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14. ABSTRACT The Burn State of the Science Research Conference achieved its stated purpose: the identification and prioritization of burn research goals for the next decade and the delineation of the resources needed to achieve those goals. Issues ranging from acute burn care through the rehabilitative period were addressed in a single forum and published in the Journal of Burn Care and Research. Although much progress has been made in burn management, much remains to be learned. Universal definitions, endpoints of care, and grading systems which can be applied for both clinical and basic science research are lacking. Consensus in these areas is vital to conducting meaningful research, but these conclusions need to be validated via basic science, pilot clinical studies, and multicenter randomized trials to define the "best" burn care. The greatest achievement of the conference was the open interaction it fostered between researchers, clinicians, burn survivors, funding organizations, journal editors, military personnel, and international burn researchers. The findings of this conference will be the basis for the burn research of the future.					
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Introduction

Although major advances have been made in burn treatment and prevention in the last 25 years, each year more than one million people sustain burn injury. Burns are a major source of injury in military conflicts and national disasters: approximately one third of the people injured in recent terrorist attacks sustained major burn injury. To date the scope of burn research and treatment has focused on individual centers analyzing outcomes based on mortality. With the newly recognized potential for large numbers of burn injuries and the incidence of burn injury in current overseas conflicts, the priorities of burn research need to be redefined. The purpose of this conference was to unite the leaders in burn care with experts in multicenter outcomes research, basic scientists, and the military to develop and prioritize a national research agenda for evidence-based burn care. The proposed consensus conference developed a comprehensive national research agenda to 1. define the status of burn care and research and 2. identify the priorities for burn research and outcomes measurement. The findings of this conference are being disseminated both locally and nationally and will be the basis for improving the delivery of health care services to burn patients. The conclusions of this conference will be the foundation for burn outcomes research and define burn research (and burn care) for the future.

Body

The Burn State of the Science Research Consensus Conference took place October 26-28 in Washington, DC. This 2.5 day conference successfully brought together burn researchers, clinicians, burn survivors, the military, and outcomes researchers to determine the needs and priorities for burn research. The specific program agenda and speaker list is included in the Appendix. Briefly, the topics covered included: acute care (inhalation injury, resuscitation, infection/inflammation, nutrition/metabolism, wound management, and care of children and the elderly), rehabilitative care (the hand, psychological health, scar, community integration, reconstructive surgery, and restoration of function), and a final series of presentations including a journal editor forum, funding opportunities, and a presentation on the burn research teams of the future. The findings of the conference have been accepted for publication and will be published in an edition of the *Journal of Burn Care and Research* dedicated to this conference. The Appendix at the conclusion of this report has a copy of the papers that will be published in the *Journal of Burn Care and Research* from this conference. This conference developed burn research priorities and goals for each of the topics and described the resources needed to achieve those goals. Funding for an infrastructure for burn multicenter trials received the highest priority for research needs. Attaining the goals for each of the topics addressed will require the presence of this infrastructure.

Key Research Accomplishments

1. Burn State of the Science Research Conference held October 26-28, 2006
2. Total attendees: 253. Representatives included burn researchers, burn clinicians, burn survivors, military personnel, members of national grant organizations (National Institutes of Health, National Institute of Disability and Rehabilitation Research, Veteran's Administration, Shriners Hospital), basic science researchers.
3. Development of burn research priorities for each of the following topics:
 - a. Inhalation injury
 - b. Burn resuscitation
 - c. Sepsis/inflammation
 - d. Nutrition/metabolism
 - e. Wound healing
 - f. Burns in children and the elderly
 - g. Hand burn rehabilitation
 - h. Burn Scarring

- i. Burn reconstruction
 - j. Psychologic health
 - k. Community reintegration
 - l. Restoration of function
- 4. Identification of burn research needs from perspective of journal editors
- 5. Outline of available funding sources for burn research
- 6. Identification of the changing paradigm of burn research from individual projects to research teams and multicenter trials

Reportable Outcomes

- 1. Presentation of meeting findings at annual American Burn Association meeting in San Diego, April, 2007.
- 2. Publication of results of meeting in *Journal of Burn Care and Research* (publication currently in press).
- 3. Subsequent Sepsis Consensus Conference held in January, 2007 to address issues raised during State of the Science Conference.

Conclusion

The Burn State of the Science conference successfully brought together burn researchers, clinicians, burn survivors, military personnel, and other members of the burn community to define the research priorities for burns. These priorities have been clearly delineated and will be published in the *Journal of Burn Care and Research* this summer. These recommendations will be the foundation for future burn research designed to optimize burn patient management and improve patient functional outcomes.

So What Section

The knowledge gained from this project will have a direct impact both on burn researchers and on the patients they serve. The priorities listed will be the basis for focusing directed studies on problems that impact burn patients and improve their quality of life both immediately after and in the years after burn injury. The publication will provide guidance for funding and conduct of burn research in each of the topics.

References

References for each of the topics is included with the individual topic papers.

Appendix

Conference Final Agenda

Day 1: Acute Burn Care

October 26, 2006

A burn expert will present the current state of the science to all attendees, followed by separate concurrent round table discussions (one for each topic) led by the burn expert. Each round table will determine research goals and needs for the topic for the next 5 years. The individual topic discussions will be summarized for all attendees at the conclusion of the session.

Introduction	8:00-8:10 a.m.
Current Basic Science Initiatives: The Glue Grant	8:10-8:25 a.m.
Multicenter Research in Burns: Where We Were, Where We Are Now	8:25-8:40 p.m.
Introduction Topic 1: Inhalation Injury	8:40-8:55 a.m.
Introduction Topic 2: Resuscitation	8:55-9:10 a.m.
Introduction Topic 3: Inflammation/Sepsis	9:10-9:25 a.m.
Break to Round Table	9:25-9:30 a.m.
Concurrent Round Table Discussions Inhalation Injury Resuscitation Inflammation/Sepsis	9:30-11:00 a.m.
Break/Return to Auditorium	11:00-11:15 a.m.
Round Table Results: Research Priorities Inhalation Injury: Resuscitation: Inflammation/Sepsis:	11:15-12:15 p.m.
Lunch	12:15-12:45 p.m.
Introduction Topic 4: Metabolism/Nutrition	12:45-1:00 p.m.
Introduction Topic 5: Burns in Children and the Elderly	1:00 -1:15 p.m.
Introduction Topic 6: Wound Healing	1:15-1:30 p.m.
Break to Round Tables	1:30-1:35 p.m.
Concurrent Round Table Discussions Metabolism/Nutrition Burns in Children and the Elderly Wound Healing	1:35-3:05 p.m.

Break/Return to Auditorium	3:05-3:20 p.m.
Round Table Results: Research Priorities Metabolism/Nutrition Burns in Children and the Elderly Wound Healing	3:20-4:20 p.m.
Summary of Acute Burn Research Priorities and Needs: The Next 10 Years	4:20-4:50 p.m.
Final Comments/Adjournment	4:50-5:00 p.m.

Day 2: Rehabilitation Research

October 27, 2006

The structure of day 2 is similar to the first day. A moderator will introduce the topic, followed by a panel discussion which will spend 12-15 minutes discussing what is not known and what should be known about each topic. A 30 minute audience participation/discussion will further identify rehabilitation needs. The session will be closed by a brief wrap up of the topic by the moderator. Each topic may include basic science, translational and clinical research elements.

8AM: Welcome, Introduction

Topic 1: The Hand	8:15-9:15 a.m.
Topic 2: Psychological Health	9:20-10:20 a.m.
Coffee Break	10:20-10:40 a.m.
Topic 3: Scar Management	10:40-11:40 a.m.
12:00-1:00: Lunch	
Topic 4: Community Integration	1:00-2:00 p.m.
Topic 5: Reconstructive Surgery	2:00-3:00 p.m.
Coffee Break	3:00-3:15 p.m.
Topic 6: Restoration of Function	3:15-4:15 p.m.
Survivor Perspective	4:15-5:15 p.m.
Concluding Remarks	5:15-5:30 p.m.

Day 3

October 28, 2006

Introduction	8:00-8:15 a.m.
Editor's Roundtable	8:15-9:15 a.m.

Journal of Burn Care and Research: Richard Gamelli MD, FACS
Burns: Steve Wolf MD, FACS
Journal of Trauma: Basil Pruitt, MD, FACS
Archives of Physical Medicine and Rehabilitation

Funding Opportunities	9:15-10:15 a.m.
NIGMS	
NIDRR	
VA	
Shriners Hospital	
Coffee Break	10:15-10:30 a.m.
Building Research Teams of the Future: Changing the Paradigm	10:30-11:30 a.m.
Summary and Concluding Remarks	

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Burn Research State of the Science: Introduction

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There have been tremendous advances in the medical and surgical management of burn injuries over the past several decades. Injuries that were uniformly fatal as recently as 25 to 30 years ago are now typically survivable. Despite this incredible progress there are numerous areas for improvements and innovations in both patient care and research.

Each year more than one million people sustain burn injury. There are several at-risk populations for burn injury in the United States including a number of underserved groups: children under 4 (for whom burn injury represents one of the leading causes of disability), adults over 65, African and Native Americans, the poor, and people living in rural areas or substandard housing.¹⁻⁵ In addition, burns represent a significant source of injury in national disasters: approximately one third of the people injured in recent terrorist attacks sustained major burn injury. Military personnel also sustain burn injury from explosions, fires, and accidents.

Traditionally, there have been many challenges to the conduct of burn research. The unique aspects of burn injury, such as the hypermetabolic response and high incidence of infection, have resulted in the exclusion of burn patients from traditional research studies. The limited number of burn patients admitted to any given center also limits the type of study that can be performed. Therefore, to date, the scope of burn research studies has been limited to individual centers analyzing rudimentary outcomes such as mortality. In addition, there has been an increasing emphasis nationally on improving the quality of outcomes research. In the past 5 years alone there have been several significant changes in the conduct of clinical research including: the requirement to register all clinical trials, adherence to new health information privacy (HIPPA) regulations, assurance of patient safety via a separate monitoring board, the CONSORT statement, and new comprehensive Human Subject Review Board regulations. While these changes are long overdue, they pose challenges to the clinical research team.

The persistent risk of burn injury, the potential for large numbers of burn injuries from war and national disasters combined with the increasing need for quality basic science and clinical research made it quite clear that the priorities and strategies for conduct of burn research needed to be examined and potentially redefined. This need for a burn research specific conference was recognized by leaders both within the ABA's Multicenter Trials Group and the National Institute on Disability and Rehabilitation Research Burn Model Systems program. Given the overlapping interests between these groups for the conduct of sound and meaningful research, the decision was made to combine forces and resources to organize a State of the Science of Burn Research conference--the first national burn research meeting in over two decades. The purpose of the conference was to review what is not known but needs to be known about critical aspects of acute and rehabilitative burn care and to construct a research agenda for burn research for the next decade. Additional support for the State of the Science conference was obtained from the Shriners Hospital for Children, the U.S. Army Medical Research and Materiel Command, the Veteran's Administration, the American Burn Association, and the National Institute for the General Medical Sciences (NIGMS).

Previously, the American Burn Association (ABA), in conjunction with Shriners Hospitals for Children (SHC) sponsored by the Association for Health Care Research and Quality (AHRQ) to identify key research issues to promote improvements in the delivery of health services to pediatric burn patients and to develop priorities for future research in outcomes measurement for children with burns. The recommendations developed in this multidisciplinary conference

were not only published, but implemented. As a result of this conference, the ABA Shriners Quality of Life Questionnaire was developed and validated for children 0-4 and 5-18 years in both Spanish and English. The tool is now being used to assess quality of life outcomes for children with burn injury. In addition, the conference set the standard for burn outcomes research: prospective multicenter clinical trials to evaluate health care outcomes. However, other than this focused pediatric research conference, there had not been a national conference dedicated to burn research in over two decades.

The overall goal of the State of the Science conference was to develop a comprehensive national research agenda covering all aspects of burn care from the acute phase through the rehabilitative by: 1) defining the status of burn care and research; 2) identifying specific priorities for burn research and outcomes measurement; and 3) delineating the requirements, including funding, manpower, and infrastructure, needed to accomplish those goals.

In order to achieve this goal of creating a national research agenda, the conference gathered burn experts from various disciplines, including members of the American Burn Association, European clinicians and investigator, leading burn-related journal editors, burn survivors and members of several major burn funding agencies to present the status of burn care in both the acute and rehabilitative phases. The two and a half day conference was held October 26-29 at the JW Marriott in Washington, DC. The day of the conference was dedicated to issues related to acute burn care, the second day was dedicated to burn rehabilitation and third half day included a journal editors roundtable, a panel discussion on opportunities for funding and a capstone lecture on building research teams of the future.

The first day of the conference on acute burn issues began with an overview by Dr. Ronald Tompkins of the Inflammation and Host Response to Injury multicenter NIH funded Glue Grant—the largest federally funded burn research initiative and an update by Dr. Jeffrey Saffle on the activities of the ABA Multicenter Trials Group. The remainder of the day was dedicated to discussion of six fundamental topics in acute burn care: inhalation injury, resuscitation, metabolic issues, care of children and the elderly, and wound healing. Following the initial topic introductions, conference attendees broke out into round table discussions, during which each topic moderator led a discussion with the group on the needs and priorities for that topic. The day concluded with a plenary session summarizing the burn research needs and priorities as defined in the group discussions. The second day of the conference included discussion of six issues fundamental to burn rehabilitation: the hand, psychological health, scar, community integration, reconstructive surgery, and restoration of function. The final panel of the day was presented by three burn survivors who provided their perspective on priorities for future burn research. The final day rounded out the program by discussing funding sources for burn research, presenting an editors round table on their perspective of burn research goals and needs from the perspective of their journal, and concluded with a discussion of the changing research paradigm and the burn research teams of the future.

In this issue of the Journal of Burn Care and Research, articles summarizing each of the State of the Science sessions are presented. These articles represent the input of the experts who moderated each panel and the input of conference attendees. Each article has been organized to include a statement of the topic, a description of what is currently known about that topic, discussion of what needs to be known and a list of the top 4 or 5 priorities for future research in each topic area. By necessity, many meaningful topics were not included in this conference. However, we believe that the topics and research priorities developed at the Burn State of the Science conference represent key areas for the future of collaborative burn research that can help not only elevate the state of the science of burn research but the state of burn care as a whole.

References

1. CDC. Deaths resulting from residential fires and the prevalence of smoke alarms – United States 1991-1995. *Morbidity and Mortality Weekly Report* 1998;47(38):803-6.

2. CDC, National Center for Health Statistics (NCHS). National vital statistics system. Hyattsville (MD): U.S. Department of Health and Human Services, CEC, National Center for Health Statistics; 1998.
3. Istre GR, McCoy MA, Osborn L, Barnard JJ, Bolton A. Deaths and injuries from house fires. *New England Journal of Medicine* 2001;344:1911-16.
4. Runyan CW, Bangdiwala SI, Linzer MA, Sacks JJ, Butts J. Risk factors for fatal residential fires. *New England Journal of Medicine* 1992;327(12):859-63. 5.
5. Ahrens M. The U.S. fire problem overview report: leading causes and other patterns and trends. Quincy (MA): National Fire Protection Association; 2001.

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Introduction

Tremendous progress in burn treatment has been achieved in the past several decades, much of it the result of clinical research. Effective fluid resuscitation, topical antibiotics, early surgical excision and grafting, customized nutritional and metabolic support, critical care, and rehabilitation have all progressed to the point that very few burn patients die, and the burn care community is now turning its efforts to measuring and improving the quality of life for survivors.

In the face of these achievements, it may seem at first glance unnecessary to evaluate the current state of clinical research in burns. However, throughout medicine a ubiquitous emphasis on objectivity is demanding that clinicians both measure the consequences of their treatments and demonstrate improved outcomes in as many ways as possible. This impetus has been driven by a number of disparate societal forces, including growing consumer distrust of the traditional physician model, the explosion of information occasioned by the computer age, and the crisis of cost in health care. These have combined in the “outcomes movement”, which demands that clinicians gather, pool, and disseminate information on a massive scale. Termed the “third revolution” in medicine, this movement have forced a re-examination of almost every aspect of health care delivery in the US[1].

The ripples generated by this concept have led to development of many practices which have become modern catchwords including “Evidence-Based Medicine” [2], “continuous quality management”[3], the shift by the Joint-Commission to outcomes-based hospital accreditation, the recent concept of “Pay-for-Performance”[4], and the development of Practice Guidelines. Taken together, these forces were expected to create a “clinical trials machine” [5], which seeks to fill in the gaps exposed in objective knowledge by rigorous testing of best practices.

As the burn care community entered this modern era, it appeared unprepared to keep pace with new demands for objectivity. Many of the most widely-accepted concepts in burn care appear to be based, at best, on consensus of experts. A review by Childs in 1998 found relatively few good quality randomized controlled trials (RCT's) in burn care. She concluded that "There is little evidence that burn care is an evidence-based practice".[6] This finding further encouraged the burn care community, already stimulated by the ubiquitous forces outlined previously, to embark on a systematic effort to improve the scientific basis of current burn treatment, and to create the infrastructure necessary to improve it.

Burn Practice Guidelines

As a first step, a task force was assembled to create a set of practice guidelines for acute burn care. Practice guidelines (PG's) are "recommendations for management of specific medical problems, supported by objective and comprehensive reviews of literature, that seek to define the current best and most cost-effective methods of treatment." [2] PG's require critical review and interpretation of the medical literature according to levels of scientific certainty; rules for both the grading of literature, and the construction of rigorous PG's, were followed in our project.[7-9] Based on the quality of supporting evidence, PG's permit three different recommendations for clinical care. These are presented in Table 1. This terminology has become widely accepted and utilized in the modern practice of evidence-based medicine.

At the initial meeting of the task force in May, 1998, we decided to develop a set of PG's for the acute (first 24 hours) of initial burn care. The task force met repeatedly during 1998-1999, and produced a set of PG's for 13 topics, including organization and delivery of burn care, fluid resuscitation, inhalation injury, electrical injury, nutrition, and prophylaxis of deep venous thrombosis. Results of this project were presented at the annual meeting of the ABA in 2000.[10] Worthy of note is that not a *single* standard was created in this effort, and that evidence could be found to support creation of only 5 Guidelines. This effort underscored the paucity of rigorous evidence in burn care, and, it was hoped, would serve as a starting point for the performance of multicenter RCT's within the burn care community.

Ongoing Initiatives

Three ongoing projects support the multicenter trial effort. First, the ABA is continuing to review and publish updated practice guidelines on an annual basis.[11, 12] Second, the ABA's computerized burn patient registry, initially developed in 1988, has been re-organized as the National Burn Repository (NBR).[13] At present the NBR contains records on over 126,000 patients admitted to US Burn Center Hospitals. This effort provides a huge amount invaluable demographic and outcome data on acute burn care, which is already being utilized for "data mining" and research.[14-16] Participation in the NBR is now a requirement for verification as a Burn Center by the ABA and American College of Surgeons.

Third, the ABA has created a multicenter trials group (MCTG) for the purpose of encouraging multicenter clinical research. Beginning in 2000, open meetings of the group have been held at the annual meeting of the ABA. Already this fledgling effort has been remarkably successful; to date six peer-reviewed publications have been produced, and additional abstracts are in process.[15, 17-21] While most of these projects have been retrospective, multicenter reviews, our publications include our first prospective RCT of oxandrolone in acute burn care. The group has created a website for ongoing communications (<www.abaresearch.org>) which now has over 100 participants.

The Future

What next steps should follow these initial efforts? Clearly, both an infrastructure and a referendum has been created for the performance of rigorous, multicenter clinical trials in burn care. A host of topics are waiting to be investigated, and a steering committee has been formed to construct the infrastructure needed to conduct such trials successfully. Funding remains a major obstacle; the MCTG has accumulated a remarkable track record with essentially no funds, larger studies cannot be conducted without the resources to support data collection, quality control, and subcommittee oversight. In the coming year, a major effort for the group will be to identify feasible topics for multicenter investigation, and submit grants for their performance. As this moves forward, burn care will truly take its place in the realm of evidence-based medicine.

REFERENCES

1. Epstein AM. The outcomes movement--will it get us where we want to go? *N Engl J Med.* 1990;323:266-70.
2. Eddy DM. Clinical decision making: from theory to practice. Practice policies --what are they? *Jama.* 1990;263:877-8, 80.
3. Mayer TA. Industrial models of continuous quality improvement. Implications for emergency medicine. *Emerg Med Clin North Am.* 1992;10:523-47.
4. Russell TR. The future of surgical reimbursement: quality care, pay for performance, and outcome measures. *Am J Surg.* 2006;191:301-4.
5. Ellwood PM. Shattuck lecture--outcomes management. A technology of patient experience. *N Engl J Med.* 1988;318:1549-56.
6. Childs C. Is there an evidence-based practice for burns? *Burns.* 1998;24:29-33.
7. Eddy DM. Clinical decision making: from theory to practice. Guidelines for policy statements: the explicit approach. *Jama.* 1990;263:2239-40, 43.
8. American Medical Association. Office of Quality Insurance and Health Care Organization's Attributes to Guidelines Development of Practice Parameters. Chicago: American Medical Association; 1990.
9. Rosenberg J, Greenberg MK. Practice parameters: strategies for survival into the nineties. *Neurology.* 1992;42:1110-5.
10. Saffle JR. (ed). Practice guidelines for burn care. Published as a Supplement to the *Journal of Burn Care and Rehabilitation.* *Journal of Burn Care and Rehabilitation.* 2001;22:S1-69.
11. Arnoldo B, Klein M, Gibran NS. Practice guidelines for the management of electrical injuries. *J Burn Care Res.* 2006;27:439-47.
12. Gibran NS. Practice Guidelines for burn care, 2006. *J Burn Care Res.* 2006;27:437-8.
13. Miller SF, Bessey PQ, Schurr MJ, et al. National Burn Repository 2005: a ten-year review. *J Burn Care Res.* 2006;27:411-36.
14. Kerby JD, McGwin G, Jr., George RL, et al. Sex differences in mortality after burn injury: results of analysis of the National Burn Repository of the American Burn Association. *J Burn Care Res.* 2006;27:452-6.
15. Kagan RJ, Gamelli R, Kemalyan N, et al. Tracheostomy in thermally injured patients: does diagnosis-related group 483 adequately estimate resource use and hospital costs? *J Trauma.* 2004;57:861-6.
16. Santaniello JM, Luchette FA, Esposito TJ, et al. Ten year experience of burn, trauma, and combined burn/trauma injuries comparing outcomes. *J Trauma.* 2004;57:696-700; discussion -1.
17. Palmieri TL, Caruso DM, Foster KN, et al. Effect of blood transfusion on outcome after major burn injury: a multicenter study. *Crit Care Med.* 2006;34:1602-7.
18. Palmieri TL, Greenhalgh DG. Blood transfusion in burns: what do we do? *J Burn Care Rehabil.* 2004;25:71-5.
19. Palmieri TL, Greenhalgh DG, Saffle JR, et al. A multicenter review of toxic epidermal necrolysis treated in U.S. burn centers at the end of the twentieth century. *J Burn Care Rehabil.* 2002;23:87-96.
20. Warner PM, Kagan RJ, Yakuboff KP, et al. Current management of purpura fulminans: a multicenter study. *J Burn Care Rehabil.* 2003;24:119-26.
21. Wolf SE, Edelman LS, Kemalyan N, et al. Effects of Oxandrolone on Outcome Measures in the Severely Burned: A Multicenter Prospective Randomized Double-Blind Trial. *J Burn Care Res.* 2006;27:131-9.

TABLE 1: Levels of Recommendation in Practice Guidelines

STANDARDS: Standards represent accepted principles of patient management that reflect a high degree of clinical certainty. Standards usually are based on Class I evidence; however, strong Class II evidence may form the basis for a standard, especially if the issue does not lend itself to testing in a randomized format. Conversely, weak or contradictory Class I evidence may not support a standard. Standards are intended to be applied rigidly. Standards are rules.

GUIDELINES: Guidelines represent a particular strategy or range of management strategies that reflect a moderate clinical certainty. Guidelines are based on significant Class II evidence and a preponderance of Class III evidence. Guidelines should be followed in most cases. Guidelines can and should be tailored to fit individual patient needs.

OPTIONS: Options represent strategies for patient management that lack strong scientific evidence but represent the panel' current state of care recommendations. Options are based on strong Class III evidence. Options have value as credible recommendations, as tools for educational purposes, and for use in guiding future studies. They are reasonable and available strategies to be considered by the physician in the care of patients.

Classes of Evidence:

CLASS I: The "gold standard" of evidence-based medicine: evidence provided by prospective, randomized, controlled trials that include appropriate design and methodology and sufficient patient numbers.

CLASS II: Clinical studies in which the data are collected prospectively or retrospectively, and retrospective analyses that are based on clearly reliable data. Types of studies so classified include observational studies, cohort studies, prevalence studies, and case control studies.

CLASS III: Evidence provided by clinical series, comparative studies, case reviews, case reports, and expert opinion.

Inhalation Injury: Research Progress and Needs

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Introduction

Smoke inhalation continues to be a major source of morbidity and mortality in burn patients despite recent advances in critical care and wound management.¹ Approximately 10-20% of patients admitted to burn centers have inhalation injury, and the incidence increases with burn size. Inhalation injury, in conjunction with age and burn size, is an important determinant of survival, prolonged ventilator dependence, hospital stay, and death in burn patients.²⁻⁵ However, determining the extent of pulmonary injury and standardizing optimal therapy continue to be elusive. Mortality in combined burn/smoke inhalation injury remains high due to progressive pulmonary and cardiac dysfunction.⁶⁻⁸ Treatment modalities used in inhalation injury range from specialized modes of ventilation to the use of nitric oxide. Research into the pathophysiology of inhalation injury has been productive, but there continue to be significant gaps in our understanding of inhalation injury.

Although “inhalation injury” contributes to increasing mortality after burn injury, a universally accepted clinical definition and/or diagnostic criteria for inhalation injury is lacking. For practical purposes inhalation injury has been divided into different phases: injury caused at the site of the fire due to noxious gases, upper airway heat injury, and lower airway chemical injury. Each aspect of inhalation injury has a different pathophysiology, treatment, and long-term implications. Laboratory and clinical advances have been made in each aspect of inhalation injury despite the current challenges. The goal of this paper is to discuss the major advances in our knowledge of inhalation injury, outline the areas requiring further study and determine the priorities for future inhalation injury research (as discussed in the break-out sessions), and discuss the resources that will be needed to accomplish those goals.

What We Know About Inhalation Injury

The first insult to the airway during the inhalation of smoke is the effects of noxious gases produced from the combustion of common household items. The vast majority of patients who die at the scene of a fire die from inhalation of toxic compounds.⁹ Research has revealed that a multitude of gases, including hydrogen cyanide, ammonia, aldehydes, acrolein, sulfur dioxide, and isocyanates are generated during the combustion of common household items such as carpeting, furniture, and decorations.¹⁰ Treatment algorithms for such gases as carbon monoxide and hydrogen cyanide have been developed.¹¹ Further identification of gases released during the burning process may reveal additional treatment needs.

Although the identification of inhaled gases can help direct treatment modalities, perhaps the most significant research advances in inhalation injury involve the description of the pathophysiology of heated smoke on the upper and lower airways. The upper airway is injured when hot air (temperatures in excess of 150°C) cause heat injury to the respiratory epithelium. Animal models have confirmed that this edema is due to increased microvascular hydrostatic pressure, increased interstitial oncotic pressure, decreased interstitial hydrostatic pressure, decreased reflection coefficient, reduced plasma oncotic pressure, and increased lung lymph flow.¹²⁻¹⁵ These studies confirmed that airway edema after burn injury was due to the injury itself, not just to the fluid administered after burn injury. The clinical impact of these studies was to support early intubation after significant upper airway burn injury to avoid airway obstruction and to reinforce the need for adequate resuscitation after burn injury.

The final aspect of inhalation injury that has undergone extensive study is the effects of smoke particles on the pulmonary parenchyma. Inhaled toxic particles cause sloughing of the airway-lining epithelium, mucus secretion, inflammation, atelectasis, and airway obstruction.^{16,17} Additional effects include mucosal edema, ulceration, ciliary damage, increased lung and bronchial blood flow, surfactant inactivation, pulmonary edema, tissue hypoxia, acidosis, shunting, V/Q mismatch, and cast formation. As a result, patients frequently develop reactive airway disease, ARDS, and pneumonia. In patients with large burns (>30% TBSA) capillary hyperpermeability occurs not only at the injured site but also in regions distant from the injury.^{14, 18, 19}

Ventilator support after severe burn inhalation injury has undergone extensive study. The VDR (volumetric diffusive respirator), a time-cycled pressure regulated high frequency ventilator, underwent extensive animal testing, followed by several retrospective human studies, in the early 1990s.²⁰⁻²² These studies suggested that early use of the VDR in inhalation injury can decrease nosocomial pneumonia rates, lower peak airway pressures, and decrease mortality. Although these studies are extremely valuable, more recent prospective, randomized studies using a low-tidal volume strategy (not used in the VDR studies) has demonstrated a significant decrease in morbidity and mortality in patients with ARDS. In addition, several new modes of ventilator support, including oscillatory ventilation and pressure release ventilation have recently been introduced in the treatment of inhalation injury.²³ Neither of these methods have been tested against the VDR. Thus, the ideal ventilatory strategy for patients with inhalation injury remains undetermined.

Testing of other therapeutic interventions in inhalation injury have also had varied results. Early tracheostomy was found to be beneficial in children, but not in adults with inhalation injury, and the use of percutaneous tracheostomy has appeared in case reports.²⁴⁻²⁶ The effects of numerous agents, ranging from albuterol to vitamin E, have been studied in

animals with inhalation injury, yet there is a paucity of prospective multicenter randomized trials evaluating the effects of these agents in patients.²⁷⁻³¹ Hence, the appropriate use of these agents remains undefined.

Tremendous progress has been made in determining the pathophysiology and anatomical changes that occur after inhalation injury. However, significant gaps in our knowledge remain. The lack of a universal definition and grading system for inhalation injury presents a significant roadblock for clinical trials studying this disease. Although significant advances have been made in the development of specialized ventilatory modes, recent advances in the management of ARDS have not been assessed in inhalation injury. Finally, although multiple therapeutic regimens for inhalation injury have been tested in animal models, there is a lack of translational research assessing the effectiveness of these treatments in patients. We have made a great deal of progress in the understanding and treatment of inhalation injury, but we have only scratched the surface of the problem.

Group Discussion: What Should the Priorities Be?

Priority 1: Diagnosis and Grading of Inhalation Injury

The overwhelming discussion regarding inhalation injury centered on the need for accurate and agreed upon criteria for diagnosis and grading of inhalation injury. Diagnostic tests have been used primarily to assist clinician decision-making in terms of patient triage, therapeutic interventions, and prognosis. Numerous studies have attempted to establish criteria for the diagnosis and grading of inhalation injury, but these studies generally are retrospective, involve small numbers of patients in a single center, or employ techniques that are not practical in the clinical setting to diagnose the severity of injury.³²⁻⁴⁴ The validity measurements of these studies are complicated by the evolving nature of inhalation injury. Lung dysfunction after inhalation injury develops over 24 to 72 hours, making prospective identification of inhalation injury problematic.⁴⁵ The host response to injury as well as the presence of premorbid conditions also makes the validation and assessment of inhalation injury challenging.

Currently methods for identification of inhalation injury are primarily non-invasive, and include a combination of history (burns sustained in a closed space, unconscious at scene, prolonged extrication), physical findings (singled facial hair, carbonaceous deposits in the oropharynx or sputum, facial burn), combined with other diagnostic modalities. Modalities that have been used include measurement of carbon monoxide levels, bronchoscopy^{32,33,37,41,44}, serial chest x-ray,^{35, 36} computed tomography,⁴³ tracheobronchial cytology/biopsy,^{39,41} radionuclide imaging (technetium, xenon),^{32,34,40} pulmonary function studies,^{33,37} and combinations of the above interventions. At the present time none of the identification systems are used consistently in the diagnosis of inhalation injury. The use of biochemical markers, molecular mechanisms and markers, and newly developed radiologic techniques (such as MRI) for the identification of inhalation injury have yet to be investigated.

Grading inhalation injury severity, although a separate issue from identifying the presence of injury, is inextricably linked to the diagnosis of inhalation injury. Several grading systems for inhalation injury have been developed, but none are universally applied due to the frequent need for invasive procedures such as bronchoscopy or specialized facilities (such as the radiography suite).^{46,47} Grading systems for children and adults for ARDS exist, but their applicability to patients with inhalation injury remains unclear.^{48,49} Grading of inhalation injury severity clearly needs to be included in the validation of the definition of inhalation injury.

Priority 2: Treatment of Inhalation Injury

The second priority identified in the group discussion was the identification of the optimal treatment of inhalation injury. Consensus was that this priority required a uniform definition and grading system for inhalation injury. Treatment modalities were divided into several categories, including ventilator management strategies, use of inhalational or intravenous agents to modify the lung response to injury, defining the role of tracheostomy in inhalation injury, and developing evidence-based “best practices” for the treatment of inhalation injury.

Ventilator Management of Inhalation Injury

As described above, studies performed in the 1980s supported the use of high frequency percussive ventilation (VDR) as the optimal ventilator strategy in the treatment of inhalation injury.²⁰⁻²² Universal use of the VDR in inhalation injury has been limited by its

complexity, lack of availability, and labor-intensive monitoring and maintenance requirements. The VDR was initially compared to conventional ventilation strategies using relatively high tidal volumes (10-12 ml/kg). However, the standard of care for mechanical ventilation in acute respiratory distress syndrome changed after a prospective randomized multicenter trial demonstrated that the use of high tidal volumes is detrimental in patients with ARDS.^{50,51} Comparison of VDR to lower volume ventilation (6 ml/kg) has yet to be performed. Additional methods of ventilation, such as oscillating ventilation, pressure release ventilation, and liquid ventilation have been reported, but have yet to be tested prospectively in patients with inhalation injury.^{23,52,53} Testing of these modalities will require multicenter prospective studies. Additional aids to ventilatory support, such as extracorporeal membrane oxygenation (ECMO) and selective CO₂ removal are being investigated, and require further prospective testing.⁵⁴

Systemic and Inhalational Agent Treatment for Inhalation Injury

The burn community has long been searching for the “magic bullet” for the treatment of inhalation injury. Studies have ranged from analysis of agents administered topically to the lung (inhalation agents) to the administration of systemic anti-inflammatory substances.²⁸⁻³¹ These studies have either used animal models (which require further validation in humans), single center retrospective studies, or single center small trials. These studies are confounded by the lack of a uniform definition and grading system for inhalation injury and from the variability of the host response to injury. Clearly, the determination of the best treatment for inhalation injury will require the translation of basic science findings, which help us understand the molecular mechanisms and potential therapeutic modalities for inhalation injury, into the clinical arena. Validation of any given treatment needs to be done via prospective, randomized, multicenter trials.

The Role of Tracheostomy in Inhalation Injury

Maintaining airway patency is essential to the care of the patient with severe inhalation injury, yet there continues to be debate on how to accomplish this goal. Early reports of tracheostomy in burn injury cited an increased risk of infection, pneumonia, and complications with the use of tracheostomy.^{55,59} A single center retrospective pediatric study reported the safety of prolonged endotracheal intubation in 98 intubated children.⁶⁰ A recent prospective single center trial demonstrated no difference in survival in adults after tracheostomy.²⁴ Other single center studies report improved outcomes with the use of tracheostomy after burn injury in children.^{25,56,61} In addition, the use of percutaneous tracheostomy in burns has been reported, but not tested prospectively.²⁶ The timing, methodology, and appropriateness of tracheostomy in inhalation injury needs to be addressed in a randomized multicenter prospective trial to answer this important question.

Priority 3: Long-Term Outcomes After Inhalation Injury

To date the vast majority of inhalation injury studies have been survival studies conducted during hospitalization. Little data exists regarding the long-term (months to years after injury) impact of severe inhalation injury on pulmonary function or quality of life in burn survivors.^{57,58} Studies of the long-term lung function are severely limited by the lack of uniform definitions and grading systems for inhalation injury, yet this is an essential next step in improving the overall quality of care for the patient with inhalation injury. The impact of inhalation injury on physical function, including the ability to perform activities of daily living, job performance, and exercise, have had little study. Quality of life, interpersonal interactions, and psychological function after inhalation injury also merit additional study.

Priority 4: Mechanistic Investigations and Translational Research

Although much progress has been made in the elucidation of the molecular mechanisms behind inhalation injury, much work needs to be done. Understanding the genomic, proteomic, and metabolomic alterations after inhalation injury will form the basis for new and innovative medical interventions that can improve treatment. Application of new methodologies, such as gene arrays and mathematical modeling, will always be at the forefront of burn research. It is vital, however, that the findings from the laboratory be applied to the human model. This type of translational research represents the long-term future for burn care and needs to remain a priority.

Inhalation Injury Research: What Do We Need?

The study and treatment of inhalation injury has made tremendous progress in the past 60 years. However, it is clear that much work needs to be done. The top four priorities for inhalation injury, as discussed in the consensus conference, are listed in Table 1. The key questions, however, are: 1. How do we address those priorities and 2. What resources do we need to complete this important research? Traditional burn research has been primarily single center studies with limited numbers of patients and resources. However, it is clear that no single center or institution can answer these questions. The burn research of the future will require a shift in the research paradigm. The team concept adopted by burn centers in the treatment of patients will need to be adopted in the research realm, and researchers will need to work together to solve problems. Consensus on definitions and grading systems will need to be reached, and the definitions developed will require testing via meticulous multicenter randomized prospective clinical trials.

Multicenter trials, however, require more than just investigator cooperation. They require an infrastructure to ensure appropriate study design, data collection, patient safety, statistical analysis, and study conduct. To date no such infrastructure exists for burn research, although individual investigators have been able to put together infrastructure for individual studies.

Conclusion

The treatment and understanding of the pathophysiology of inhalation injury has evolved over the last century, as evidenced by improved survival after burn injury. However, consensus on definitions and grading systems, and the accuracy of these systems needs to be achieved in order to conduct rigorous multicenter trials. Further significant advances in inhalation injury will require a significant commitment of personnel, time, and resources focused on achieving the four research priorities: 1. definition of and grading system for inhalation injury 2. optimizing treatment modalities for inhalation injury 3. assessing and improving long-term outcomes after inhalation injury and 4. better understanding the molecular mechanisms of inhalation injury and translating that understanding to the patient.

Table 1: Priorities for Inhalation Injury Research

1. Define and develop a universally applicable grading system.
2. Develop “best practice” guidelines for treatment (ventilator management, systemic agents, inhalational agents, airway access).
3. Assess and improve long-term outcomes (physical, functional, psychological).
4. Elucidate the genomic, proteomic, and metabolomic alterations after inhalation injury and translate those findings to patient care.

Bibliography

1. Saffle JR, Davis B, Williams P. Recent outcomes in the treatment of burn injury in the United States: A report from the American Burn Association patient registry. *J Burn Care Rehabil* 1995;16:219-32.
2. Smith DL, Cairns BA, Ramadan F, et al. Effect of inhalation injury, burn size, and age on mortality: a study of 1447 consecutive burn patients. *J Trauma* 1994;37:655-9.
3. Shirani KZ, Pruitt Ba Jr, Mason AD Jr. The influence of inhalation injury and pneumonia on burn mortality. *Ann Surg* 1987;205:82-7.
4. Sellers BJ, Davis BL, Larkin PW, Morris SE, Saffle JR. Early prediction of prolonged ventilator dependence in thermally injured patients. *J Trauma* 1997;43:899-903.
5. Tredget EE, Shankowsky HA, Taerum TV, Moysa GL, Alton JD. The role of inhalation injury in burn trauma. A Canadian Experience. *Ann Surg* 1990;212:720-7.
6. Clark, WR. Smoke inhalation: diagnosis and treatment. *World J Surg* 16:24-29, 1992.
7. Sobel JB, Goldfarb IW, Slater H, and Hammell EF. Inhalation injury: a decade without progress. *J Burn Care Rehabil* 13:573-575, 1992.
8. Wolf SE, Rose JK, Desai MH, Mileski JP, Barrow RE, and Herndon DN. Morality determinants in massive pediatric burns. An analysis of 103 children with > or = 80% TBSA burns. *Ann Surg* 225:554-565, 1997.
9. Birky MM, Clark FB. Inhalation of toxic products from fires. *Bull NY Acad Med* 1981;57:997-1013.
10. Prien T, Traber DL. Toxic smoke compounds and inhalation injury-a review. *Burns Incl Therm Inj* 1988;14:451-60.
11. Demling RH. Burn care in the immediate resuscitation period. In *ACS Surgery: Principles and Practice*. Ed Wilmore. New York: Web MD Corporation, 2002, 50-54.
12. Pitt RM, Parker JC, Jurkovich GJ, Taylor AE, Curreri PW. Analysis of altered capillary pressure and permeability after thermal injury. *J Surg Res* 1987;42:693-702.
13. Lund T, Wiig H, Reed RK. Acute postburn edema: role of strongly negative interstitial fluid pressure. *Am J Physiol* 1988;255:H1069-74.
14. Harms BA, Bodai BI, Kramer GC, and Demling RH. Microvascular fluid and protein flux in pulmonary and systemic circulations after thermal injury. *Microvasc Res* 23:77-86, 1982.
15. Isago T, Noshima S, Traber LD, Herndon DN, Traber DL. Analysis of pulmonary microvascular permeability after smoke inhalation. *J Appl Physiol* 1991;71:1403-8.
16. Abdi S, Evans MJ, Cox RA, Lubbesmeyer H, Herndon DN, Traber DL. Inhalation injury to tracheal epithelium in an ovine model of cotton smoke exposure. Early phase (30 minutes). *Am Rev Respir Dis* 142:1436-9, 1990.
17. Cox RA, Burke AS, Soejima K, Murakami K, Katahira J, Traber LD, Herndon DN, Schmalstieg FC, Traber DL, Hawkins HK. Airway obstruction in sheep with burn and smoke inhalation injuries. *Am J Respir Cell Mol Biol*. 29:295-302, 2003.
18. Carvajal HF, Linares HA, and Brouhard BH. Relationship of burn size to vascular permeability changes in rats. *Surg Gynecol Obstet* 149:193-202, 1979.
19. Ward PA and Till GO. Pathophysiologic events related to thermal injury of skin. *J Trauma* 30:S75-79, 1990.
20. Cioffi WG, deLemos RA, Coalson JJ, Gerstmann DA, Pruitt BA Jr. Decreased pulmonary damage in primates with inhalation injury treated with high-frequency ventilation. *Ann Surg*. 1993;218:328-35.
21. Rodeberg DA, Housinger TA, Greenhalgh DG, Maschinot NE, Warden GD. Improved ventilatory function in burn patients using volumetric diffusive respiration. *J Am Coll Surg*. 1994;179:518-22.
22. Cioffi WG Jr, Rue LW 3rd, Graves TA, McManus WF, Mason AD Jr, Pruitt BA Jr. Prophylactic use of high-frequency percussive ventilation in patients with inhalation injury. *Ann Surg*. 1991;213:575-80.
23. Cartotto R, Ellis S, Smith T. Use of high-frequency oscillatory ventilation in burn patients. *Crit Care Med*. 2005;33:175-81.

24. Saffle JR, Morris SE, Edelman L. Early tracheostomy does not improve outcome in burn patients. *J Burn Care Rehabil.* 2002;23:431-8.
25. Palmieri TL, Jackson W, Greenhalgh DG. Benefits of early tracheostomy in severely burned children. *Crit Care Med.* 2002;30:922-4.
26. Gravvanis AI, Tsoutsos DA, Iconomou TG, Papadopoulos SG. Percutaneous versus conventional tracheostomy in burned patients with inhalation injury. *World J Surg.* 2005;29:1571-5.
27. Tasaki O, Mazingo DW, Dubick MA, Goodwin CW, Yantis LD, Pruitt BA Jr. Effects of heparin and lisofylline on pulmonary function after smoke inhalation injury in an ovine model. *Crit Care Med.* 2002;30:637-43.
28. Morita N, Shimoda K, Traber MF, Westphal M, Enkhbaatar P, et al. Vitamin E attenuates acute lung injury in sheep with burn and smoke inhalation injury. *Redox Rep.* 2006;11:61-70.
29. Palmieri TL, Enkhbaatar P, Bayliss R, Traber LD, Cox RA, et al. Continuous nebulized albuterol attenuates acute lung injury in an ovine model of combined burn and smoke inhalation. *Crit Care Med.* 2006;34:1719-24.
30. Morita N, Traber MG, Enkhbaatar P, Westphal M, Murakami K, et al. Aerosolized alpha-tocopherol ameliorates acute lung injury following combined burn and smoke inhalation injury in sheep. *Shock.* 2006;25:277-82.
31. Enkhbaatar P, Kikuchi Y, Traber LD, Westphal M, Morita N, et al. Effect of inhaled nitric oxide on pulmonary vascular hyperpermeability in sheep following smoke inhalation. *Burns.* 2005;31:1013-9.
32. Agee RN, Long JM ed, Hunt JL, et al. Use of ¹³³xenon in early diagnosis of inhalation injury. *J Trauma* 1976;16:218-24.
33. Petroff PA, Hander EW, Clayton WH, Puritt BA. Pulmonary Function studies after smoke inhalation. *Am J Surg* 1976;132:346-51.
34. Schall GL, McDonald HD, Carr LB, Capozzi A. Xenon ventilation-perfusion lung scans. The early diagnosis of inhalation injury. *JAMA* 1978;240:2441-5.
35. Teixidor HS, Rubin E, Novick GS, Alonso DR. Smoke inhalation: radiologic manifestations. *Radiology* 1983;149:383-7.
36. Peitzman AB, Shires GT 3rd, Teixidor HS, Curreri PW, Shires GT. Smoke inhalation injury: evaluation of radiographic manifestations and pulmonary dysfunction. *J Trauma* 1989;29:1232-8.
37. Brown DL, Archer SB, Greenhalgh DG, Washam MA, James LE, Warden GD. Inhalation injury severity scoring system: a quantitative method. *J Burn Care Rehabil* 1996;17:552-7.
38. Hollingsed TC, Saffle JR, Barton RG, Craft WB, Morris SE. Etiology and consequences of respiratory failure in thermally injured patients. *Am J Surg* 1993;166:592-6.
39. Khoo AK, Lee ST, Poh WT. Tracheobronchial cytology in inhalation injury. *J Trauma* 1997;42:81-5.
40. Lin WY, Kao CH, Wang SJ. Detection of acute inhalation injury in fire victims by means of technetium-99m DTPA radioaerosol inhalation lung scintigraphy. *Eur J Nucl Med* 1997;24:125-9.
41. Masanes MJ, Legendre C, Lioret N, Saizy R, Lebeau B. Using bronchoscopy and biopsy to diagnose early inhalation injury. Macroscopic and histologic findings. *Chest* 1995;107:1365-9.
42. Ryan CM, Shoenfeld DA, Thorpe WP, Sheridan RL, Eassem EH, Tompkins RG. Objective estimates of the probability of death from burn injuries. *N Engl J Med* 1998;338:362-6.
43. Reske A, Bak Z, Samuelsson A, Morales O, Seiwerts M, Sjoberg F. Computed tomography—a possible aid in the diagnosis of smoke inhalation injury? *Acta Anaesthesiol Scand.* 2005;49:257-60.
44. Madnani DD, Steele NP, de Vries E. Factors that predict the need for intubation in patients with smoke inhalation injury. *Ear Nose Throat J.* 2006;85:278-80.
45. Pruitt BA Jr, Erickson DR, Morris A. Progressive pulmonary insufficiency and other pulmonary complications of thermal injury. *J Trauma* 1975;15:369-79.
46. Brown DL, Archer SB, Greenhalgh DG, Washam MA, James LE, Warden GD. Inhalation injury severity scoring system: a quantitative method. *J Burn Care Rehabil* 1996;17:552-7.

47. Masanes MJ, Legendre C, Lioret N, Maillard D, Saizy R, Lebeau B. Fiberoptic bronchoscopy for the early diagnosis of subglottal inhalation injury: comparative value in the assessment of prognosis. *J Trauma* 1994;36:59-67.
48. Kuttig M, Zobel G, Grubbauer HM, Trop M. A clinical score system for children with ARDS. *Anaesthetist* 1991;40:282-6.
49. Pepe PE, Thomas RG, Stager MA, Hudson LD, Carrico CJ. Early prediction of the adult respiratory distress syndrome by a simple scoring method. *Ann Emerg Med* 1983;12:749-55.
50. Ventilation with lower tidal volumes as compared with traditional tidal volumes for acute lung injury and the acute respiratory distress syndrome: the Acute Respiratory Distress Syndrome Network. *N Engl J Med*. 2000;342:1301-8.
51. Amato MB, Barbas CS, Medeiros DM, et al. Effect of a protective-ventilation strategy on mortality in the acute respiratory distress syndrome. *N Engl J Med*. 1998;338:347-54.
52. Cindrick LL, Gore DC, Herndon DN, Traber LD, et al. Bronchoscopic lavage with perfluorocarbon decreases postprocedure hypoxemia in an ovine model of smoke inhalation. *J Trauma* 1999;46:129-135.
53. Leach CL, Fuhrman BP, Morin FC, Rath MG. Perfluorocarbon-assisted gas exchange (partial liquid ventilation) in respiratory distress syndrome: a prospective, randomized, controlled study. *Crit Care Med*. 1993;21:1270-78.
54. Pierre EJ, Zwischenberger JB, Angel C, Upp J, Cortiella J, et al. Extracorporeal membrane oxygenation in the treatment of respiratory failure in pediatric patients with burns. *J Burn Care Rehabil* 1998;19:131-4.
55. Lund T, Goodwin CW, McManus WF, Shirani KZ et al. Upper airway sequelae in burn patients requiring endotracheal intubation or tracheostomy. *Ann Surg*. 1985;201:374-82.
56. Barret JP, Desai MH, Herndon DN. Effects of tracheostomies on infection and airway complications in pediatric burn patients. *Burns*. 2000;26:190-3.
57. Tasaka S, Kanazawa M, Mori M, Fujishima S, et al. Long-term course of bronchiectasis and bronchiolitis obliterans as late complication of smoke inhalation. *Respiration*. 1995;62:40-2.
58. Fogarty PW, George PJ, Solomon M, Spiro SG et al. Long term effects of smoke inhalation in survivors of King's Cross underground station fire. *Thorax*. 1991;46:914-18.
59. Moylan JA Jr., West JT, Nash G, Bowen JA, Pruitt BA Jr. Tracheostomy in thermally injured patients: a review of five years' experience. *Am Surg*. 1972;38:119-23.
60. Kadilak PR, Vanasse S, Sheridan RL. Favorable short- and long-term outcomes of prolonged translaryngeal intubation in critically ill children. *J Burn Care Rehabil*. 2004;25:262-5.
61. Barret JP, Desau MH, Herndon DN. Effects of tracheostomies on infection and airway complications in pediatric burn patients. *Burns*. 2

Burn Resuscitation

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Introduction

One of the great advances in burn care, developing a strategy for treating burn shock resuscitation, occurred in the 1960s and 1970s. Prior to this period, most people with extensive burns (>30 % total body surface area [TBSA]) would simply expire within hours, or if they survived, would suffer from renal failure. Currently, burn shock resuscitation has become an afterthought that is relegated to residents and nursing staff. Calculations are performed based on protocols and it is known that fluid rate titration should be based on urine output. Recently, however, concerns have arisen that suggest that over-resuscitation has become common. "Fluid creep" has become the term to describe a trend in giving patients too much fluid¹⁻⁴. The issue of "fluid creep" seems to be substantiated by increased numbers of publications describing complications such as compartment syndromes, especially abdominal compartment syndrome⁵⁻⁸. These realizations suggest that there still is a long way to go in understanding the mechanisms of burn shock. The purpose of this review will be to summarize the presentation; discussions and conclusions of burn resuscitation at the recent "State of the Science Meeting" which took place in Washington, DC, October 26, 2006.

The goal of the review will be to ask several questions:

- ☐ Have we made progress in our resuscitation formulas?
- ☐ Can we do a better job with resuscitation?
- ☐ Do we need to do a better job?
- ☐ What is the pathophysiology of burn shock?
- ☐ Is there agreement on resuscitation formulas?
- ☐ What is the best resuscitation fluid?
- ☐ How do newer technologies assist with resuscitation?
- ☐ What should the endpoints of resuscitation be?
- ☐ Can we alter the capillary leak of burn shock?

The answers to these questions are, unfortunately, not simple. We have made progress, but not enough. There is not even universal agreement on which formula to use. We know that the ultimate goal is optimal perfusion but we still do not have adequate indicators of perfusion. One guideline for resuscitation has been clearly defined: urine output. Are we following urine output like we should? Often enough, we are not. Is urine output good enough? Maybe urine output leads to over-resuscitation. Does it really matter if we do a good job with resuscitation or not? Most patients tolerate our inaccuracies and do just fine despite our mistakes. According to the recent publication by the Institution of Medicine, this attitude will not be tolerated⁹. There are increased efforts to reduce medical errors. We cannot tolerate doing an "adequate" job when we can put forth a "good" or excellent" effort. The challenge to our colleagues, then, is to improve our knowledge of the science of resuscitation to reduce errors and improve the outcomes of our patients.

History

_____The first documented interest in studying burn shock resuscitation was tied to burn disasters. Underhill published his experience with the Rialto Theater fire in 1921¹⁰. He documented the understanding that burn shock was related to fluid loss. The Coconut Grove disaster in 1942 was an impetus for many developments in burn care. One of the topics of the landmark publication of Cope and Moore was related to fluid shifts in burn resuscitation¹¹. They suggested that edema contributes to the shock state after a burn. They also suggested that resuscitation should be tied to the body weight and the severity of burn and introduced a "body-weight burn budget" formula for resuscitation. The first burn resuscitation formula based on body surface area burn and bodyweight was described by Evans in 1952¹². The "Evans Formula" was the standard for years. In 1965, Moyer, Margraf and Monafu suggested that burn edema sequesters a large amount of fluid¹³. They introduced the first crystalloid-only resuscitation. They also suggested that extracellular sodium depletion plays a role in burn shock. Arturson was another key investigator who suggested that capillary leak was the major cause of fluid shifts after a burn injury¹⁴.

Clearly, a major focus of research during the 1960s and 1970s was the investigation of fluid shifts during the first 24 hours after burn injury. There has not been such an effort since

that time. One of the key figures in burn resuscitation was Charles Baxter, who was instrumental in developing the Parkland Formula, which today is the most frequently used resuscitation formula. Baxter, along with Shires, performed isotope studies to indicate that the fluid leaking from the capillaries had a similar protein content to serum¹⁵. This finding suggested that providing protein during burn shock resuscitation was not indicated since most of the supplemental proteins would leak into the interstitial space. He and his colleagues understood that fluid requirements should be dictated by the urine output of the burn patients. They determined that patients required 4 ml/kg/% TBSA burn in 24 hours¹⁶. As a rough indicator of the 24 hour requirements, they suggested that fluid delivery could be divided so that one half of the fluids could be given in the first 8 hours and the second half in the remaining 16 hours. He also realized that this was an approximation and the best indicator of fluid requirements should be based on urine output. The “Parkland Formula” has remained the most commonly used formula today.

Dr. Baxter spent much of his early career studying the mechanisms of burn shock. One of his key findings was that in response to a burn injury there is a “cellular shock” that is manifested by a change in the transmembrane potential of the cell¹⁶. In patients with burns over 30% TBSA there is a systemic decrease in the transmembrane potential of the cell. The cause of the transmembrane decrease is related to an increase in intracellular sodium. The burn has effects on the membrane-associated ion channels. Further studies are needed to elucidate these effects but research has tended to focus on other aspects of the response to injury.

Around the same time as Dr. Baxter’s work, Dr. Pruitt and Dr. Moncrief characterized the hemodynamic effects of burn shock with and without resuscitation¹⁷. They developed the Brooke Formula (named after the military base in San Antonio, Texas) with a resuscitation volume that was lower than the Parkland Formula (2 ml/kg/% TBSA burn). They also stressed that the actual fluid volume given should be titrated to the physiologic response (urine output). While the initial formula suggested the use of a colloid for resuscitation, it was eventually changed to the “Modified Brooke Formula” suggesting the use of Lactated Ringers solution at 2 ml/kg/% TBSA burn.

Also in the early 1970s, Monafo started examining the efficacy of using a hypertonic saline solutions (240 – 300 mEq of Na⁺) for resuscitation^{18,19}. The concept was that hypertonic saline would shift water from the intracellular to the intravascular space. The other benefit would be that with a lower volume of resuscitation there would be less edema and its associated complications. Initially, there was great interest in using a hypertonic sodium chloride solution but interest waned in the subsequent years. At least two prospective trials have been performed with varying results^{20,21}. A more recent study suggested that there was an increase in renal failure with hypertonic saline²². Another study suggested that the use of a hypertonic saline resuscitation reduces the risk of abdominal compartment syndrome by reducing the volume of resuscitation²³. In the early 1990s, Warden suggested the use of a “modified hypertonic resuscitation” using Lactated Ringers solution with 50 mEq of NaHCO₃ per liter²⁴. This creates a sodium concentration of 180 mEq. The results of another study suggested that addition of NaHCO₃ would not alter the outcome of resuscitation²⁵. The interest in hypertonic resuscitation has recently been rekindled with findings that suggest that hypertonic saline may enhance the immune response to injury²⁶.

More recently, the concept of using colloids for resuscitation has been revived. Fresh frozen plasma, Dextran 40, Dextran 70, and other colloid formulas have been proposed.^{27,28,29,30,31} Recent studies utilizing colloids have not substantially influenced the practice of burn resuscitation since the development of the Parkland Formula.

In 1978, approximately 30 years prior to the current State of the Science Meeting, an NIH “Consensus Conference” on burn shock resuscitation was held to determine the optimal resuscitation for a burn patient³². Although there was no consensus on the best resuscitation formula, what was agreed upon was that the resuscitation fluids should be minimized to decrease iatrogenic complications. The consensus conference acknowledged that physiologic parameters, including urine output, were important for monitoring the efficacy of resuscitation and suggested that replacing sodium was key to an adequate resuscitation. Since that conference there has been no concerted efforts to improve burn shock resuscitation.

The Pathophysiology of Burn Edema

The pathophysiology of burn edema has been extensively studied. Demling³³ has recently published an excellent review from which I will summarize key issues. Burn edema forms rapidly after a burn injury; the extent varies with the depth of injury. For instance, after a superficial burn the maximal amount of edema forms after 12 hours. Ninety percent of the edema, however, is present by 4 hours. The rapid increase in edema is due to increased perfusion to the injured area. This increases local blood flow that in turn “pushes” more fluid out of the capillaries. To a great extent, the edema tends to reside within the dermis. Resorption of water begins around 4 hours and is complete by 4 days. The edema dissipates in a partial thickness burn more rapidly than in a full thickness burn due to the functional lymphatic network and increased perfusion of a partial-thickness burn.

Edema formation in deep burns is different, mainly because of the damage to dermal vascular and lymphatic plexus. The rate of tissue edema peaks later (maximal at 18 hours) and resorption is much delayed because of damage to the lymphatics. Approximately 25% of the excess water is still present at one week. The edema fluid also tends to reside in the subcutaneous tissue (because the skin itself is destroyed).

The fluid mechanics of edema are best understood by the modern version of the Starling Equation:

$$Q = Kf(P_{cap} - P_i) + (\pi_p - \pi_i)$$

While there is a general simplistic view that an increase in capillary permeability drives injury-related edema, all factors of the formula are affected after a burn.

Q refers to the “Fluid Filtration Rate” which peaks within 1-2 hours after a burn injury. The increase in fluid filtration rate (**Q**) persists for days after a burn but is soon balanced by very efficient resorption by lymphatics. Clearly, if there is damage to the local lymphatics then resorption of fluids will be delayed.

Kf refers to “Capillary Filtration Coefficient” which depends on the capillary surface area and hydraulic conductivity. This coefficient increases to 2-3 times normal after a burn injury.

P_{cap} refers the “Capillary Hydrostatic Pressure” which is increased in superficial burns due to the increase vasodilation in response to local mediator release. The **P_{cap}** increases from a normal of 24 mmHg to 48 mmHg after a burn injury.

P_i refers to the “Interstitial Hydrostatic Pressure” which, surprisingly, becomes negative after a burn either from the breakdown of large proteins into smaller osmotically active particles that create a vacuum-like effect or due to the “Hydraulic Theory of Interstitial Matrix Pressure”, which suggests that coiling of tethered collagen and hyaluron macromolecules creates a negative pressure.

σ refers to the “Reflection Coefficient” and describes the permeability characteristics of the capillary to macromolecules. A reflection coefficient of 1 indicates that no large molecule will pass across the capillary (i.e. it is impermeable). A value of 0 means that there is free flow of macromolecules across the capillary. Normal **σ** is 0.9 for the skin and 0.7 for the lung. The peak in permeability occurs within the first day post-burn and persists for days.

π_p refers to “Plasma Oncotic Pressure” or “Plasma Colloid Osmotic Pressure”. The plasma oncotic pressure decreases significantly as protein levels drop during resuscitation. The value drops by around 50% in a major burn.

π_i refers to “Interstitial Oncotic Pressure” or “Interstitial Colloid Osmotic Pressure”, which increases after burn injury due to proteins leaking into the interstitium.

Another factor is important in the production of edema: interstitial compliance. With destruction of the tissues, the interstitial compliance increases due to destruction of local collagen and other extracellular matrix molecules. This contributes to edema by increasing the compliance of the tissues to extra fluid. Other factors in the formation of edema are the lymphatics and the production of free oxygen radicals from leukocytes. The oxygen-free radicals lead to further tissue destruction, mediator production and prolonged changes in capillary permeability.

The Current State of Resuscitation

The majority of burn centers use a crystalloid solution (Lactated Ringer’s) along with some variation of the Parkland Formula for resuscitation (Table 1) and adjust resuscitation

based on urine output. Resuscitation of a burn patient remains problematic. The fact that there are multiple formulas for resuscitation implies that our current resuscitation guidelines do not apply to all situations. There have been several publications that suggest that our resuscitation efforts frequently lead to over-resuscitation¹⁻⁴. Many centers deliver much more fluid than 4 ml/kg/% TBSA burn, thus suggesting that “fluid creep” does indeed occur. The excessive fluid delivery has led to descriptions of increased complications such as abdominal compartment syndrome⁵⁻⁸. Why does “fluid creep” occur? The answer is not clear but it is known that actual urine output levels frequently are higher than the targeted ½ to 1 ml/kg/hour. Is the lack of adherence to urine output due to lack of training or are staff members not paying attention to urine output? One hypothesis for over-resuscitation is that with increased use of narcotics there are increased fluid demands³⁴. The term “opioid creep” has been coined to correspond to “fluid creep”. This interesting hypothesis needs to be tested.

Other factors may be related to the timing and initial volume of resuscitation. Delay in resuscitation increases fluid requirements³⁵ so with the regionalization of burn units, delays may lead to increasing fluid requirements. A comment during the State of the Science Meeting was that once over-resuscitation has been initiated, it is impossible to “turn off” the need for a high fluid resuscitation rate. This interesting hypothesis needs to be tested. Improved instruction and communication should help reduce initial over-resuscitation. Another key question is: is urine output an adequate monitor of resuscitation? Dries suggested that urine output might not be an accurate indicator of adequate resuscitation³⁶. Are other parameters any better? Clearly, these questions need to be answered.

Age is another important factor affecting the volume of resuscitation. The actual fluid required for pediatric burn resuscitation turns out being approximately 6 ml/kg/% TBSA burn^{37,38}. Small children have relatively large daily basal fluid requirements. This volume contributes to the fluid needed for burn resuscitation. For instance, a 10 kg child (body surface area of 0.5 meters squared) needs approximately 1000 ml/day for daily basal fluid requirements. If that child sustains a 50% TBSA burn, the Parkland Formula indicates that they need $4 \times 10 \times 50 = 2000$ ml in 24 hours. Addition of the basal requirement to the Parkland formula yields 6 ml/kg/% TBSA burn. In an adult or older child, the daily basal requirements become much smaller in comparison, and are already included in the resuscitation formula. For example, a 100 kg man needs approximately 3000 ml per day in basal fluids. If he sustains 80% burns the Parkland formula suggests $4 \times 100 \times 80 = 32,000$ ml for the first 24 hours. The 3000 ml is relatively inconsequential in influencing the fluid rate for resuscitation.

Anecdotal reports of using alternative solutions, such as Ringer’s ethyl pyruvate solution (REPS), as an alternative crystalloid solution for other types of shock have recently been published^{39,40}. The theory is that pyruvate, the second to last product of glycolysis, helps to improve the cell’s capability to deal with metabolic stress. Studies by Fink have suggested that REPS has anti-inflammatory and anti-oxidant activities. There have been no reports of using this solution in burn shock resuscitation. Additional reports indicate that Lactated Ringer’s solution contains both L and D-lactate isomers⁴¹⁻⁴³. The D-lactate isomer has been found to be toxic to the cells and increases apoptosis^{42,43}. The L-lactate isoform lacks toxicity and thus might be better for routine resuscitation. These findings have not been confirmed in clinical studies⁴¹. Other fluids that may have some benefit include D- hydroxybutyrate in a Ringer’s solution⁴³, “Normosol”⁴⁴, “Isosal-D”⁴⁵, or “Gelofusine” (used for burn resuscitation in China)⁴⁶. Prospective randomized trials on these solutions are lacking.

The use of colloids in resuscitation has long been debated. The first formula described by Evans utilized albumin (NS at 1 ml/kg/% burn + Colloid at 1 ml/kg/% burn)¹². The original Brooke formula also utilized colloid (LR at 1.5 ml/kg/% burn + Colloid at 0.5 ml/kg/% burn), but the formula was later switched to LR at 2 ml/kg/% TBSA burn¹⁷. As described above, Slater suggested that the use of fresh frozen plasma in addition to LR (LR 2l/24 hours + FFP at 75 ml/kg/24 hours)²⁷. Demling reported the use of a complicated formula of Dextran 40 in normal saline at 2ml/kg/hour with LR added to maintain adequate urine output. He then added FFP at 0.5 ml/kg/hr starting at 8 hours and continuing for 18 hours²⁷. The Haifa group uses serum for their resuscitation formula³¹. Many other burn units will utilize the Parkland formula (or another crystalloid resuscitation) and then give small amounts of human albumin after 12 – 24 hours if

the patient fails to resuscitate adequately. Although maintaining normal albumin levels is not justified, once levels drop below 2.0 mg/dL albumin may be indicated, and albumin does not decrease the incidence of multiple organ dysfunction^{47,48}. The issue of the relative roles of crystalloid versus colloid resuscitation is still unresolved.

The other question related to resuscitation is whether inotropic support (such as dopamine, dobutamine, epinephrine, norepinephrine or vasopressin) is indicated during burn shock. "Goal-directed resuscitation" was popular for managing sepsis during the 1990's⁴⁹ but controlled trials suggested that it did not improve patient outcomes⁵⁰. Several publications that suggest that a major burn releases a "cardiac depression factor" that impairs cardiac function^{51,52}, so inotropic support might be of value in selected cases. Determining which patients, if any, would benefit from cardiac support may improve the outcomes of burn shock resuscitation.

Endpoints of Resuscitation

The most important message derived from the State of the Science Meeting was that *endpoints of resuscitation* are poorly defined. Cancio, et al, tried to find variables to predict who would not respond to resuscitation and was unable to do so⁵³. No single formula should be used to dictate fluid resuscitation during burn shock. There are many other factors that influence fluid requirements during resuscitation besides TBSA burn involvement. Other factors such as burn depth, inhalation injury, associated injuries, age, delay in resuscitation, need for escharotomies/fasciotomies, and use of alcohol or drugs influence fluid requirements. Clearly, the formulas are just indicators for the initiating fluid resuscitation rate. Fluid rates need to be adjusted based on physiologic endpoints, such as urine output (1/2 ml/kg/ hour for adults and 1 ml/kg/hour for small children). The value of using urine output to adjust fluid rates during burn shock has been challenged³⁶. Studies also suggest that the adjustment of resuscitation fluids based on urine output is inconsistent¹⁻⁴. Methods for improving our response to urine output as an endpoint are in order.

Other indicators of resuscitation have been challenged in recent years. The use of invasive monitoring, such as the central venous pressure (CVP) or pulmonary artery catheter (PAC) theoretically should help, especially in the elderly, but studies do not support their use⁵⁴⁻⁵⁷. One study suggests that the CVP is influenced more by intra-abdominal pressures than actual right atrial pressures⁵⁸. Pulmonary artery catheters (PAC) have the capability to provide more information, but recent studies suggest that the PAC does not change mortality in other diseases⁵⁴⁻⁵⁷.

Invasive monitors continue to become more sophisticated. Pulmonary artery catheters have the capability of measuring continuous cardiac output and mixed venous oxygen saturation. It is also possible to measure such parameters as ventricular-arterial coupling⁵⁶. There have been a few studies using what is described as intermittent transpulmonary thermodilution using the "COLD system" (Pulsion Medical Systems, Munich, Germany). This system utilizes two systems of thermodilution, 0.3 mg/kg indocyanine green dye mixed with iced 5% glucose solution through a central line in the superior vena cava and a "thermistor-tipped fiberoptic catheter" placed in the femoral artery is used to measure such parameters as intrathoracic blood volume (ITBV), cardiac output, total blood volume index (TBVI), and extravascular lung water (EVLW)⁵⁶⁻⁵⁹. Although preliminary studies suggest that these devices may aid in resuscitation, the one randomized trial did not support these findings⁵⁷. A surprising conclusion was that the use of the Baxter (Parkland) formula led to under-resuscitation! This conclusion is certainly in contrast to the concerns about "fluid creep".

Another potential aid in estimating cardiac output, "pulse contour analysis", is based on the shape of an arterial waveform⁶⁰⁻⁶³. Pulse contour analysis has been found to be effective using both femoral and radial arterial catheters⁶². These devices have not been prospectively tested in burn patients. Other methods include measuring trans-esophageal echocardiography⁶³, partial carbon dioxide rebreathing⁶³ and impedance electrocardiography⁶⁴. Comparisons of these various techniques demonstrate that they are somewhat reliable for determining cardiac output⁶³. While these devices are interesting, their use for burn resuscitation is undefined.

Tissue perfusion monitors, such as gastric tonometers⁶⁵ or devices to measure O₂ and CO₂ saturations in the subcutaneous tissues⁶⁶ (both below the burn and in normal skin), have also been tested. These devices are of marginal utility in dictating resuscitation; they demonstrate low perfusion despite other signs of adequate resuscitation. All of these findings suggest that we do not have adequate devices to monitor the adequacy of resuscitation. A major focus for the future will be to develop more reliable endpoints for resuscitation.

Oral Resuscitation

Oral resuscitation was one of the earliest methods of providing fluids for patients. Oral resuscitation is a potential source of fluids in two situations – burns in the third world and in the case of a disaster when intravenous supplies may not keep up with medical demand. Resources in many countries cannot support the use of intravenous fluids for many of their population. With a sizeable burn these patients often are not resuscitated and thus expire. Oral resuscitation fluids can be created in kitchens and are very inexpensive to create and administer. There are two excellent reviews that detail the specifics of oral resuscitation in burn patients^{67,68}. What has piqued interest in oral resuscitation has been the success of using oral fluids to treat cholera and other epidemic forms of diarrhea. The World Health Organization (WHO) has developed guidelines for using oral resuscitation for severe diarrheal diseases^{69,70}. These same formulations should be helpful for burn patients. The key question is at what size burn is oral resuscitation ineffective? Anecdotal studies suggest that oral resuscitation is helpful for at least patients with smaller burns⁷¹. The value of oral resuscitation for larger burns has not been established. It is conceivable that encouraging early oral fluid intake prior to intravenous access could improve resuscitation in massive burns. This strategy would also be helpful for soldiers suffering from burns while they await definitive care. The combination of oral and intravenous fluids would place less of a burden on supplies in a mass casualty situation.

A major problem with oral resuscitation, which may be related to the use of narcotics, is that vomiting may limit the volume delivered to the patient. One suggestion made at the State of the Science Meeting was that oral opioid antagonists might improve gastrointestinal function. Clearly, early feeding is tolerated through naso-duodenal feeding tubes. The placement of naso-duodenal or naso-gastric tubes may facilitate oral resuscitation.

Another quandary of oral resuscitation is what type of fluid do we provide? Studies have suggested the use of hypo- and hypertonic solutions (Table 2). The current World Health Organization solution is somewhat hypotonic, and the literature suggests that hypotonicity really does not matter for severe diarrheal disease⁷³. Studies also suggest that the addition of glucose will aid in the delivery of water⁷⁴. The ideal solution and the best mode of delivery are currently not known (Table 2 and 3). Finally, there has been a description of delivering resuscitation fluids per rectum (“proctoclysis”) ⁷⁵. The “Murphy’s Drip” solution, originally described in 1913, is made of NaCl (1.77g) and CaCl₂ (1.77g) in 473 mL (1 pint) and delivered per rectum as 1-2 pints every hour. While these techniques are not frequently used, further studies are needed to test oral and rectal resuscitation strategies. The use of simplified resuscitation formulas could greatly enhance survival in third world countries.

Pharmacologic Manipulation of Resuscitation

The other key question of burn shock is whether the shock process can be reversed or inhibited by pharmacologic manipulation. Although burn shock involves the loss of fluid across from the intravascular to the interstitial space, the exact pathophysiology of the capillary leak is not totally known. Local mediators such as histamine, serotonin, prostaglandins, and others have been implicated in the development of capillary leakage⁷⁶⁻⁷⁸. Many studies have been performed that utilize blockers of these different mediators to prevent capillary leakage⁷⁹⁻⁸¹. However, these mediators appear to reduce, but do not eliminate, edema. Pre-injury treatment is obviously not feasible for treating our patients. Post-injury studies have not proven to be of much value.

Another promising substance in reducing the amount of fluid required for burn shock resuscitation is high dose Vitamin C^{82,83}. The clinical studies, performed in Japan, suggest that Vitamin C treatment might be an inexpensive and effective means for reducing fluid requirements for burn patients⁸⁴. These studies have not been duplicated in other institutions. Multi-institutional prospective randomized trials are needed to substantiate these findings.

Finally, both plasmapheresis and exchange transfusions have been used to decrease inflammation and edema formation⁸⁵⁻⁸⁷. The theory of “removing the evil humors” makes sense, since the techniques can reduce cytokine levels. Plasmapheresis was reserved for adults and exchange transfusions were utilized for children. While these studies were encouraging, burn teams rarely use these techniques, due to the extensive personnel and equipment requirements.

Resuscitation – the Future

In reality, there has been little progress made in understanding and treating burn shock in the last 2-3 decades. The formulas have not changed since the seventies and the attention paid to monitoring resuscitation may have deteriorated. There has been an increase in over-resuscitation and its associated complications. One may wonder whether our teams are trained as well in adjusting fluids as they were in the past. One new idea is to develop “closed-loop” resuscitation, in which the amount of urine produced is measured and intravenous fluids are adjusted automatically by a computer⁸⁸. Publications that suggest that “closed-loop” resuscitation does as well as human monitors.

The simple question of which type of resuscitation fluid is the best still needs to be answered. Crystalloid use is inexpensive and is effective for the majority of patients. Some patients, however, benefit from the addition of colloid. Who are these patients and when should colloids be added? What are we to do if there is a burn-related disaster? We would quickly run out of our IV solutions. Do we need to have easily produced alternatives? The use of oral resuscitation formulas and treatment protocols is also necessary if we can improve the outcome of burns in the outcome of burns in the third world. Studies are necessary to develop the optimal types of solution and to improve the tolerance of oral resuscitation.

One must also wonder whether urine output is really an accurate enough indicator of tissue perfusion. Frequently the patient may have adequate urine output but is hemodynamically unstable. Abdominal compartment syndrome is thought to be a problem of “over-resuscitation” but frequently occurs in the face of inadequate urine output. The other monitors of tissue perfusion (gastric, rectal, skin tonometers) are of limited utility. A challenge for the future will be to develop monitors of tissue perfusion that are more accurate than our current standards.

We must also develop a better understanding of the hemodynamic demands of burn shock so that we can truly understand whether supplementation with inotropic support is indicated or of true value. The ability to alter the cellular responses to a burn injury would also be helpful. Is vitamin C treatment worthwhile? Can we develop an effective blockade of capillary leak that is effective hours after burn injury? Data needs to be obtained on the molecular and cellular mechanisms of burn shock. One of the key problems has been that there has been little interest in resuscitation research for the last several decades. Maybe it is time to rekindle that interest in burn resuscitation.

Recommendations from the State of the Science Meeting

Listed below is a summary of the key issues stressed by the participants of the State of the Science Meeting. Several key questions were asked of the participants so the questions will be listed along with key areas for future concern. It is hoped that these points will be used as guidelines for future investigations related to burn shock resuscitation.

- ☐ The most important area of research should be to define endpoints of resuscitation.
 - ☐ Urine output alone is probably not an adequate endpoint.
 - ☐ Multiple endpoints exist that may conflict. The interpretation of these endpoints should be better defined.
 - ☐ The role of invasive and noninvasive monitoring needs to be defined.
 - ☐ Should pulmonary artery catheters be used?
 - ☐ What is the role of newer monitoring techniques?
 - ☐ Better indicators of perfusion need to be determined.
 - ☐ Current measures of tissue perfusion (gut or skin) are inadequate.
 - ☐ What is the role of base deficit and lactate levels?
 - ☐ What is the role of the laser Doppler?
 - ☐ What are the cellular markers of resuscitation?

- What is the best resuscitation solution?
 - Lactated Ringer's solution has problems but is still used by the vast majority of burn units.
 - Some units use other types of crystalloid solutions, such as acetate.
 - Colloid solutions are used in about 5% of the units throughout resuscitation.
 - Most units add a colloid (usually albumin) during the first 24-48 hours, with a trend to adding albumin earlier during resuscitation. One person stated; "everyone cheats" by adding colloids to the resuscitation.
 - A multi-center trial to examine the role of colloids in resuscitation is warranted.
 - The role of hypertonic saline but its role still needs to be evaluated.
- Avoiding over-resuscitation is an important goal.
 - Over-resuscitation is a major cause of complications such as compartment syndromes and acute respiratory distress syndrome.
 - Once over-resuscitation has started, it is difficult to stop.
 - Better teaching of pre-hospital personnel, emergency department staff, house staff and nursing will reduce early over-resuscitation and its complications.
 - Quality improvement projects should be set up to reduce over-resuscitation. The urine output target should continue to be ½ ml/kg/hour for adults and 1 ml/kg/hour for children <30 kg.
 - Any center that participates in a resuscitation study will improve compliance with urine output goals.
 - The influence of narcotics, alcohol and other drugs on over-resuscitation should be investigated.
 - The role of computer-based "closed-loop" resuscitation systems should be investigated.
- Research should focus on the pathophysiology of both burn shock and edema formation.
 - Research focus on cardiovascular changes in burn shock, including causes of myocardial depression.
 - Research should define the cellular and molecular changes in the response to burn injury.
 - Mathematical modeling may be a methodology for research
- Oral resuscitation techniques should be investigated.
 - Oral resuscitation should improve survival in third world countries.
 - Oral resuscitation may be a strategy for early resuscitation when intravenous access is unavailable (soldiers burned in action or during a disaster).
 - Studies should focus on ways to improve tolerance of oral resuscitation strategies, including types of fluids and methods of delivery.
 - Narcotics may decrease tolerance to oral resuscitation. Their role in oral intolerance to fluids should be investigated.
- The role of inotropic agents during resuscitation needs to be determined.
 - Goal-directed resuscitation has not been proven effective in the ICU.
 - A study to evaluate the role of inotropes should be performed.
 - Vasopressin may be an important inotrope to study during resuscitation.
- Research should focus on methods to stop the capillary leak during burn shock
 - The role of narcotics in capillary leak should be determined.
 - A multi-center trial to examine the role of vitamin C during burn shock resuscitation should be performed.
 - A "cocktail" should be developed to treat capillary leak. For instance, vitamin E (a vitamin with anti-oxidant effects) might reduce the leak.
 - The role of activated protein C (Xigris™, Eli Lilly, Incorporated, Indianapolis, IN) was mentioned as an interesting agent to reduce capillary leak. At present it is cost-prohibitive.
 - Endpoints of resuscitation need to be defined prior to these studies.

Conclusion – Top 5 Priorities for Burn Resuscitation Research

There are still gaps in our knowledge of burn resuscitation. While there are many issues that should be investigated, the following questions should receive top priority (Table 4):

- 1) The top priority for burn resuscitation research is to define the *endpoints of resuscitation*. It has become obvious that urine output is not good enough but at the same time, newer measures of cardiovascular function have also been questioned. This needs to precede all other resuscitation studies.
- 2) There should be investigations that clearly identify the reasons for “fluid creep” in burn resuscitation. Have we become complacent or are there physiologic reasons for the increase in delivered fluids? Will performance improvement strategies reverse this trend?
- 3) The pathophysiology of burn edema should be determined. We need to determine what initiates the leak and determine why there are changes in the entire cardiovascular system.
- 4) The role of oral resuscitation should be investigated. Improving oral resuscitation strategies should enhance survival in third world countries and after disasters.
- 5) The last topic for investigation is to test an agent that will reduce the capillary leak that occurs during burn shock. The investigation of high dose vitamin C seems to make the most sense for the first trial.

References

- 1) Engrav LH, Colescott PL, Kemalyan N, et al. A biopsy of the use of the Baxter formula resuscitate burns or Do we do it like Charlie did it? *J Burn Care Rehabil* 2000;21:91-5.
- 2) Pruitt BA Jr. Protection from excessive resuscitation: pushing the pendulum back. *J Trauma* 2000;49:387-91.
- 3) Shah A, Kramer GC, Grady JJ, Herndon DN. Meta-analysis of fluid requirements for burn injury 1980-2002. *J Burn Care Rehabil* 2003;24:S118.
- 4) Friedrich JB, Sullivan SR, Engrav LH, et al. Is supra-Baxter resuscitation in burns patients a new phenomenon? *Burns* 2004;30:464-6.
- 5) Greenhalgh DG, Warden GD. The importance of intra-abdominal pressure measurements in burned children. *J Trauma* 1994;36:685-90.
- 6) Latenser BA, Kowel-Vern A, Kimball D, Chakrin A, Dujovny N. A pilot study comparing percutaneous decompression with decompressive laparotomy for acute abdominal compartment syndrome in thermal injury. *J Burn Care Rehabil* 2002;23:190-5.
- 7) Hobson KG, Young KM, Ciraulo A, Palmieri TL, Greenhalgh DG. Release of abdominal compartment syndrome improves survival in patients with burn injury. *J Trauma* 2002;53:1129-34.
- 8) Oda J, Inoue KYT, Harunari N, et al. Resuscitation volume and abdominal compartment syndrome in patients with major burns. *Burns* 2006;32:151-4.
- 9) Institute of Medicine. *To Err is Human: Building a Safer Health System*. Washington, DC: National Academy Press, 1999.
- 10) Underhill FP. The significance of anhydremia in extensive surface burn. *JAMA* 1930;95:852-7.
- 11) Moore FD. The body-weight burn budget: Basic fluid therapy for the early burn. *Surg Clin North Am* 1970;50:1249-65.
- 12) Artz CP, Moncrief JA. The burn problem. In *The Treatment of Burns*, Artz CP, Moncrief JA, eds., Philadelphia, WB Saunders Co, 1969; pp 1-22.
- 13) Moyer CA, Margraf HW, Monafo WW. Burn shock and extravascular sodium: Treatment with Ringer's solution with lactate. *Arch Surg* 1965;90:799-811.
- 14) Arturson G. Microvascular permeability to macromolecules in thermal injury. *Acta Physiol Scand (Suppl)* 1979;463:111-222.
- 15) Baxter CR, Shires GT. Physiological response to crystalloid resuscitation of severe burns. *Ann NY Acad Sci* 1968;150:874-94.
- 16) Baxter CR. Fluid volume and electrolyte changes in the early post-burn period. *Clin Plast Surg* 1974;1:693-703.
- 17) Pruitt BA Jr, Mason AD Jr, Moncrief JA. Hemodynamic changes in the early postburn patient: The influence of fluid administration and of a vasodilator (hydralazine). *J Trauma* 1971;11:36-46.
- 18) Monafo WW. The treatment of burn shock by the intravenous and oral administration of hypertonic lactated saline solution. *J Trauma* 1970;10:575-86.
- 19) Monafo WW, Halverson JD, Schechtman K. The role of concentrated sodium solutions in the resuscitation of patients with severe burns. *Surgery* 1984;95:129-35.
- 20) Caldwell FT, Boswer BH. Critical evaluation of hypertonic and hypotonic solutions to resuscitate severely burned children: A prospective study. *Ann Surg* 1979;189:546-52.
- 21) Gunn ML, Hansbrough JF, Davis JW, Furst SR, Field TO. Prospective randomized trial of hypertonic sodium lactate vs. lactated Ringer's solution for burn shock resuscitation. *J Trauma* 1989;29:1261-7.
- 22) Huang PP, Stucky FS, Dimick AR, et al. Hypertonic sodium resuscitation is associated with renal failure and death. *Ann Surg* 1995;221:543-57.
- 23) Oda J, Ueyama M, Yamashita K, et al. Hypertonic lactated saline resuscitation reduces the risk of abdominal compartment syndrome in severely burned patients. *J Trauma* 2006;60:64-71.
- 24) Warden GD. Burn Shock Resuscitation. *World J Surg* 1992;16:16-23.

- 25) Berger MM, Pictet A, Revelly JP, Frascarolo P, Chiolerio RL. Impact of a bicarbonated saline solution on early resuscitation after major burns. *Intensive Care Med* 2000;26:1382-5.
- 26) Rizoli SB, Rhind SG, Shek PN, et al. The immunomodulatory effects of hypertonic saline resuscitation in patients sustaining traumatic hemorrhagic shock. *Ann Surg* 2006;243:47-57.
- 27) Du G, Slater H, Goldfarb IW. Influences of different resuscitation regimens on acute early weight gain in extensively burned patients. *Burns* 1991;17:147-50.
- 28) O'Mara MS, Slater H, Goldfarb IW, Saushaj PF. A prospective, randomized evaluation of intra-abdominal pressures with crystalloid and colloid resuscitation in burn patients. *J Trauma* 2005;58:1011-8.
- 29) Demling RH, Kramer GC, Gunther R, Nerlich M. Effect of non-protein colloid on post-burn edema formation in soft tissues and lung. *Surgery* 1984;95:593-602.
- 30) Onarheim H, Missavage AE, Kramer GC, Gunther RA. Effectiveness of hypertonic saline-dextran 70 for initial fluid resuscitation of major burns. *J Trauma* 1990;30:597-603.
- 31) Fodor L, Fodor A, Ramon Y, et al. Controversies in fluid resuscitation for burn management: Literature review and our experience. *Injury Int J Care Injured* 2006;37:374-9.
- 32) Schwartz SL. Consensus summary on fluid resuscitation. *J Trauma* 1979;19(suppl):876-7.
- 33) Demling RH. The burn edema process: Current concepts. *J Burn Care Rehabil* 2005;26:207-27.
- 34) Sullivan SR, Friedrich JB, Engrav LH, et al. "Opioid creep" is real and may be the cause of "fluid creep". *Burns* 2004;30:583-90.
- 35) Barrow RE, Jeschke MG, Herndon DN. Early fluid resuscitation improves outcomes in severely burned children. *Resuscitation* 2000;45:91-6.
- 36) Dries DJ, Waxman K. Adequate resuscitation of burn patients may not be measured by urine output and vital signs *Crit Care Med* 1991;19:327-9.
- 37) Merrell SW, Saffle JR, Sullivan JJ, et al. Fluid resuscitation in thermally injured children. *Am J Surg* 1986;152:664-669.
- 38) Graves TA, Cioffi WG, McManus WF, Mason AD Jr, Pruitt BA Jr. Fluid resuscitation of infants and children with massive thermal injury. *J Trauma* 1988;28:1656-9.
- 39) Fink MP. Ringer's ethyl pyruvate solution: A novel resuscitation fluid for the treatment of hemorrhagic shock and sepsis. *J Trauma* 2003;54:S141-3.
- 40) Fink MP. Ethyl pyruvate: A novel anti-inflammatory agent. *Crit Care Med* 2003;31:S51-6.
- 41) Delman K, Malek SK, Bundz S, et al. Resuscitation with lactated Ringer's solution after hemorrhage: Lack of cardiac toxicity. *Shock* 1996;5:298-303.
- 42) Jaskille A, Alam HB, Rhee P, et al. D-lactate increases pulmonary apoptosis by restricting phosphorylation of Bad and eNOS in a rat model of hemorrhagic shock. *J Trauma* 2004;57:262-70.
- 43) Jaskille A, Koustova E, Rhee P, et al. Hepatic apoptosis after hemorrhagic shock in rats can be reduced through modification of conventional Ringer's solution. *J Am Coll Surg* 2006;202:25-35.
- 44) Personal communication from Richard Kagan, MD, Shriners Hospitals for Children Cincinnati.
- 45) Milner SM, Kinsky MP, Guha SC, et al. A comparison of two different 2400 mOsm solutions for resuscitation of major burns. *J Burn Care Rehabil* 1997;18:109-15.
- 46) Huag Y, Yan B, Yang Z. Clinical study of a formula for delayed rapid fluid resuscitation for patients with burn shock. *Burns* 2005;31:617-22.
- 47) Greenhalgh DG, Housinger TA, Kagan KJ, et al. Maintenance of serum albumin levels in pediatric burn patients. A prospective, randomized trial. *J Trauma* 1995;39:67-74.
- 48) Cooper AB, Cohn SM, Zhang HS, et al. Five percent albumin for adult burn shock resuscitation: Lack of effect on daily multiple organ dysfunction score. *Transfusion* 2006;46:80-9.

- 49) Shoemaker WC, Appel PL, Kram HB. Oxygen transport measurements to evaluate tissue perfusion and titrate therapy: dobutamine and dopamine effects. *Crit Care Med* 1991;19:672-88.
- 50) Gattinoni L, Brazzi L, Pelosi P, et al. A trial of goal-oriented hemodynamic therapy in critically ill patients. SvO₂ Collaborative Group. *N Engl J Med* 1995;333:1025-32.
- 51) Baxter CR, Cook WA, Shires GT. Serum myocardial depressant factor of burn shock. *Surg Forum* 1966;17:1-2.
- 52) Raffa J, Trunkey DD. Myocardial depression in acute thermal injury. *J Trauma* 1978;18:90-3.
- 53) Cancio LC, Reifenberg L, Barillo DJ, et al. Standard variables fail to identify patients who will not respond to fluid resuscitation following thermal injury: brief report. *Burns* 2005;31:358-65.
- 54) Shah MR, Hasselblad V, Stevenson LW, et al. Impact of the pulmonary artery catheter in critically ill patients: Meta-analysis of randomized clinical trials. *JAMA* 2005;294:1664-70.
- 55) Martin RS, Norris PR, Kilgo PD, et al. Validation of stroke work and ventricular arterial coupling as markers of cardiovascular performance during resuscitation. *J Trauma* 2006;60:930-5.
- 56) Rocca GD, Costa MG, Pompei L, Coccia C, Pietropaoli P. Continuous and intermittent cardiac output measurement: Pulmonary artery catheter versus aortic transpulmonary technique. *Br J Anaesth* 2002;88:350-6.
- 57) Holm C, Mayr M, Tegeler J, et al. A clinical randomized study on the effects of invasive monitoring on burn shock resuscitation. *Burns* 2004;30:798-807.
- 58) Kuntscher MV, Germann G, Hartmann B. Correlations between cardiac output, stroke volume, central venous pressure, intra-abdominal pressure and total circulating blood volume in resuscitation of major burns. *Resuscitation* 2006;70:37-43.
- 59) Holm C, Mayr M, Horbrand F, et al. Reproducibility of transpulmonary thermodilution measurements in patients with burn shock and hypothermia. *J Burn Care Rehabil* 2005;26:260-5.
- 60) Rocca G, Costa MG, Coccia C, et al. Cardiac output monitoring: Aortic transpulmonary thermodilution and pulse contour analysis agree with standard thermodilution methods in patients undergoing lung transplantation. *Can J Anesth* 2003;50:707-11.
- 61) McGee WT, Horswell JL, Calderon J. Validation of a continuous cardiac output measurement using arterial pressure waveforms. *Crit Care* 2005;9:24-5.
- 62) De Wilde RBP, Breukers RBGE, van den Berg PCM, Jansen JRC. Monitoring cardiac output using the femoral and radial arterial pressure waveform. *Anaesthesia* 2006;61:743-6.
- 63) Bajorat J, Hofmockel R, Vagts DA, et al. Comparison of invasive and less-invasive techniques of cardiac output measurement under different haemodynamic conditions in a pig model. *Eur J Anaesth* 2006;23:23-30.
- 64) Wynne JL, Ovadjie LO, Akridge CM, et al. Impedance cardiography: A potential monitor for hemodialysis. *J Surg Res* 2006;133:55-60.
- 65) Holm C, Horbrand F, Mayr M, et al. Assessment of splanchnic perfusion by gastric tonometry in patients with acute hypovolemic burn shock. *Burns* 2006;32:689-94.
- 66) Venkatesh B, Meacher R, Muller MJ, Morgan TJ, Fraser J. Monitoring tissue oxygenation during resuscitation of major burns. *J Trauma* 2001;50:485-94.
- 67) Thomas SJ, Kramer GC, Herndon DN. Burns: Military options and tactical solutions. *J Trauma* 2003;54:S207-18.
- 68) Cancio LC, Kramer GC, Hoskins SL. Gastrointestinal fluid resuscitation of thermally injured patients. *J Burn Care Res* 2006;27:561-9.
- 69) Avery ME, Snyder JD. Oral therapy for acute diarrhoea: the underused simple solution. *N Engl J Med* 1990;323:891-4.
- 70) Victora CG, Bryce J, Fontaine O, Monasch R. Reducing deaths from diarrhoea through oral rehydration therapy. *Bull World Health Organ* 2000;78:1246-55.
- 71) Iwuagwu FC, Bailie F. Oral fluid therapy in paediatric burns (5-10%): An appraisal. *Burns* 1998;24:470-4.

- 72) Brown TL, Hernon C, Owens B. Incidence of vomiting in burns and implications for mass burn casualty management. *Burns* 2003;29:159-62.
- 73) Alam NH, Yunus M, Faruque AS, et al. Symptomatic hyponatremia during treatment with reduced osmolarity oral rehydration solution. *JAMA* 2006;296:567-73.
- 74) Farthing MJ. Oral rehydration: An evolving solution. *J Pediatr Gastroenterol Nutr* 2002;34(Suppl 1):S64-S67.
- 75) Murphy JB. Recurrent appendicitis-retrocecal appendix, with description of Dr. Murphy's proctoclysis. In: *The Surgical Clinics of John B. Murphy MD at Mercy Hospital, Chicago, Vol. 2*. Philadelphia: W.B. Saunders Co.; 1913. p. 345-52.
- 76) Majno G, Palide GE. Studies on inflammation. I. The effect of histamine and serotonin on vascular permeability. *J Cell Biol* 1961;11:571-605.
- 77) Majno G, Shea SM, Leventha M. Endothelial contractions induced by histamine type mediators. *J Cell Biol* 1969;42:647-72.
- 78) Heggors JP, Loy GL, Robson MM, DelBaccaro EJ. Histological demonstration of prostaglandins and thromboxanes in burned tissue. *J Surg Res* 1980;28:110-7.
- 79) Carvajal HF, Brouhard BH, Linares HA. Effect of antihistamine, antiserotonin and ganglionic blocking agents upon increased capillary permeability following burn edema. *J Trauma* 1975;15:969-75.
- 80) Boykin JV Jr, Crute SL, Haynes BW Jr. Cimetidine therapy for burn shock: A quantitative assessment. *J Trauma* 1985;25:864-70.
- 81) Holliman CJ, Meuleman TR, Larsen KR, et al. The effect of ketanserin, a specific serotonin antagonist, on burn shock hemodynamic parameters in a porcine burn model. *J Trauma* 1983;23:867-71.
- 82) Matsuda T, Tanaka H, Shimazaki S, et al. High dose vitamin C therapy for extensive second degree burns. *Burns* 1991;2:127-31.
- 83) Tanaka H, Matsuda H, Shimazaki S, et al. Reduced resuscitation fluid volume for second-degree burns with delayed initiation of ascorbic acid therapy. *Arch Surg* 1997;132:158-61.
- 84) Tanaka H, Matsuda T, Miyagantani Y, et al. Reduction of resuscitation fluid volumes in severely burned patients using ascorbic acid administration: a randomized, prospective study. *Arch Surg* 2000;135:326-31.
- 85) Warden GD, Stratta RJ, Saffle JR, Kravitz M, Ninnemann JL. Plasma exchange therapy in patients failing to resuscitate from burn shock. *J Trauma* 1983;23:945-51.
- 86) Kravitz M, Warden GD, Sullivan JJ, Saffle JR. A randomized trial of plasma exchange in the treatment of burn shock. *J Burn Care Rehabil* 1989;10:17-26.
- 87) Stratta RJ, Saffle JR, Kravitz M, Ninnemann JL, Warden GD. Exchange transfusion therapy in pediatric burn shock. *Circ Shock* 1984;12:203-12.
- 88) Hoskins SL, Elgjo GI, Lu J, et al. Closed-loop resuscitation of burn shock. *J Burn Care Res* 2006;27:377-385.

Table 1: Burn resuscitation formulas current and past.

Crystalloid Formulas (Usually use lactated Ringer's solution, newer isotonic fluids may be utilized)

Parkland (Baxter) Formula – 4 ml/kg/%TBSA burn, give $\frac{1}{2}$ in the first 8 hours and $\frac{1}{2}$ in the next 16 hours. Adjust rate based on urine output. For second 24 hours give 20-60% of calculated plasma volume as colloid. (The recommendation for the second 24 hours is usually not followed.)

Modified Brooke Formula – 2 ml/kg/%TBSA burn, give $\frac{1}{2}$ in the first 8 hours and $\frac{1}{2}$ in the next 16 hours. Adjust rate based on urine output. For second 24 hours give 0.33-0.5 ml/kg/%TBSA burn as colloid plus D₅W to maintain urine output.

Hypertonic Formulas (No colloid)

Monafo – 250 mEq/liter Na⁺ + 150 mEq lactate + 100 mEq Cl⁻. Adjust rate based on urine output. For second 24 hours – 1/3 isotonic salt given orally.

Warden – Lactated Ringer's plus 50 mEq NaHCO₃ (180 mEq of Na⁺) per liter for first 8 hours (based on the Parkland Formula). Switch to lactated Ringer's when pH normalizes or at 8 hours. Adjust rate based on urine output.

Colloid Formulas

Burn Budget Formula of F.D. Moore – Lactated Ringer's 1000-4000 ml + 0.5 normal saline 1200 ml + 7.5% of body weight colloid + 1500-5000 ml D₅W. For second 24 hours use same formula except for colloid 2.5% of weight.

Evans Formula – Normal saline at 1 ml/kg/%TBSA burn + colloid at 1 ml/kg/%TBSA burn. For second 24 hours give $\frac{1}{2}$ of first 24 hour requirements + D₅W (dextrose 5% in water) 2000 ml.

Brooke Formula (original) – Lactated Ringer's at 1.5 ml/kg/%TBSA burn + colloid at 0.5 ml/kg/%TBSA burn. Switch to D₅W 2000 ml for second 24 hours.

Slater Formula – Lactated Ringers 2000 ml + Fresh Frozen Plasma at 75 ml/kg/24 hours. Adjust rate based on urine output.

Haifa Formula – Plasma at 1.5 ml/kg/%TBSA burn + lactated Ringer's at 1 ml/kg/%TBSA burn. Adjust rate based on urine output.

Demling Formula – Dextran40 in normal saline at 2 ml/kg/hour for 8 hours. Fresh Frozen Plasma at 0.5 ml/kg/hour starting at 8 hours. Lactated Ringer's given to maintain urine output.

Table 2: The content of various solutions used for oral resuscitation. (Adapted from Cancio, Kramer and Hoskins⁶⁸)

Formula	Carbohydrate	Na⁺	Cl⁻	K⁺	Buffer	mOsM
WHO ORS (1975)	111	90	80	20	30	331
WHO ORS (2002)	75	75	65	20	10	245
Gatorade	250	20	20	3	3	280
Pedialyte	139	45	35	20	30	250
Rehydralyte	139	75	65	20	30	325
Fox's Na Lactate	0	161	0	0	161	321
Moyer's Citrated NaCl	0	85	63	0	29	160
Monafo's HTS	0	300	200	0	100	600
Liquidsorb	222	60	44	4	28	370
Jiang's Burn Drink	252	48	28	0	20	347
Ricelyte	3 (%wt/vol)	50	45	25	34	200
AstroAde (NASA)	0	164	76	0	40	253
Lactated Ringer's	0	130	109	4	28	270
0.9% NaCl	0	154	154	0	0	308

(Carbohydrates in mM, Osmolarity in mOsM, WHO ORS = World Health Organization Oral Rehydration Solution, HTS = hypertonic saline)

Table 3: Recipes for Homemade Oral Resuscitation Fluids (Adapted from Cancio, Kramer and Hoskins⁶⁸)

Base Ingredient	Volume	Sugar	Salt*	Baking Soda
Clean water	1 liter	8 tsp	½ tsp	½ tsp
Gatorade	Quart Bottle	No addition	¼ tsp	¼ tsp
Lactated Ringer's	1 liter	8 tsp sugar or glucose	No addition	No addition

(* - In the absence of baking soda, double the salt, tsp = teaspoon)

Table 4: The top five topics for investigation in burn shock resuscitation.

- 1) Define the endpoints of burn shock resuscitation.
- 2) Develop a better understanding of the pathophysiology of burn shock edema.
- 3) Determine the cause of “fluid creep”.
- 4) Develop a oral resuscitation protocol.
- 5) Perform a multicenter trial with an agent that reduces the capillary leak of burn shock.
The role of high dose vitamin C seems to make the most sense at this time.

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Introduction

A critical burn injury is a unique trauma, which often is accompanied by significant metabolic disturbances as well as perturbation of innate and adaptive immunity (1, 2). Human skin is not only a barrier against environmental insults and against colonization of pathogenic microbes but, more importantly, it is an immune organ with significant surveillance and thermoregulatory functions (3). Therefore it is hardly surprising that loss of large portions of skin due to burns results in impaired immunity, metabolic compromises, fluid shifts and heat loss.

Through improvements in resuscitation, critical care, nutritional support, and early closure of the burn wound over the past two decades our ability to care for burn patients has resulted in a marked reduction in morbidity and mortality. However, nosocomial wound or pulmonary infections especially in patients requiring ventilator assistance remain a major problem.

Inflammation in Burns and its Consequences

Inflammation is an essential and primordial component of normal healing when wounds are small and localized. Prompt wound closure resolves this response (4,5). However, inflammatory responses in a critical burn injury are often deranged because there is global involvement of multiple tissue beds and their constituent immune and non-immune cells placing significant metabolic and energy requirements on the repair process. For example, the extent of inflammation and energy requirements are directly proportional to the severity of injury sustained by the patient (6). The spectrum of inflammation runs from a mild elevation in cytokines associated with inflammation that largely go unnoticed clinically to a system-wide severe inflammatory response that eventually leads to microcirculatory failure of capillaries supplying individual vital organs, acute respiratory syndrome (ARDS), severe coagulopathy, and the development of the multiple organ failure.

Any critical injury of a large magnitude causes activation of multiple biological cascades in a temporal fashion. During this dynamic time course response, an acute phase of hyper-reactive immune response is followed by a hypo-reactive phase. Traditionally, the hyper-reactive phase is often called “systemic inflammatory response syndrome” or SIRS and the subsequent hypo-reactive phase as “counter anti-inflammatory response syndrome” or CARS. SIRS is often associated with enhanced production of pro-inflammatory cytokines and chemokines, increased free radical production through reactive oxygen species (ROS), and activation of complement and coagulation cascades (7, 8). The net pathophysiological impact of these responses is manifested in increased vascular permeability, fever, leukocytosis, tachypnea, peripheral vascular resistance and increased leukocyte mobilization and recruitment and the resultant bacterial killing (9). Activation of coagulation can precipitate disseminate intravascular coagulation (DIC) which increases the risk of mortality. Later during their clinical course, critically injured burn patients experience CARS, which is punctuated by the production of anti-inflammatory cytokines, leukocytopenia, severely impaired neutrophil phagocytosis, edema, and an increased risk for nosocomial infections(10-12).

Innate and Adaptive Immunity are the Effectors of Host-Defense

Central to the host-defense in any severe injury is the robust and balanced participation of leukocytes, especially the polymorphonuclear neutrophils (PMN) and monocyte/macrophages(13). In a critical burn, host defense mechanisms become critical to the survival of the host. Significant loss of vital skin tissue signals inflammatory responses and recruitment of PMN and monocytes initially and T-cells and B-cells at a later stage (14). The influx of phagocytic cells is essential for controlling bacterial colonization and preventing the development of invasive wound infections but also serves the important function of clearing cellular debris and sets in motion the wound healing process(13). However, in large burns, especially in a full thickness or a third-degree burn injury where there is a profound loss of keratinocyte progenitors that prevent wound closure through the growth of new skin, wound healing will not occur without successful skin grafting. Partial thickness or second-degree burns, on the other hand, still contain much of the dermis and the keratinocyte progenitors and therefore will heal unless the wound site becomes infected. In the event of an infection, bacterial

and fungal products damage or destroy the underlying tissue due to proteolysis and exotoxins. The consequence of such an infection can be a marked delay in wound closure or a conversion in the depth of injury equivalent to that of a full thickness burn. Therefore robust and continuous innate immune response to the burn wound site is of paramount importance to the wound closure, healing and the clinical outcome of these patients.

Innate Adaptive Immune Response to Burn Injury

The innate immune response to inflammation and sepsis is a rapid response that is not pathogen specific (15). It constitutes the first line of host-defense in humans and is a conserved response in all vertebrates. Leukocytes that mediate innate immunity are primarily PMNS, monocyte/macrophages, natural killer cells (NK cells) and natural killer T- cells (NK-T cells)(9, 16). Although the biology of each type of leukocytes is often discussed individually in the context of any disease process, including severe trauma and burn injury, they seldom act alone. They communicate and interact with each other in the tissue micro-environment through the ligands they produce and respond to the matrix molecules that surround them. It is essential to understand that the concerted action of all the constituents of innate immune cell system is required if the functional integrity of the innate immune response is to be maintained.

Aside from limiting microbial entry and growth in the burn wound and underlying tissues, innate immunity forms the bridge to the longer lasting pathogen specific adaptive immune response. The immune cells that bridge the two arms of immune response are dendritic cells and macrophages, both of which can present pathogen specific antigens to T- and B-cells to initiate cellular and humoral immunity (17, 18). Antigen presentation requires phagocytosis and intracellular killing of the pathogen, digestion of associated proteins and lipids and presentation of the pathogen specific peptides through the MHC class II complex to the T and B cells (19).

In a critical burn injury where inflammation is sustained for a significant period of time after the injury, demands placed on the innate and adaptive immune response are significant. The durability of the immune response under these conditions is dictated by the hormonal response to stress (catecholamines, glucocorticoids etc), the nutritional status, and the age of the patient as well any preexisting co-morbidities. In a burn patient with a significant injury alterations in the tissue microenvironment can further perturb burn induced metabolic demands and physiologic response and further increase the risk of contracting a nosocomial infection. The therapeutic interventions that are required in the care of a burn patient such as multiple surgical procedures, anesthesia, and blood transfusions add further to the risk for an infection (9, 20).

Bacterial infections and sepsis, in particular, pose a significant clinical problem in all ICU patients, including those that are treated in the burn ICU. After the discovery of inflammation-associated cytokines, many immuno-therapies directed at neutralizing these bioactive compounds have been tried. While many of them yielded somewhat promising results in animal models, they have failed to produce meaningful treatment alternatives in large clinical trials (21, 22). A potential reason for the ineffectiveness of many of the sepsis immunotherapies is perhaps due to the fact that they are monotherapies directed against a single component of the inflammatory cascade (23). The immune response to inflammation and infection is a complex cascade of pro- and anti-inflammatory molecules that change with the duration and severity of a critical injury. It is not surprising that an approach such as anti-TNF- α antibody or IL-1 receptor antagonists have not proven to be effective treatment modalities in sepsis as the timing and intensity of the response to be manipulated in a given patient is dynamic and likely needs to be modulated over time.

Microbial Resistance to Antibiotics and Burn Care

One of the difficulties in effectively treating septic patients is the emergence of increasing number of bacterial pathogens with resistance to multiple antibiotics. In recent years, *Staphylococcus aureus*, *Pseudomonas aeruginosa* and *Acinetobacter baumannii* have posed a significant risk to critically injured burn patients because of their drug resistant patterns. In the US alone approximately 90,000 patients die of hospital acquired infections. According to Infectious Society of America (IDSA) 70% of these mortalities are due to multi-drug resistant bacterial strains (24). As the incidence of sepsis is rising, much of the current research in the fields of critical care and sepsis has focused on host-response (25). While this focus has

generated much useful information, unfortunately it has provided only a partial picture of the pathophysiology of sepsis (26). In the last five years through a nation-wide multi-center effort spearheaded through a NIH Inflammation and Host Response to Injury Glue Grant, we are beginning to accumulate extensive genomic and proteomic data from different tissues including blood, skin, muscle and fat from burn patients. While the data collection phase is extensive, it is an essential component in our understanding of the importance of the genomic and proteomic oscillations in the pathophysiology of inflammation associated with burn injury, and sepsis (27-29). To date, no direct correlations have emerged from these studies. If such correlations are established, it will be necessary to test the hypothesis that they are indeed the causative factors and not associative responses to assure us of their utility in the development of either novel diagnostic or therapeutic modalities.

These potential advancements in understanding the human response to burn injury, however, do not diminish the ever-increasing problem of antibiotic resistance strains. One area of research where significant improvements have not been made is in the development of new classes of antibiotics to overcome the threat. The number of newer antibiotics is currently 60% less than existed in the mid-1980s. Since 1960, only two new classes of antibiotics have been introduced for clinical use, linezolid in 2000 and daptomycin in 2003(24). In the light of these facts, how do we find new ways to meet these healthcare challenges?

Pathogen- Host Response

Similar to the responses of the host to the pathogen centered on eradicating the microbial insult, the bacterial pathogen also employs specific mechanisms that allow them to evade immune detection and ensure their survival (30). Through processes such as adherence to host tissue, active evasion of the immune system cells, and direct damage to the host through exotoxin production, bacteria are able to initiate, disseminate and sustain infections (31). In order to combat bacterial infections, especially multi-drug resistant nosocomial infections, and to devise pathogen specific antimicrobial therapy, it is essential to understand the interrelationship between the responses of the host and the bacterial pathogen.

Much our understanding of the host-response to Gram-negative bacterial infections has come from studies with purified lipopolysaccharide (LPS) in cell culture and whole animal studies. Unfortunately in many nosocomial Gram-negative pathogens LPS is a less pathogenic determinant compared to the multitude of exotoxins secreted by these pathogens that aid in their evasion and paralysis of our immunity and cause tissue damage. For example, 86 different exotoxins are secreted by *Pseudomonas aeruginosa*, which range from proteases including elastases, collagenases, peptidases to hemolysins and exotoxins A, T, U and S all of which can cause immune cell inactivation and tissue damage (32). Similarly, another difficult to treat multi-drug resistant pathogen, *Staphylococcus aureus*, secretes multiple exotoxins which are harmful to host tissues and facilitates in the dissemination and survival of the *Staphylococcus*.

In the last decade, it has become apparent that bacteria communicate with each other specifically through “quorum sensing” mechanisms (33). Recent studies have begun to elucidate how bacteria proactively respond to our immune response while attempting establish an infection by turning on specific genes that counteract the killing ability of the phagocytes. For example, *Yersinia pestis*, the causative agent of bubonic plague, specifically up regulates nitroso active stress response genes that neutralize intracellular nitric oxide mediated bacterial killing during the early stages of infections when it is most susceptible to elimination by PMN and macrophages. However, when the *Yersinia pestis* migrates to the local lymph node, the achievement of quorum enables them to turn on Type III exotoxins which are directly injected into immune cells through a needle like mechanism to inactivate the cytoskeleton, thus disabling their phagocytic capacity (34). Interestingly, the *Yersinia pestis* does not turn on *oxyR* or *soxR* genes that combat superoxide and hydrogen peroxide mediated killing as they are less susceptible to these agents (35). *Pseudomonas aeruginosa* on the other hand, up regulates the transactivator OxyR to produce catalases and hydroperoxidases to neutralize hydrogen peroxide and hydroperoxide mediated killing by PMN and macrophages (36). Our own studies with *oxyR* deletion mutant in a *Pseudomonas aeruginosa* burn wound sepsis model, showed that OxyR expression is essential for inhibiting bone marrow progenitor differentiation into

dendritic cells but not monocyte/macrophages although these two cell types are derived from the same myeloid progenitor cell (37).

Therefore the proper study of sepsis cannot just be a study of the host response to infection but must include understanding the inter-relationship between biological systems of the host and the pathogen that are engaged in a biochemical tango of survival. Such studies can be broadly classified as 'Pathogen-Host Response'. One may ask what new information we might gain from this approach? Establishing the specific gene and protein expression patterns of bacteria at different stages of infection and sepsis and correlating them with corresponding host-response genomic and proteomic expression patterns opens the way to early detection of bacterial infections through better and high throughput pathogen specific diagnostics. This is essential knowledge if we are to tailor our antibacterial therapies to individual patient needs rather than on an empiric basis as is currently practiced. The clinical decision making quandary that faces all critical care physicians is knowing when to start and when to stop treating a critically ill patient with antibacterial agents because of the lack of proper tools that will promote the practice of evidence based medicine in this area.

Second, understanding the genomic and proteomic expression changes in bacteria during an infection or sepsis that occur as an adaptive response in an attempt at evading immune detection and elimination will lead to a new class of anti-bacterials that are directed at preventing or impeding a) the changes bacteria invoke to evade detection and b) the toxins they produce to cause tissue destruction. For example, if we could devise compounds that delay or inhibit the establishment of "quorum" by inactivating quorum sensing molecules such as acyl homoserine lactones, we might have an opportunity to prevent the pathogen from becoming virulent by turning off their exotoxins (38, 39). By preventing the adjustments that bacteria make during the process of establishing and disseminating an infection, we may be able to more effectively use currently available less toxic antibiotics perhaps at a lower dose for a shorter time. The most irresistibly logical reason to promote studies of "Pathogen-Host Response" is that it provides the simultaneous opportunity to develop both better diagnostics and better primary or adjunct therapy for multi-drug resistant nosocomial infections that are currently a bane in our ability to care for critically injured burn patients.

Priorities in Sepsis/Inflammation: Break-Out Session Discussions

The major unanswered questions regarding sepsis and inflammation in burns, as listed in Table 1, were used to begin the dialog for the round table discussions. Several specific areas for future research were defined. (Table 2) These areas can be divided into four categories: definitions, early identification, treatment optimization, and mechanistic studies.

Although sepsis, SIRS, and infection have been defined for a variety of populations, the pathophysiology of the burn wound and the host's response to the burn make the application of these definitions problematic. The key question discussed was: Do the current definitions meet the needs of burns? Current definitions are frequently used as proxies for quality or standard of care; thus, the accuracy of these definitions assumes increased importance. The group concluded that a consensus needs to be reached on the definitions of infection, sepsis, and SIRS to provide a framework for research and for objective evaluation of patient outcomes.

Infection increases hospital costs, decreases patient survival, and has long-term effects on patient outcomes. Early detection of infection yields improved survival; therefore, the second priority for inflammation research is to develop methods for early detection of infection. Potential areas of investigation include identifying markers (serum, genomic, physiologic) for early identification of infection/inflammation, development of a system for stratification of inflammation severity, and identifying methods of preventing/containing infection once it occurs.

Although the early identification or avoidance of infection will decrease the incidence of sepsis, the treatment of infection and sepsis continues to be a priority. Currently the treatment of infection in burns centers around the use of antibiotics. Optimal use of antibiotics including antibiotic type, timing of antibiotic administration, and length of antibiotic use need to be defined. The role of antibiotic rotation to avoid the emergence of resistant pathogens in the burn center may decrease the number and severity of nosocomial infections. Finally, the role of gut decontamination needs to be defined in burns. This priority for burn research will involve both

clinical and basic science studies: we need to understand the mechanisms behind the efficacy of antibiotics and the inflammatory process to design appropriate therapeutic choices.

The final priority discussed in the break out session was the determination of the role of inflammation in burns. Although inflammation can often be deleterious after burn injury, it is also necessary for wound healing and patient recovery. One of the key research questions relating to burns is: When does inflammation become deleterious and how do we identify this time point? The answer to this question will need to factor for multiple issues, including burn size, patient age, genomics, and environmental factors. Multiple agents have been utilized to modify the inflammatory response, including glycemic control, beta blockade, and the use of anabolic agents. The timing and use of these agents needs to be defined through further prospective, randomized trials and mechanistic studies.

Conclusions

Inflammation and sepsis represent major challenges to the critically ill burn patient, and studies improving our knowledge of inflammation and sepsis after burn injury are vital to improving patient outcomes. The top research priorities for infection and sepsis involve defining infection and sepsis, identifying patients at risk, optimizing treatment, and modifying the inflammatory response. Accomplishing these goals will require the integration of clinical and basic science techniques and knowledge, as well as support for multidisciplinary projects.

References

1. Schwacha MG. Macrophages and post-burn immune dysfunction. *Burns* 2003;29:1-14.
2. Sparkes BG. Immunological responses to thermal injury. *Burns* 1997;23:106-113.
3. Williams IR, Kupper TS. Immunity at the surface: homeostatic mechanisms of the skin immune system. *Life Sci* 1996;58:1485-1507.
4. DiPietro LA. Wound healing: the role of the macrophage and other immune cells. *Shock* 1995;4:233-240.
5. Martin P, Leibovich SJ. Inflammatory cells during wound repair: the good, the bad and the ugly. *Trends Cell Biol* 2005;15:599-607.
6. Herndon DN, Hart DW, Wolf SE, et al. Reversal of catabolism by beta-blockade after severe burns. *N Engl J Med* 2001;345:1223-1229.
7. Takahashi H, Tsuda Y, Takeuchi D, et al. Influence of systemic inflammatory response syndrome on host resistance against bacterial infections. *Critical care medicine* 2004;32:1879-1885.
8. Nystrom PO. The systemic inflammatory response syndrome: definitions and aetiology. *The Journal of antimicrobial chemotherapy* 1998;41 Suppl A:1-7.
9. Smith JW, Gamelli RL, Jones SB, et al. Immunologic responses to critical injury and sepsis. *J Intensive Care Med* 2006;21:160-172.
10. Bone RC. A personal experience with SIRS and MODS. *Critical care medicine* 1996;24:1417-1418.
11. Bone RC. Sir Isaac Newton, sepsis, SIRS, and CARS. *Critical care medicine* 1996;24:1125-1128.
12. Bone RC. The sepsis syndrome. Definition and general approach to management. *Clinics in chest medicine* 1996;17:175-181.
13. Faist E. The mechanisms of host defense dysfunction following shock and trauma. *Curr Top Microbiol Immunol* 1996;216:259-274.
14. Delves PJ, Roitt IM. The immune system. First of two parts. *N Engl J Med* 2000;343:37-49.
15. Oberholzer A, Oberholzer C, Moldawer LL. Sepsis syndromes: understanding the role of innate and acquired immunity. *Shock* 2001;16:83-96.

16. Goldmann O, Chhatwal GS, Medina E. Contribution of natural killer cells to the pathogenesis of septic shock induced by *Streptococcus pyogenes* in mice. *The Journal of infectious diseases* 2005;191:1280-1286.
17. Fujiwara N, Kobayashi K. Macrophages in inflammation. *Curr Drug Targets Inflamm Allergy* 2005;4:281-286.
18. Steinman RM, Hemmi H. Dendritic cells: translating innate to adaptive immunity. *Curr Top Microbiol Immunol* 2006;311:17-58.
19. Jutras I, Desjardins M. Phagocytosis: at the crossroads of innate and adaptive immunity. *Annu Rev Cell Dev Biol* 2005;21:511-527.
20. Dunne JR, Malone DL, Tracy JK, et al. Allogenic blood transfusion in the first 24 hours after trauma is associated with increased systemic inflammatory response syndrome (SIRS) and death. *Surgical infections* 2004;5:395-404.
21. Abraham E, Anzueto A, Gutierrez G, et al. Double-blind randomised controlled trial of monoclonal antibody to human tumour necrosis factor in treatment of septic shock. NORASEPT II Study Group. *Lancet* 1998;351:929-933.
22. Suntharalingam G, Perry MR, Ward S, et al. Cytokine Storm in a Phase 1 Trial of the Anti-CD28 Monoclonal Antibody TGN1412. *N Engl J Med* 2006;355.
23. Abraham E. Why immunomodulatory therapies have not worked in sepsis. *Intensive Care Med* 1999;25:556-566.
24. von Bubnoff A. Seeking new antibiotics in nature's backyard. *Cell* 2006;127:867-869.
25. Martin GS, Mannino DM, Eaton S, et al. The epidemiology of sepsis in the United States from 1979 through 2000. *N Engl J Med* 2003;348:1546-1554.
26. Hotchkiss RS, Karl IE. The pathophysiology and treatment of sepsis. *N Engl J Med* 2003;348:138-150.
27. Calvano SE, Xiao W, Richards DR, et al. A network-based analysis of systemic inflammation in humans. *Nature* 2005;437:1032-1037.
28. Cobb JP, Mindrinos MN, Miller-Graziano C, et al. Application of genome-wide expression analysis to human health and disease. *Proceedings of the National Academy of Sciences of the United States of America* 2005;102:4801-4806.
29. Chung TP, Laramie JM, Meyer DJ, et al. Molecular diagnostics in sepsis: from bedside to bench. *J Am Coll Surg* 2006;203:585-598.
30. Wilson JW, Schurr MJ, LeBlanc CL, et al. Mechanisms of bacterial pathogenicity. *Postgrad Med J* 2002;78:216-224.
31. Melstrom KA, Jr., Smith JW, Gamelli RL, et al. New perspectives for a new century: implications of pathogen responses for the future of antimicrobial therapy. *J Burn Care Res* 2006;27:251-264.
32. Winsor GL, Lo R, Sui SJ, et al. *Pseudomonas aeruginosa* Genome Database and PseudoCAP: facilitating community-based, continually updated, genome annotation. *Nucleic Acids Res* 2005;33:D338-343.
33. Bassler BL, Losick R. Bacterially speaking. *Cell* 2006;125:237-246.
34. Navarro L, Alto NM, Dixon JE. Functions of the *Yersinia* effector proteins in inhibiting host immune responses. *Curr Opin Microbiol* 2005;8:21-27.
35. Sebbane F, Lemaitre N, Sturdevant DE, et al. Adaptive response of *Yersinia pestis* to extracellular effectors of innate immunity during bubonic plague. *Proceedings of the National Academy of Sciences of the United States of America* 2006;103:11766-11771.
36. Ochsner UA, Vasil ML, Alsabbagh E, et al. Role of the *Pseudomonas aeruginosa* oxyR-recG operon in oxidative stress defense and DNA repair: OxyR-dependent regulation of katB-ankB, ahpB, and ahpC-ahpF. *J Bacteriol* 2000;182:4533-4544.
37. Melstrom KA, Muthu K, He LK, et al. OxyR gene expression of *Pseudomonas aeruginosa* regulates bone marrow dendritic cell differentiation and function after burn sepsis. *J Am Coll Surg* 2006;203:S34.
38. Gonzalez JE, Keshavan ND. Messing with bacterial quorum sensing. *Microbiol Mol Biol Rev* 2006;70:859-875.
39. Smith RS, Iglewski BH. *Pseudomonas aeruginosa* quorum sensing as a potential antimicrobial target. *J Clin Invest* 2003;112:1460-1465.

Table 1

Sepsis-The challenges and the unanswered questions:
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- 1) What are the critical control elements responsible for the transition from the “normal state” to the burn induced inflammatory response?
- 2) How does the dynamic time course of the inflammatory response evolve in a burn patient and impact their recovery and predisposition to infections?
- 3) Could we effectively monitor and modulate innate and adaptive immune responses?
- 4) How does critical injury compromise immunity through imbalances in hormonal and metabolic demands?
- 5) Given that multi-antibiotic resistant bacterial strains are increasing at a rapid rate and that discovery of new classes of antibacterials is lagging, what are the potential options for the treatment of infections in critically injured burn patients?
- 6) Will understanding host-pathogen responses open pathways to new and rapid diagnostics and potential tailored antibacterial therapies based on interruption of metabolic actions of bacteria to host initiated defense mechanisms?

Table 2

Research Priorities for Sepsis

1. Define infection, sepsis, and SIRS in the burn patient.
2. Develop methodology for early identification of infection.
3. Optimize the treatment of infection in burns, including the use of antibiotics, gut decontamination, and length of treatment.
4. Determine the role of inflammation in burns and how we can modify the inflammatory response to improve outcomes.

NUTRITION AND METABOLISM IN BURNS: STATE OF THE SCIENCE 2007

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ABSTRACT

INTRODUCTION

Nutrition and its delivery to the severely burned in the modern burn centre almost seems second nature; its delivery is assumed by all, with a specialist (Burn ICU dietician) overseeing the process in most places. The medical staff participates actively by ordering the diet, which is usually standardised for the centre, and considering whether it is given every day while on rounds. Some even look at the calories delivered and make adjustments to the regimen. Almost all suppose that nutritional delivery is clearly necessary and cannot possibly be ignored. Numbers and formulae for the type and amount of diet are used with great certainty for the particular centre, and can be recited by heart by all but the new intern. However, what is the underpinning of these treatments? What do we really know with certainty about the diet in burned patients, and how it should be given? The general notion persists that starvation or severe underfeeding of the burned patient is associated with muscle wasting, delays in wound healing, and greater susceptibility to infection. Common sense dictates these to be true; therefore, the question of whether to starve or feed can be assumed to be answered in favor of feeding, but even this has not been shown with good scientific evidence. Furthermore, the real questions that remain to be answered are: how do we improve the nutritional prescription for the burned patient and are we delivering the best nutritional regimen to our patients? Nutritional regimens vary widely between individual centers, which suggests that we still do not know how to best feed our patients. How much should be fed? When? What? More importantly, is some of what we do with the provision of the diet actually hurting patients?

The Burn State of the Science Research conference, held in October 2006, brought leaders in the field of burns from around the world to discuss the most significant questions in burns and burn care. One of the sessions targeted Nutrition and Metabolism in burns. Through a moderator, a brief presentation of the known general and landmark data in this field was carried out, followed by a discussion among four separate groups to define the questions that should be addressed in the near future to improve the lot of the burned patient. This manuscript will briefly review what is known and generally accepted by all practitioners regarding nutrition in the burned patient, then define the questions from the group that should be answered and to which funding should be directed.

NUTRITION AND METABOLISM OF INJURY

The provision of nutrition to anyone serves two basic functions: to provide substrate for energy production through intermediary metabolism, and to provide necessary nutrients that cannot be synthesised from routine substrate that serve as co-factors, signalers, electrolytes, etc. Both of these are absolutely necessary for the biochemical processes of life. Generally, stores of substrate and nutrients are sufficient for some period of time such that continuous intake is not required; however, those stores can be depleted in multiple conditions (such as burn injury), to the detriment of the patient. One example of this is muscle wasting during starvation. Severe burn injury also represents a dramatic deviation from the normal condition in that available substrate and nutrients are maximally mobilised through a variety of mechanisms resulting in deficits in strength and muscle mass. Thus, the purpose of nutrition in the severely burned is to provide substrate and nutrients to restore deficits left by the response to the burn. Severe burn injury is not a nutritional disease, however. Nutrition is used to prevent complications associated with substrate and nutrient deficits, enable wound healing, and re-establish homeostasis.

The metabolic response to severe burn typically displays the classic “ebb and flow” physiology initially described by Moore(1). Adequate resuscitation and nutrition is necessary for the clinical signs of hypermetabolism to manifest(2). Hyperdynamic circulation with elevated cardiac output occurs with initiation of resuscitation and by six to twelve hours will already begin to exceed pre-burn levels(3). The increased energy expenditure to cope with this insult necessitates mobilization of large amounts of substrate from fat stores and active muscle for repair and fuel, leading to catabolism. Hyperpyrexia associated with this response adds to the cost. Up-regulation of acute phase proteins and a decrease in constitutive proteins leads to the

potential detriment of structure and function of essential organs(4). Another clinical manifestation is hyperglycemia. Feeding is used to abrogate some of these responses and “feed the fire” so to speak, but feeding alone is not sufficient(5). Therefore, a major problem is the hypermetabolism associated with injury, for which the mechanism and means of slowing-down has not been established.

In the 1960’s, investigators began to have interest in the delivery of nutrition to the severely injured as data became available as to its importance, with seminal early work done by Jonathon Rhoads and his group at the University of Pennsylvania. During this time, the importance of nutrition to wound healing, immunity, and wasting was noted. In the 1970’s, total parenteral nutrition became available and was used extensively in many populations, including burns. Around this time, formulas were developed for the provision of feeding of the severely burned, much of it based on little data(6). In the 1980’s, enteral tube technology and feeding were developed. It seems that the same strategies developed for parenteral nutrition in terms of delivery time and rate were interposed here without regard to normal physiology.

Studies during these time periods were characterised by high amounts of feeding with no real changes in substrate or nutrient strategies found to be clearly superior to previously established regimens. In the 1990’s more attention was paid to overfeeding with some diminution in feeding. The compilation of strategies developed during these times resulted in the current standard of care for nutrition and metabolism which is described briefly below.

CURRENT NUTRITION PRACTICES IN BURNS

In most burn centres around the world, burned patients are fed sometime during or immediately after resuscitation (first 24-72 hours) as the standard. Feeding can be either enteral or parenteral or some combination of both, and is generally continuous. It is increased from initial rates based on tolerance to reach a level which is felt to be adequate based on local standards. Significant variability exists in the type of enteral feedings in terms of substrate percentages and volumes used between units with economic and personal preference reasons. Nutrients such as vitamins and minerals are given at levels well above the Federal Drug Administration Guidelines. Some supplement iron, zinc, vitamins C and E and others at pharmacologic levels with little agreement between centres. The total volume of feeding is generally proportional to the burn size, and is again variable between centres. These feedings are continued until normal feeding by mouth can be assured with the understanding that more calorie intake than normal will be required. Exactly how much is given is variable. Once normal feeding has resumed, counseling on proper intake is generally done by the dietary personnel without direct measurement in the later phases of the hospitalisation and in convalescence. Furthermore, little consideration is taken to measuring response to the treatment and making modifications except perhaps by weight maintenance. It is probable that variability in the response will be present in the population we treat to say nothing of whether different feeding strategies are required in particular populations such as the obese and elderly.

More and more nutritional adjuncts are now available to improve nutritional parameters, including nutritional additives such as glutamine and fiber and metabolic manipulators such as propranolol and oxandrolone. To date, no general agreement exists between centres on the utilisation of these adjuncts, although data for the nutritional treatment of the severely burned exists in this realm(7-9).

BREAKOUT SESSION DISCUSSION

At the State of the Science Conference, discussion was broken into three categories from which questions could be framed. The first is central to any argument for treatment, namely, How to measure the response to treatment? What endpoints should be used? The second class of question was in regards to the method and substance of delivery. What should be fed? When? How? The third revolved around the question of nutritional adjuncts assuming that standard nutrition had been maximised. The following paragraphs provide very brief background for each of these categories followed by the questions discussed by the groups.

ENDPOINTS

It is difficult to answer the question of how well a dietary prescription is faring in helping the burned patient to recover because the real endpoint of treatment is global and therefore a compilation of many variables. What is desired in the end is to restore normal body

composition, metabolic homeostasis and thus normal function. Strategies commonly used to determine the adequacy of dietary provision in that light include total body weight(10), nitrogen balance(11), measurement of lean body mass with dual-image x-ray absorptiometry(12), and measurement of serum proteins among others. Recently, some have used functional measures like exercise tolerance to measure adequacy(13). Some also use indirect calorimetry as a means of measuring metabolic rate and thus metabolic needs. All the studies using these as primary outcome variables suffer from lack of power, with number of subjects between 10 and 40; this may not be enough to insure adequate reproducibility and thus widespread applicability. In addition, problems exist with each measure when considered individually. For weight, it was shown in severely burned children that increasing caloric intake to maintain weight resulted in fat mass gain instead of lean body mass(14) and thus did not restore normal body composition. Accurate measurement of nitrogen balance is fraught with error because of unaccounted nitrogen losses into wounds, especially with the use of vacuum assisted dressings. This difficulty diminishes when the wound is closed. Lean body mass measures with x-ray or more complicated isotope techniques suffer from errors associated with edema in the acute hospitalisation and early convalescence. Changes in serum proteins associated with nutritional adequacy are significantly affected more by inflammation associated with the burns than nutrient stores(4), and thus cannot be reliably used alone for measurement or effects. The use of exercise measurements requires the ability to perform the tasks reliably, which may be difficult during acute hospitalisation and during early convalescence.

From these, it seems that the analysis of body composition and metabolism does not have a single reliable measurement to even determine the effects of nutrition; however, it is likely that one could be devised given a determined effort from multiple centres perhaps as a joint effort to improve applicability. The adequacy of wound healing and immunity should also be included in the analysis. The optimal measure will likely be different for differing time periods, such as acute hospitalisation, early outpatient convalescence from hospital discharge to about 6 months after injury during which time most will be working towards resuming relatively normal tasks and home-life, and late convalescence marked by anabolism and gaining mass and activity. For instance, including exercise measurements would be inappropriate during acute hospitalisation, but might be appropriate during late convalescence. Furthermore, measuring wound healing is inappropriate during late convalescence, but is critical during acute hospitalisation. Standardisation of a measure that could be used by all researchers in the field would significantly improve the conclusions drawn by future studies.

METHOD AND SUBSTANCE OF DELIVERY

As stated above, the provision of nutrition to the burned patient is not in question, but the best method and exactly what to feed has not been established. Relevant questions that have not been answered include what, when, and how much feeding should be given. In addition, very little attention has been paid to determination of beneficial dietary provision during outpatient convalescence.

Two methods exist for administering nutrition: parenteral and enteral. It has been established that enteral feedings should make up the bulk of nutrition given to the severely burned(15), but the evidence is only level II at best. Supplementing enteral feeding with parenteral has been tested, again with level II evidence, and was not shown to be of benefit and was actually harmful(16). What has not been answered is whether some component of the diet, such as protein through amino acids alone might be beneficial if given parenterally and added to enteral feedings.

Available substrate in feedings include carbohydrate, fat, and protein. Commercially available formulae include varying percentages of each. What has not been established clearly is which substrate is most appropriate for the severely injured? Data exists to support that carbohydrate is the preferred fuel(17), and fat utilisation is actually relatively inhibited in critical illness suggesting that feeding regimens should be carbohydrate based. This must be weighed against potential detrimental effects of high carbon dioxide production with carbohydrate based feeding.

Recent efforts focused on early feeding of burned patients in an attempt to lessen catabolism based on the notion that early feeding would prevent depletion of substrate stores,

however, this notion has not been borne out in recent studies(18). It still remains to be established exactly when feeding of the severely burned should be started after injury. Furthermore, it has not been determined when aggressive feeding is no longer necessary or beneficial as the patient approaches discharge.

As alluded to earlier, when parenteral nutrition was developed, the feeding rate was generally continuous for logistic reasons, and I conjecture that this carried onto enteral feeding regimens. This is in contradistinction to normal physiology which is intermittent feeding usually during the day. The notion of the superiority of intermittent feeding should be tested.

Significant variability exists between burn centres on the volume of substrate (calories) given to burned patients. Recent attention has been paid to the dangers of overfeeding which has never been systematically defined in the burn population. Initial feeding prescriptions in common use were based on very few patients(6, 10). Some also use indirect calorimetry as a measure of metabolic rate and thus as an individual benchmark of metabolic and nutritional needs. It appears that total energy expenditure is clearly related to resting energy expenditure measured with indirect calorimetry(19), but, it has been shown that energy expenditure and calories given are directly related and thus mathematically coupled. In other words, giving more calories increases energy expenditure and vice versa(2). Using this measure then as a measurement of need may be in error. Curiously, very little data are currently available about how much substrate and nutrients should be given to the severely burned. Perhaps this is because the actual goal of feeding the severely burned has not been firmly established as mentioned earlier in this manuscript.

NUTRITIONAL ADJUNCTS

Significant work has been done with the use of nutritional adjuncts to bolster normal nutrition in an effort to benefit the severely burned. These adjuncts can be roughly broken into two classes, nutritional additives and pharmacologic manipulators.

Nutritional additives are additional agents that are already present in the diet, such as the amino acids glutamine(8) and arginine, or other substrates such as RNA(20). Studies have shown some benefit to these, particularly glutamine, while the data on others has been less satisfying. Further questions in this arena should be focused on the effects and mechanisms of compounds as they become known.

Pharmacologic manipulators of the hypermetabolic response to injury have been studied in depth for some time. These manipulators include propranolol which blocks one of the mediators of the response(9), namely the catecholamines, and stimulants of metabolic processes such as insulin(21) and oxandrolone(7) that increase net protein synthesis in muscle. Many of these drugs are now in common use in burn centres. Further questions should probably focus on other effects, such as on the immune system or wound healing to demonstrate further (or not) their beneficial effects.

QUESTIONS AND PRIORITIES

From the discussion above and with input from all discussants at the State of the Science Meeting in 2006, the following questions are proposed in relation to nutrition and metabolism that should receive attention from researchers in the coming years. Those that are in italics received the most discussion.

1. What is the proper endpoint for measuring the effect of nutritional treatment?
 - a. *During acute hospitalisation?*
 - b. During early convalescence (hospital discharge to 6 months after injury)?
 - c. During late convalescence (6 months after injury to 18 months after injury)?
2. What is the best method of feeding for the burned patient?
 - a. *Additional amino acids to a standard enteral diet given either parenterally or enterally, maybe the essential amino acids(22)?*
 - b. What is the proper substrate?
 - i. Carbohydrate versus fat?
 - c. When should the diet be given or artificial methods of feeding (intravenous or by tube) stopped?
 - i. During resuscitation?
 - ii. Late hospitalisation?

- iii. Intermittent feedings?
 - d. How many calories should be given?
 - i. *During acute hospitalisation?*
 - ii. During early convalescence?
 - iii. During late convalescence?
 - e. Should feeding regimens be different for different populations?
 - i. Children?
 - ii. Elderly?
 - iii. Obese?
- 3. When and what nutritional adjuncts should be given to the severely burned?
 - a. Which nutritional additives should be given?
 - i. When?
 - ii. How much?
 - b. Which pharmacologic manipulators should be given?
 - i. When?
 - ii. How much?
 - c. What are the mechanisms of action for these agents?
 - i. Do they have other beneficial effects such as on the immune system and wound healing? If so, how?

Based on these discussions, the priorities for research in burn nutrition and metabolism were developed and are listed in Table 1.

Conclusion

Although much progress has been made in the establishment of nutrition and its importance in burn patient outcomes, the optimal feeding regimen remains elusive. Prior to establishing what nutritional regimen should be employed after burn injury, accurate endpoints and goals for burn nutrition need to be developed and validated. Randomized prospective clinical trials will need to be linked to mechanistic basic science analysis of the metabolic changes after burn injury to elucidate the optimal nutritional support for the burn patient.

REFERENCES

1. Moore FD. Bodily changes during surgical convalescence. *Annals of Surgery* 1953;137:289-295.
2. Hart DW, Wolf SE, Chinkes DL, Beauford RB, Mlcak RP, Heggers JP, et al. Effects of early excision and aggressive enteral feeding on hypermetabolism, catabolism, and sepsis after severe burn. *Journal of Trauma* 2003;54:755-6.
3. Crum RL, Dominic W, Hansbrough JF, Shackford SR, Brown MR. Cardiovascular and neurohumoral responses following burn injury. *Archives of Surgery* 1990;125(8):1065.
4. Thomas S, Wolf SE, Murphy KD, Chinkes DL, Herndon DN. The long-term effect of oxandrolone on hepatic acute phase proteins in severely burned children. *Journal of Trauma* 2004;56:37-44.
5. Shaw JH, Wolfe RR. An integrated analysis of glucose, fat, and protein metabolism in severely traumatized patients. Studies in the basal state and the response to total parenteral nutrition. *Annals of Surgery* 1989;209:63-72.
6. Curreri PW, Richmond D, Marvin J, Baxter CR. Dietary requirements of patients with major burns. *Journal of the American Dietetic Association* 1974;65(4):415.
7. Wolf SE, Edelman LS, Kemalyan N, Donison L, Cross J, Underwood M, et al. Effects of oxandrolone on outcome measures in the severely burned: a multicenter prospective randomized double-blind trial. *J Burn Care Res* 2006;27(2):131.
8. Garrel D, J. P, Nedelec B, Samson L, Dorais J, Champoux J, et al. Decreased mortality and infectious morbidity in adult burn patients given enteral glutamine supplements: a prospective, controlled, randomized clinical trial. *Critical Care Medicine* 2003;31(10):2444.
9. Herndon DN, Hart DW, Wolf SE, Chinkes DL, Wolfe RR. Reversal of catabolism by beta-blockade after severe burns. *New England Journal of Medicine* 2001;345(17):1223.
10. Hildreth MA, Carvehal HF. Caloric requirements in burned children: a simple formula to estimate daily caloric requirements. *Journal of Burn Care & Rehabilitation* 1982;3:78-80.
11. Larsson J, Lennmarken C, Martensson J, Sandstedt S, Vinnars E. Nitrogen requirements in severely injured patients. *Br J Surg* 1990, 77: 413-416. *British Journal of Surgery* 1990;77:413-416.
12. Wolf SE, Thomas SJ, Dasu MRK, Ferrando AA, Chinkes DL, Wolfe RR, et al. Improved net protein balance, lean mass, and gene expression changes with oxandrolone treatment in the severely burned. *Annals of Surgery* 2003;237:801-811.
13. Suman OE, Spies RJ, Celis MM, Mlcak RP, Herndon DN. Effects of a 12-wk resistance exercise program on skeletal muscle strength in children with burn injuries. *Journal of Applied Physiology* 2001;91(3):1168-1175.
14. Hart DW, Wolf SE, Herndon DN, Chinkes DL, Lal SO, Obeng MK, et al. Energy expenditure and caloric balance after burn: increased feeding leads to fat rather than lean mass accretion. 2002;235(152-161).
15. McDonald WS, Sharp CWJ, Deitch EA. Immediate enteral feeding in burn patients is safe and effective. *Annals of Surgery* 1991;213(2):177.
16. Herndon DN, Barrow RE, Stein M, Linares H, Rutan TC, Rutan RL, et al. Increased mortality with intravenous supplemental feeding in severely burned patients. *Journal of Burn Care & Rehabilitation* 1989;10(4):309.
17. Hart DW, Wolf SE, Xhang X-J, Chinkes DL, Buffalo MC, Matin SI, et al. Efficacy of a high-carbohydrate diet in catabolic illness. 2001;29:1318-1324.
18. Peck MD, Kessler M, Cairns BA, Chang YH, Ivanova A, Schooler W. Early enteral nutrition does not decrease hypermetabolism associated with burn injury. *Journal of Trauma* 2004;57(6):1143.
19. Goran MI, Peters EJ, Herndon DN, Wolfe RR. Total energy expenditure in burned children using the doubly labelled water technique. *American Journal of Physiology* 1990;259(4 Part 1):E579-E585.

20. Saffle JR, Weibke G, Jennings K, Morris SE, Barton RG. Randomised trial of immune-enhancing enteral nutrition in burn patients. *Journal of Trauma* 1997;42:793-802.
21. Thomas SJ, Morimoto K, Herndon DN, Ferrando AA, Wolfe RR, Klein GL, et al. The effect of prolonged euglycemic hyperinsulinemia on lean body mass after severe burn. *Surgery* 2002;132(2):341-347.
22. Paddon-Jones D, Sheffield-Moore M, Urban RJ, Aarsland A, Wolfe RR, Ferrando AA. Exogenous amino acids stimulate human muscle protein anabolism without interfering with the response to mixed meal ingestion. *American Journal of Physiology* 2005;288(4):E761-E767.

Table 1. Top Priorities in Burn Nutrition and Metabolism

1. Determine the endpoints for nutrition management.
2. Optimize feeding regimens, including substrate, method, duration, and time after injury.
3. Determine the optimal nutrition strategy for different populations (elderly, children, obese, diabetes, etc).
4. Define the role of nutritional adjuncts.

Cutaneous Wound Healing

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Introduction

Overall, burns are smaller than 20 years ago, but even small burns can leave patients with debilitating scars. Management of the burn wound and resultant scarring requires integration of multiple disciplines. Despite our best efforts, the evaluation and treatment of burn wounds and burn scars has not been completely elucidated. The purpose of this paper is to describe the state of knowledge regarding wound healing, both what is known and what is not known, and to recap the priorities set by the breakout sessions of the Burn State of the Science: Research meeting. Wound challenges in 2007 include wound coverage for patients with extensive full-thickness burns, management of donor sites and partial thickness burns, and reduction of long-term morbidity from burn scars.

Background

Early excision and grafting of the burn wound has indisputably impacted burn survival more than any other intervention over the past 30 years¹. Removing the burn wound has been reported to decrease infection, shorten hospital length of stay, reduce the need for reconstructive surgery, and return patients to their pre-morbid level of function sooner². These clinical advances have created a standard of care that emphasizes use of sheet skin grafts whenever possible with meshed grafts recommended for coverage of burns in patients with larger full-thickness wounds^{3,4}. Larger wounds may benefit from coverage with skin substitutes. Existing skin substitutes include both dermal replacement templates and epidermal cultures⁵. Dermal substitutes, such as Integra[®], replace the cutaneous connective tissue and provide a template for ingrowth of indigenous cells from the wound bed^{6,7}. Dermal substitutes have been reported to reduce scar formation and improve wound pliability. Keratinocyte grafts restore the epidermal layer and restore the cutaneous barrier to infection and fluid loss. Cultured epidermal allografts, which have gained popularity for treatment of non-healing chronic wounds, have limited applicability in definitive burn treatment because of rejection. Reports of successful treatment of large burns with cultured dermal-epidermal autografts⁸⁻¹² have not yet progressed to multi-center trials due to the high expense and complexity of fabrication¹³. Whereas development of these products has advanced the field, time of preparation and expense limit their availability for treatment of patients with extensive burn injuries.

Split-thickness skin grafting unavoidably creates donor sites, which share many problems of wound healing with partial thickness burns, both of which heal spontaneously. The deeper the wound the longer it takes to heal--increasing the risk of pain, infection, and, ultimately, scar formation. Wound care has progressed significantly since fine mesh gauze was a standard donor site dressing. Now, there are many alternatives for anti-microbial impregnated dressings ranging from silver to beta-glucan. Nevertheless, our ability to modulate healing with topical growth factors or mediators has been limited despite of years of animal research in the field. Few dressings provide excellent antimicrobial coverage, pain relief, and rapid healing. This is due in part to the cytotoxicity of antimicrobial agents, which reduce wound contamination but may also delay cell migration and proliferation.

Deep partial thickness wounds often lead to hypertrophic scar formation. Despite years of research and a moderate ability to predict which wounds are at risk for scar formation, our understanding of the pathophysiology of scar has not advanced. The same treatment alternatives of pressure garments, topical silicone, and steroid injection are used today as 30 years ago. With scar formation comes the other late sequelae of hyperesthesia and itching. Our ability to treat these complications is limited to a few anti-histamine agents and anecdotal experience with drugs such as topical doxepin hydrochloride (Prudoxin[®]).

Many unanswered questions in burn wound healing center on development of improved skin substitutes. Better understanding of innate immune responses in the skin would facilitate development of cellular skin substitutes that are immunologically unreactive. Given the length of time for engraftment of currently available constructs, methods to increase vascular ingrowth will potentially improve their usefulness by increasing rates of engraftment, decreasing time to healing, and thereby shortening hospital length of stay and potentially cost. Likewise, improved microbial resistance would increase skin substitute efficacy.

Reduction of shearing of epidermal grafts may be best managed by ex vivo culture of dermal epidermal constructs as described by Boyce and colleagues^{11,12,14}. Better understanding of keratinocyte adhesion, epithelial-mesenchymal interactions, and basement membrane biology will continue to contribute to more rapid and stable wound closure with engineered skin grafts.

Absence of important epidermal appendages including hair follicles and sweat glands in split thickness skin grafts and some healed burn wounds results in potentially embarrassing areas of alopecia and inability to sweat. The role of somatic stem cells in wound healing, and the ability to promote mobilization from the bone marrow represents one area of research that may promote regeneration of more complete cutaneous anatomy and physiology.

Donor sites, regardless of size, are consistently recognized as a potential source of concern even in patients with small burns. Cost-effective interventions with novel agents that accelerate healing, decrease pain, minimize infection, and reduce scar formation would improve post-operative management of donor sites. Despite the common use of topical antimicrobials, burn wounds are often contaminated and are at risk for burn wound infection or sepsis. Recent insights into the natural behavior of bacteria raise the possibility that current topical and systemic antimicrobial agents inadequately disrupt biofilms, the protective extracellular environments created by bacteria. Currently, elimination of these networks requires excision of the non-healing wound. Pharmacologic or enzymatic destruction of biofilms may provide an important advance in treatment of burn and donor site infections by increasing the availability of topical or systemic agents, which can be used concurrently.

Pain associated with healing wounds can be directly related to the dressing itself or may be limited to dressing changes. In either case, minimizing wound pain by developing pain-free topical agents or long-acting dressings that allow regular examination of the wound would improve patient comfort when non-operative wound care is appropriate.

Altered or deficient wound innervation is a major concern to burn patients. Pruritis and hyperesthesia can be intolerable for many patients with hypertrophic scars. Conversely, even successful skin grafts are relatively numb, limiting tactile sensation and potentially manual labor. Ability to modulate reinnervation of healing wounds could significantly affect quality of life and return to function.

Conclusions from the Breakout Session

In discussion, several areas for future research were identified. (Table 1) First, development of standardized tools to assess wound healing need to be developed so that wound healing research, both clinical and basic science, will have common endpoints. Questions such as: When is a wound healed? have implications for the determination of treatment efficacy and the diagnosis of late complications of wound healing. The development of these tools is an essential first priority in the evaluation of wound healing.

The second priority for wound healing research centers on later sequelae of burn injury. Hypertrophic scars and intractable itching are the most significant long-term problems for burn survivors. These late outcomes transcend all areas of cutaneous wound healing research because scars and pruritis develop in healed partial thickness burns, donor sites and in the interstices of meshed grafts. A unified definition and grading system for pruritis and hypertrophic scars will enable researchers to have a common frame of reference when conducting clinical studies. Understanding the pathophysiology behind these processes will enable us to develop new treatment regimens.

The third priority for cutaneous wound healing research continues to be the development of innovative treatment modalities for wound and scar management. The continued need for an immunologically-neutral engineered skin substitute for major wounds that may eventually be applicable to burns smaller than 5% total body surface area would be a major advancement in burn care. This would greatly decrease donor site complications, which can actually cause more morbidity than the initial burn injury.

The final priority in wound healing and repair is the optimization of wound healing. Methods to augment keratinocyte migration and proliferation to accelerate healing of partial-thickness burns

and donor sites and development of novel delivery systems for growth factors, antimicrobial agents, and / or morphogens would improve patient outcomes. To achieve these goals, as mentioned above, standardized tools to quantify healing and scar formation need to be developed and validated. Ideally, advances in wound healing will benefit from multi-center trials that are either investigator or industry initiated.

The primary obstacle to achieving these research goals will be establishing sources of funding. Clearly, industry has the necessary research and development resources (both money & management) to bring novel wound healing modalities to market. However, the limited magnitude of the burn market has discouraged development of several promising therapies. Nonetheless, collaboration between burn research teams and researchers in the health-care industry will be essential for advances in this field. Early consultation by industry with burn experts will maximize likely successes of industry-sponsored clinical trials by outlining clinically relevant sources of morbidity and mortality.

A larger challenge will be identification of funding for an infrastructure that facilitates clinician-initiated clinical trials. The National Institutes of Health (NIH) has recognized this need and addressed it in the NIH Roadmap with establishment institutional awards for clinical and translational research (<http://grants.nih.gov/grants/guide/rfa-files/RFA-RM-06-002.html>). These mechanisms of funding are crucial to the continued reduction of morbidity and mortality in patient populations at high risk. Coordination of activities among burn researchers, NIH and industry holds the greatest potential to study and intervene in the biologic and medical mechanisms that contribute to morbidity and mortality in victims of burn injuries.

Conclusions

Research in cutaneous wound healing after burn injury has resulted in the adoption of several clinical practices, such as early excision and grafting, which have impacted patient outcomes. However, the future progress of cutaneous wound healing research will rely on the development of consistent definitions of wound healing and pruritis as well as the development of an understanding of the pathophysiology underlying these processes. Development of cutting edge wound healing technologies, such as skin substitutes, and methodologies for accelerating wound healing form the framework for future studies. Interdisciplinary translational research has the potential to further advances in this area, but funding mechanisms need to be developed to support these types of research and improve patient outcomes.

References

1. Burke JF, Quinby WC, Bondoc CC. Early excision and prompt wound closure supplemented with immunosuppression. *Surg Clin North Am* 1978; 58:1141-1150.
2. Burke JF, Bondoc CC, Quinby WC. Primary burn excision and immediate grafting: a method shortening illness. *J Trauma* 1974; 14:389-395.
3. Housinger TA, Warden GD, Lang D et al. The use of sheet skin grafts in pediatric burn patients. *Proc Amer Burn Assn* 1991; 23:32.
4. Warden GD, Saffle JR, Kravitz M. A two-stage technique for excision and grafting of burn wounds. *J Trauma* 1982; 22:98-103.
5. Boyce ST, Supp DM. Skin Substitutes: Theoretical and Developmental Considerations. In: McCauley RL ed. *Functional and Aesthetic Reconstruction of Burn Patients*. New York: Marcel Dekker; 2005:113-128.
6. Yannas IV, Burke JF. Design of an artificial skin. I Basic design principles. *J Biomed Mater Res* 1980; 14:65-81.
7. Boyce ST, Warden GD. Principles and practices for treatment of cutaneous wounds with cultured skin substitutes. *Am J Surg* 2002; 183:445-456.
8. Hansbrough JF, Boyce ST, Cooper ML et al. Burn wound closure with cultured autologous keratinocytes and fibroblasts attached to a collagen-glycosaminoglycan substrate. *JAMA* 1989; 262:2125-2130.
9. Boyce ST, Goretsky MJ, Greenhalgh DG et al. Comparative assessment of cultured skin substitutes and native skin autograft for treatment of full-thickness burns. *Ann Surg* 1995; 222(6):743-752.
10. Boyce ST, Kagan RJ, Meyer NA et al. The 1999 Clinical Research Award. Cultured skin substitutes combined with Integra to replace native skin autograft and allograft for closure of full-thickness burns. *J Burn Care Rehabil* 1999; 20:453-461.
11. Boyce ST, Kagan RJ, Yakuboff KP et al. Cultured skin substitutes reduce donor skin harvesting for closure of excised, full-thickness burns. *Ann Surg* 2002; 235:269-279.
12. Boyce ST, Kagan RJ, Greenhalgh DG et al. Cultured skin substitutes reduce requirements for harvesting of skin autograft for closure of excised, full-thickness burns. *J Trauma* 2006; 60:821-829.
13. Boyce ST. Fabrication, quality assurance, and assessment of cultured skin substitutes for treatment of skin wounds. *Biomed Eng J* 2004; 20:107-112.
14. Boyce ST, Supp AP, Swope VB et al. Vitamin C regulates keratinocyte viability, epidermal barrier, and basement membrane in vitro, and reduces wound contraction after grafting of cultured skin substitutes. *J Invest Dermatol* 2002; 118:565-572.

Table 1. Priorities in Wound Healing Research

1. Development and validation of standardized tools to assess wound healing.
2. Defining, grading, and understanding the pathophysiology of hypertrophic scarring and pruritis.
3. Development of innovative treatment modalities for wound healing and scarring.
4. Optimization of wound healing.

Burns at the Extremes of Age

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Introduction

Tremendous progress has been made in the last 50 years in the overall survival after burn injury. However, improvement in outcomes for the very young and the very old, both of whom have a higher incidence of burn injury, has lagged behind. Young children and the elderly continue to have increased mortality and morbidity when compared to older children and young adults with injuries of similar severity. Despite this, little research examines how the unique physiology and psychosocial needs of the seriously injured at the extremes of age impacts outcomes. Hence, one of the categories for research discussed at the Burn State of the Science research conference was management of burns in young children and the elderly. The purpose of this manuscript is to first delineate the unique aspects of care for young children and the elderly that impact the treatment of burn injury followed by a discussion of the research priorities for young children and the elderly generated from the breakout discussion sessions.

Airway Considerations

Children

Children have anatomic and physiologic differences which impact airway management. The child's trachea is shorter and glottis more anterior than the adult's, making airway access more difficult to obtain, secure, and maintain in children. (1) Children, due to their smaller airway diameter, will develop significant airway obstruction more readily than an adult. Timely and appropriate intubation after burn or inhalation injury in a child is paramount. Yet the optimal timing and method for airway access in children continues to be debated. Uncuffed endotracheal tubes have been traditionally used in young children, but can be associated with problematic air leaks when children develop respiratory failure. Low-pressure cuffed tubes are now available in virtually all sizes and should be used if children are at risk of developing respiratory failure, particularly if they have facial and upper airway edema, which makes endotracheal tube exchange more hazardous (2). In addition, the indications and timing of tracheostomy in burned young children remains to be defined, with data supporting both early tracheostomy and endotracheal intubation. (3-5)

Maintaining airway access in children continues to be problematic. Unplanned extubation carries substantial morbidity and mortality, especially in the markedly edematous burned child. (6) Although not possible to eliminate completely, it can be minimized with adequate sedation, regular assessment of endotracheal tube security, and adequate staffing. (7)

Children have a tendency to bronchospasm, particularly after inhalation injury. (8) Young children tolerate fluid overload poorly, so accurate repletion is important. Narrow pediatric airways are easily occluded with endobronchial debris and secretions. Therapies to decrease cast formation and improve bronchospasm have been investigated in animal models and to a limited extent in humans. (9, 10) Virtually all practitioners attempt to limit overdistention and inflating pressures. (11) In extraordinary cases, nitric oxide, albuterol, high-frequency ventilation, or extracorporeal membrane oxygenation have been used. (12-14)

Older Adults

Even in lungs not injured by smoking or occupational exposures, reduced pulmonary function is a routine part of aging. (15) In many older adults, further reductions in pulmonary function, including chronic obstructive lung disease or chronic bronchitis, have developed secondary to cigarette smoke or occupational exposures. Therefore, elderly patients often have little pulmonary reserve resulting in limited gas exchange and susceptibility to air trapping. Elders who suffer burn injury, especially if complicated by respiratory failure, often have a protracted need for positive pressure support. This is likely due to the combination of underlying lung disease, the hypermetabolism associated with burn injury, and baseline muscle weakness. Such patients are often best managed with early tracheostomy. (16) The elderly may have pulmonary complications after even a small burn due to limitations from donor site pain, immobility, and underlying co-morbidities. Data regarding the appropriate acute airway management, timing and indications for long-term airway access, and the long-term implications of tracheostomy in the elderly have yet to be defined.

Cardiovascular/Resuscitation Considerations

Children

Children usually have robust cardiac function. However, children can have markedly impaired cardiac function after burn injury. Children at risk for cardiac dysfunction include those less than one year of age, low birth weight or premature infants, children with congenital cardiac anomalies, and children with concomitant inhalation injury (17). Children should be resuscitated to age-specific endpoints; however, randomized prospective trials delineating the ideal resuscitation regimen for children are lacking. (18) Very young children and infants have immature renal concentrating ability and may need to receive fluid infusions adequate to allow for 1 cc/kg/hour of urine output.

Older Adults

Survival in the elderly after burn injury is influenced by a variety of factors. Elders often have overt or occult coronary artery or valvular disease, which can manifest as myocardial dysfunction or infarction during the stress of injury. (19) The use of invasive monitoring, such as the pulmonary artery catheter, to optimize fluid management in the elderly has not been validated in multicenter clinical trials. In addition, occult arterial occlusive disease may be present, which can compromise renal or gut function during periods of injury-related stress. (20) Diffuse coronary artery disease can result in difficulties in vascular access and wound healing due to insufficient nutrient delivery. The use of beta blockers has been proposed as a method for improving outcomes in the elderly. (21)

The decision to proceed with resuscitation in the elderly with a major burn injury is challenging. Multiple mortality models have been published; however, these are primarily limited to single center studies of patients spanning the age continuum. There is a lack of a single predictive scoring system for the elderly that has been validated in a multicenter fashion. Development of such a scoring system is a priority for the elderly, as it would obviate unnecessary patient suffering from the delivery of futile care and provide families with information vital to end-of-life decision making.

Nutrition Considerations

Children

In general, children have a higher metabolic rate and need for substrate, minerals and trace elements than adults. (22) High loads of parenteral glucose are not utilized. (23) Children rapidly develop a negative nitrogen balance, suggesting that feeding should be continued, enterally or parenterally, during the perioperative period. (24) Although enteral nutrition is the preferred method of feeding, parenteral support may be required during periods of sepsis-induced ileus. Selected children with large burn injury (>40% TBSA) may benefit from anabolic agents to improve donor site healing and improve lean muscle mass. (25) Compounding the increased need for nutrients is the frequent presence of fever in the absence of infection, which increases metabolic rate and nutritional requirements. (26) The use of beta blockers has been shown in single center studies to decrease heart rate and improve lean muscle mass in children with severe burn injury. (27)

Older Adults

Substrate needs are poorly predicted in the critically ill elderly. (28) The elderly may have overt or occult diabetes and tolerate glucose loads poorly, necessitating insulin infusion to maintain metabolic homeostasis. (29) The ideal substrate, rate of infusion, type of infusion, and route of administration of enteral feedings has not been defined, and, similar to children, the endpoints for nutrition in the elderly have not been well-delineated. The elderly often have underlying malnutrition, which impacts both the immune and metabolic systems. Selected elders may benefit from anabolic agents, particularly oxandrolone, which is inexpensive and administered enterally. (30, 31)

Elders may also have a higher incidence of occult endocrine problems such as hypothyroidism and adrenal insufficiency (32). In general, these follow predictable patterns (33), but atypical presentation is common. (34) A high index of suspicion for endocrine abnormalities needs to be maintained. In some cases, osteoporosis may complicate rehabilitation efforts. (35)

Neurologic/Pain Considerations

Children

In young children, pain and anxiety may be difficult to assess, requiring a sensitivity on the part of the bedside nursing staff to ensure adequate comfort. (36) The development and validation of age-appropriate pain scales, protocols for narcotic and benzodiazepine use, and sedation is sorely needed.

The incidence of Attention Deficit Hyperactivity Disorder has been estimated as high as 20% in the population of children requiring burn center admission. (37) This should be addressed during both the acute treatment period and recovery to optimize participation in rehabilitation and scar management efforts, and to prevent repeat injury. As many as 30% of burn-injured children will develop injury and treatment-related Acute and Post-Traumatic Stress Disorder (38) This should be anticipated and treatment offered if present.

Older Adults

Older adults may present with variable degrees of baseline organic brain dysfunction, sometimes contributing to the injury (39) This may make orientation to the hospital environment and burn rehabilitation more difficult. (40) They seem to awaken more slowly from a period of intensive care. At times, delirium and agitation may result in management difficulty (41) In some cases, a syncopal episode of cardiac or neurovascular origin may have caused the injury. This possibility should be pursued in suspicious clinical settings (42)

An additional consideration in the elderly is their response to medications. The compromised renal function associated with age may slow the metabolism of commonly used narcotics. Elders may also have difficulty in expressing pain, making the treatment of pain and anxiety problematic. Elderly patients are often taking powerful pharmacologic agents when they are injured. Beta-blockers are particularly common and can mask tachycardia as a sign of volume depletion or pain. In addition, the elderly may have occult renal disease, making them more susceptible to nephrotoxic drug effects.

Wound Healing Considerations

Children

Young children have a thinner skin with a lesser density of appendages, resulting in deeper burns for a given mechanism of injury and more protracted healing of donor sites (43) The use of full thickness donor sites, when possible, will limit donor site debility. In massive burns, split thickness grafts will need to be taken and dermal substitutes may be of particular value in patients with massive burns. (44) Although many grafting techniques have been described, there is a paucity of studies demonstrating the long-term superiority of any single approach.

Older Adults

As we age, our skin becomes atrophic, with a thinner dermis and fewer appendages. (45) The clinical result is a proclivity to compromised spontaneous burn wound and donor site healing. (46) This may result in a greater need for surgery than in young adults with similar mechanisms, and more protracted donor site healing. Although early excision and grafting has been adopted for young adults, the benefits of early versus delayed excision in the elderly has not been clearly demonstrated. (47, 48) The risk/benefit ratio of excision and grafting needs to be carefully weighed in this population. In theory thin skin grafts with the use of dermal substitutes may decrease donor site morbidity, but no prospective randomized trials have been conducted to evaluate this approach in the elderly. Another approach that may prove useful in this population is the use of full thickness grafts, which take advantage of the loss of skin turgor that accompanies age, resulting in redundant skin.

Prevention Considerations

Children

Children are dependent on others for many aspects of their physical safety. (49) They have a lesser awareness of danger and an increased curiosity which implores them to explore their surroundings. Many prevention campaigns have been developed for this population. Particularly effective targets are legislative initiatives, such as children's sleepwear standards and hot water heater factory set-points. However, much work needs to be done. (50,51)

Older Adults

Older adults value their independence, despite the fact that they may have reduced mobility, strength, and coordination. Some tasks of daily living may become increasingly difficult, presenting increased risks. This is especially true in the cooking and in bathing. (52) As these deficits develop very gradually, elders may have a lesser awareness of danger. Prevention campaigns directed at this unique population should be developed. (53)

Break Out Session Discussion

The breakout session centered on identifying the many unmet research needs in burn care for children and the elderly (Table 1). These ranged from issues in critical care to outcomes research. Topics included development of a composite skin substitute, understanding the metabolic differences at the extremes of age, understanding special resuscitation needs at the extremes of age, defining the unique psychosocial needs of the very old and very young, and developing more sophisticated techniques of outcomes research. Work in any of these areas is likely to be fruitful and to benefit both current and future patients.

The final list of priorities is depicted in Table 2. Investigation of the metabolic and resuscitative needs and mechanisms for both children and the elderly is needed. These populations have unique physiologic changes after burn injury that need to be investigated. Airway management and pain management in children after burn injury are also topics that require further investigation. Although airway and pain management were also cited as important topics for the elderly, development of an accurate model for outcome prediction in the elderly was considered to be the highest priority, as it would obviate many unnecessary resuscitations. Open wounds, including the donor site, continue to be one of the major causes of morbidity in the elderly. The optimization of wound closure, whether with newly developed technologies or modifications of already existing techniques, is a priority for the elderly. Investigation into artificial skin and new innovative technologies may well improve the overall survival in this patient population.

Studies in multiple different areas of research will be needed to accomplish these goals. Consensus conferences will be needed to define endpoints, develop protocols for testing, and delineate areas of further investigation. Epidemiologic studies will elucidate outcomes and provide potential strategies for clinical trials. Mechanistic studies of metabolism, nutrition, and resuscitation will provide the foundation for new methods that can then be tested in pilot translational research and multicenter clinical trials.

Conclusions

Children and the elderly with burn injury have unique physiologic and metabolic needs. Understanding these differences will be the key to the development of optimal therapeutic regimens after burn injury in these patients. The priorities for children and the elderly include airway management, resuscitation, nutrition, pain management, wound closure, and outcome prediction models. Achieving these priorities will require researchers and clinicians to unite to develop and validate treatment modalities.

REFERENCES

1. McNiece WL, Dierdorf SF. The pediatric airway. *Semin Pediatr Surg.* 2004;13:152-165.
2. Sheridan RL. Uncuffed endotracheal tubes should not be used in seriously burned children. *Pediatr Crit Care Med.* 2006 May;7(3):258-9.
3. Palmieri TL, Jackson W, Greenhalgh DG. Benefits of early tracheostomy in severely burned children. *Crit Care Med.* 2002 Apr;30(4):922-4.
4. Saffle JR, Morris SE, Edelman L. Early tracheostomy does not improve outcome in burn patients. *J Burn Care Rehabil.* 2002 Nov-Dec;23(6):431-8.
5. Kadilak PR, Vanasse S, Sheridan RL. Favorable short- and long-term outcomes of prolonged translaryngeal intubation in critically ill children. *J Burn Care Rehabil.* 2004 May-Jun;25(3):262-5.
6. Sadowski R, Dechert RE, Bandy KP, Juno J, Bhatt-Mehta V, Custer JR, Moler FW, Bratton SL. Continuous quality improvement: reducing unplanned extubations in a pediatric intensive care unit. *Pediatrics.* 2004 Sep;114(3):628-32.
7. Marcin JP, Rutan E, Rapetti PM, Brown JP, Rahnamayi R, Pretzlaff RK. Nurse staffing and unplanned extubation in the pediatric intensive care unit. *Pediatr Crit Care Med.* 2005 May;6(3):254-7.
8. Fitzpatrick JC, Cioffi WG Jr. Ventilatory support following burns and smoke-inhalation injury. *Respir Care Clin N Am.* 1997 Mar;3(1):21-49.
9. Murakami K, McGuire R, Cox RA, Jodoin JM, et al. Heparin nebulization attenuates acute lung injury in sepsis following smoke inhalation in sheep. *Shock.* 2002;18:236-41.
10. Palmieri TL, Enkhbaatar P, Bayliss R, Traber L, Cox RA, Hawkins HK, Herndon DN, Greenhalgh DG, Traber DL. Continuous Nebulized Albuterol Attenuates Acute Lung Injury in an Ovine Model of Combined Burn and Smoke Inhalation. *Critical Care Medicine.* 2006;34:1719-1724.
11. Silver GM, Freiburg C, Halerz M, Tojong J, Supple K, Gamelli RL. A survey of airway and ventilator management strategies in North American pediatric burn units. *J Burn Care Rehabil.* 2004 Sep-Oct;25(5):435-40a).
12. Sheridan RL, Zapol WM, Ritz RH, Tompkins RG. Low-dose inhaled nitric oxide in acutely burned children with profound respiratory failure. *Surgery.* 1999 Nov;126(5):856-62.
13. Cartotto R, Ellis S, Smith T. Use of high-frequency oscillatory ventilation in burn patients. *Crit Care Med.* 2005 Mar;33(3 Suppl):S175-81.
14. Kane TD, Greenhalgh DG, Warden GD, Goretsky MJ, Ryckman FC, Warner BW. Pediatric burn patients with respiratory failure: predictors of outcome with the use of extracorporeal life support. *J Burn Care Rehabil.* 1999 Mar-Apr;20(2):145-50.
15. Medbo A, Melbye H. Lung function testing in the elderly-Can we still use FEV(1)/FVC<70% as a criterion of COPD? *Respir Med.* 2007 Jan 17; [Epub ahead of print].
16. Sprung J, Gajic O, Warner DO. Review article: Age related alterations in respiratory function – anesthetic considerations. *Can J Anaesth.* 2006 Dec;53(12):1244-57.
17. Behrman RE, Klingman RM, Jenson HB. *Nelsons Textbook of Pediatrics*, 17th ed. Elsevier, 2004.
18. Sheridan RL, Schnitzer JJ. Management of the high-risk pediatric burn patient. *J Pediatr Surg.* 2001 Aug;36(8):1308-12.
19. Meyers DG, Hoestje SM, Korentager RA. Incidence of cardiac events in burned patients. *Burns.* 2003 Jun;29(4):367-8.
20. Wilson DB, Mostafavi K, Craven TE, Ayerdi J, Edwards MS, Hansen KJ. Clinical course of mesenteric artery stenosis in elderly Americans. *Arch Intern Med.* 2006 Oct 23;166(19):2095-100).
21. Arbabi S, Ahrns KS, Wahl WL, Hemmila MR, Wang SC, Brandt MM, Taheri PA. Beta-blocker use is associated with improved outcomes in adult burn patients. *J Trauma.* 2004 Feb;56(2):265-9.
22. Prelack K, Sheridan RL. Micronutrient supplementation in the critically ill patient--strategies for clinical practice. *J Trauma* 2001;51(3):601-620.

23. Sheridan RL, Yu YM, Prelack K, et al. Maximal parenteral glucose oxidation in hypermetabolic young children: a stable isotope study. *Journal of Parenteral and Enteral Nutrition* 1998;22(4):212-21.
24. Herndon DN, Tompkins RG. Support of the metabolic response to burn injury. *Lancet*. 2004 Jun 5;363(9424):1895-902.
25. Przkora R, Herndon DN, Suman OE, Jeschke MG, Meyer WJ, Chinkes DL, Mlcak RP, Huang T, Barrow RE. Beneficial effects of extended growth hormone treatment after hospital discharge in pediatric burn patients. *Ann Surg*. 2006 Jun;243(6):796-801.
26. Parish RA, Novack AH, Heimbach DM, Engrav LR. Fever as a predictor of infection in burned children. *J Trauma*. 1987 Jan;27(1):69-71.
27. Hart DW, Wolf SE, Chinkes DL, Lal So, et al. Beta-blockage and growth hormone after burn. *Ann Surg*. 2002;236:450-6.
28. Ryan CM, Sheridan RL, Schoenfeld DA, Warshaw AL, Tompkins RG. Post-burn pancreatitis. *Ann Surg* 1995;222:163-170.
29. Weekers F, Giulietti AP, Michalaki M, Coopmans W, Van Herck E, Mathieu C, Van den Berghe G. Metabolic, endocrine, and immune effects of stress hyperglycemia in a rabbit model of prolonged critical illness. *Endocrinology*. 2003 Dec;144(12):5329-38.
30. Demling RH, DeSanti L. Oxandrolone induced lean mass gain during recovery from severe burns is maintained after discontinuation of the anabolic steroid. *Burns*. 2003 Dec;29(8):793-7.
31. Wolf SE, Edelman LS, Kemalyan N, Donison L, et al. Effects of oxandrolone on outcome measures in the severely burned: a multicenter prospective randomized double-blind trial. *J Burn Care Res*. 2006 Mar-Apr;27(2):131-9.
32. Noth RH, Mazzaferri EL. Age and the endocrine system. *Clin Geriatr Med*. 1985 Feb;1(1):223-50.
33. Rehman HU, Masson EA. Neuroendocrinology of ageing. *Age Ageing*. 2001 Jul;30(4):279-87.
34. Gambert SR, Escher JE. Atypical presentation of endocrine disorders in the elderly. *Geriatrics*. 1988 Jul;43(7):69-71, 76-8.
35. Ekstrom H, Elmstahl S. Pain and fractures are independently related to lower walking speed and grip strength: results from the population study "Good Ageing in Skane". *Acta Orthop*. 2006 Dec;77(6):902-11.
36. Sheridan RL, Hinson M, Blanquiere M, et al. Development of a Pediatric Burn Pain and Anxiety Management Program. *J Burn Care Rehabil* 1997;18:455-9.
37. Mangus RS, Bergman D, Zieger M, Coleman JJ. Burn injuries in children with attention-deficit/hyperactivity disorder. *Burns*. 2004 Mar;30(2):148-50.
38. Stoddard F, Ronfeldt H, Kagan J, Drake J, Snidman N, Murphy M, Saxe G, Burns J, Sheridan R. Young burned children: the course of acute stress, physiological and behavioral responses. *Am J Psychiatry* 2006;163:1084-1090.
39. Kaimal AB, Nair UV. Organic brain dysfunction in late-onset depression. *Br J Psychiatry*. 2005 Sep;187:288.
40. Marik PE. Management of the critically ill geriatric patient. *Crit Care Med*. 2006 Sep;34(9 Suppl):S176-82.
41. Ranhoff AH, Rozzini R, Sabatini T, Cassinadri A, Boffelli S, Trabucchi M. Delirium in a sub-intensive care unit for the elderly: occurrence and risk factors. *Aging Clin Exp Res*. 2006 Oct;18(5):440-5.
42. Kadri N, Chassagne P, Benichou J, Hellot MF, Delangre T, Derambure V, Druetne L, Bentot C, Bercoff E. The value of clinical characteristics from a standard questionnaire to discriminate cardiac from neurological syncope in the elderly. *J Nutr Health Aging*. 2006 Nov-Dec;10(6):546-53.
43. Sheridan RL, Remensnyder JP, Prelack K, Petras L, Lydon M. Treatment of the seriously burned infant. *J Burn Care Rehabil* 1998;19:115-8.
44. Heimbach DM, Warden GD, Luterman A, Jordan MH, Ozobia N, Ryan CM, Voigt DW, Hickerson WL, Saffle JR, DeClement FA, Sheridan RL, Dimick AR. Multicenter postapproval clinical trial of Integra dermal regeneration template for burn treatment. *J Burn Care Rehabil*. 2003 Jan-Feb;24(1):42-8.

45. Koehler MJ, Konig K, Elsner P, Buckle R, Kaatz M. In vivo assessment of human skin aging by multiphoton laser scanning tomography. *Opt Lett*. 2006 Oct 1;31(19):2879-81.
46. Rao K, Ali SN, Moiemmen NS. Aetiology and outcome of burns in the elderly. *Burns*. 2006 Nov;32(7):802-5.
47. Pereira C, Barrow A, Sterns H, Hawkins C, et al. Age-dependent differences in survival after severe burns: a unicentric review of 1674 patients and 179 autopsies over 15 years. *J Am Col Surg*. 2002;536-48.
48. Kim DS, Luce EA. Early excision and grafting versus conservative management of burns in the elderly. *Pl and Recon Surg*. 1998;102:1013-1017.
49. Carlsson A, Uden G, Hakansson A, Karlsson ED. Burn injuries in small children, a population-based study in Sweden. *J Clin Nurs*. 2006 Feb;15(2):129-34.
50. Diller KR. Adapting adult scald safety standards to children. *J Burn Care Res*. 2006 May-Jun;27(3):314-22.
51. Cagle KM, Davis JW, Dominic W, Gonzales W. Results of a focused scald-prevention program. *J Burn Care Res*. 2006 Nov-Dec;27(6):859-63.
52. Bessey PQ, Arons RR, Dimaggio CJ, Yurt RW. The vulnerabilities of age: burns in children and older adults. *Surgery*. 2006 Oct;140(4):705-15.
53. Ryan CM, Thorpe WP, Mullin PA, Daly WD, Tompkins DM, Kelleher P, Sheridan RL, Tompkins RG. A persistent fire hazard for older adults: cooking related clothing ignition. *The Journal of the American Geriatric Society* 1997;45(10):1283-1285.

Table 1 Selected Unmet Needs in Burn Research

Unmet Needs-Critical Care

- Support of respiratory failure
- Non-invasive monitoring
- Vascular and airway access
- Pain Control and Monitoring
- Antimicrobials
- Control of burn shock

Unmet Needs-Nutritional Support

- Better understanding of biology of catabolic illness
- Better monitoring tools for LBM
- Clarification of the role of anabolic agents

Unmet Needs-Wound Evaluation and Excision

- Early determination of the ability of burns to heal
- Blood conserving techniques
- Tissue glues

Unmet Needs-Wound Closure

- Autologous composites
- Safe temporary membranes to facilitate healing and pain control

Unmet Needs-Rehabilitation and Reconstruction

- Durable permanent skin substitute
- Biology and control of scar formation
- A greater understanding of emotional recovery

Table 2: Priorities for Research

Children

1. Determine optimal airway management after burn injury.
2. Define the endpoints of resuscitation for children after burn injury.
3. Define the metabolic changes after burn injury and optimize nutritional support.
4. Determine the optimal pain and sedation management after burn injury.

Older Adults

1. Develop an accurate model for outcome prediction.
2. Define and optimize resuscitation endpoints.
3. Delineate the metabolic changes after burn injury and optimize nutritional support.
4. Define the optimal strategy for wound closure, including timing, procedure, and perioperative support.

Overview of Day 2: Burn Rehabilitation

Matthew B. Klein, M.D.

It is quite difficult to separate acute care for burn rehabilitation as so many of the long-term burn effects are impacted by events which occur in the early post-injury period. As we began to set the agenda for the rehabilitation day of the State of the Science Conference we found identifying topics worthy of discussion was quite easy, however narrowing the list to seven topics was quite challenging. Adequate discussion of each topic could easily fill an entire day—let alone a single hour. We selected a renowned group of moderators and panelists to lead the discussion of the following topics: psychological health, the burn scar, community integration, burn reconstruction, the hand and restoration of function. While these topics seem distinct in many ways, there is still an enormous amount of overlap between them. For example, scar and hand function can significantly impact psychological health and, ultimately, impact potential for successful community integration.

The final panel of the rehabilitation day of the SOS provided the burn survivor perspective. Optimizing the quality of life burn survivors is the ultimate goal of all of our efforts in both the acute and rehabilitative phases of burn care. The inclusion of the burn survivor perspective at a conference for setting a burn research agenda was clearly essential.

The format of the rehabilitation day was a bit different than the acute care day. All sessions were held in the main lecture hall. The moderator for each session provided a 2-3 minute overview of the topic and then two expert panelists provided a summary of what is not known but what needs to be known about each topic. Then the remainder of each session was dedicated to audience participation.

The following papers summarize the proceedings of each session. Each paper presents a statement of the topic, brief background and discussion of what is currently known and discussion of what is not known. Finally, the authors of each paper have provided a “top five” list of research priorities. While these written summaries provide a synthesis of the panelists’ presentations and the issues raised by audience participants they are by no means exhaustive reviews. Rather, they represent experts’ opinions on the priorities for the future of burn research.

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Topic:

Hand burns occur commonly both as part of larger burn injuries as well as isolated injuries and are a leading cause of impairment following burn injury.¹ However, there continues to be an overwhelming number of unanswered questions in nearly every facet of hand burn management. Even the issue of optimal timing for skin closure, which seemed to have been well answered, has been called into question and recent articles suggest that even this fundamental question may require further exploration.² Other aspects of hand burn management including graft types (i.e. full vs. split thickness), post-operative positioning, use of Kirshner wires, timing for range of motion and use of splinting remain unresolved. The analysis of hand outcomes has also been an ongoing challenge primarily due to the lack of validated assessment tools that correlate the extensive data one can collect on range of motion at each joint, hand strength and sensation with overall functional outcome. The purpose of the hand panel was to identify gaps in our knowledge in several different aspects of hand burn management and identify specific priorities for future research in the broad and complex domain of hand burns.

Background:

Hand burns occur quite commonly and the outcome of hand burns can significantly impact daily function and overall health related quality of life. The management of hand burns is typically dictated by the depth of the burn. Superficial and partial thickness burns that are likely to heal within a timely manner (two to three weeks) are managed with wound care and aggressive range of motion to preserve hand function. Conversely, deeper partial thickness and full thickness burns that will require longer time to heal are better managed with wound excision and skin grafting. There have been a number of studies which have examined the optimal management and outcomes of patients with both partial thickness and full thickness burns of the hand. Sheridan studied 305 hands with partial thickness tissue loss that did not require surgery and found that 97% of patients had good functional outcome defined as normal or near normal based on staff impression.³ These findings contradict the opinion of “universally” good outcomes for this burn depth and suggests that more studies are needed to try to determine the sources of suboptimal outcome following partial thickness injuries (i.e. patient compliance with therapy, chronic pain).

Many of the studies on surgical management of hand burns have focused on the timing of excision and the techniques of skin grafting. Full thickness hand burns have been described as having mostly good outcomes.³ van Zuijlen’s evaluated the outcome of 88 patients (143 hand burns) using the Jebsen Taylor Hand Test (JTHT) and found 80% of the hands had normal function on all 7 tasks.⁴ No distinction was made for joint ankylosis or exposed or rupture tendons and there was no correlation found between surgery timing and outcome. Only three

patients in the series underwent amputation and these patients tended to have greater functional impairment.⁴ Sheridan studied 309 hands with deep dermal or full thickness injuries that required grafting.³ Of these, 81% had normal or near normal function based on staff impression but no formal functional assessment or range of motion measurements were performed. Eighteen percent could perform ADL's with adaptive equipment and less than 1% of the hands were unable to perform ADL's.³ Cartotto evaluated 29 patients with deep partial or full thickness hand burns. At greater than a year post injury, these subjects had normal mean pinch strength but decreased grip strength and a mean TAM of 225 degrees which is considered functional but is clearly well below the norm of 260 degrees.⁵ Although early excision and grafting is standard for full thickness hand burns, factors such as total body surface area (TBSA), medical stability and other complicating conditions may impact the timing of surgery, other management strategies and ultimate outcome.

Deep full thickness hand burns involving the extensor mechanism, joint capsule or bone are rare making up less than 5% of all hand burns but have been described as having universally poor outcomes regardless of treatment.^{6,7} Sheridan studied 56 hands with fourth-degree injuries. His protocol included immobilization with axial Kirschner wires with staged autografting when avascular structures were covered with granulation tissue. The majority of patients (89%) required Kirschner wire fixation and 61% required one or more partial or complete digital amputations. Of this group, only 9% had normal or near normal hand function, 81% could perform ADL's with equipment and 9% were unable to perform ADL's. Although these findings are consistent with the clinical impressions of the burn community no actual functional assessments were performed.³ Holavanahalli studied 32 burn survivors with deep full thickness hand burns.⁸ She found severe impairment with more than 50% amputations and 22% with a Boutonniere deformity. Forty percent of subjects had poor functional range with a TAM of less than 180°. Scores on JHT were lower than the norms, and subjects reported most difficulty in performing MHQ-Activities of Daily Living.⁸ These data clearly demonstrates the profound impairments found with this depth of burn. It is obvious that this group requires extensive research to find better ways of protecting the tendons and maximizing functional outcomes.

Regardless of burn depth, range of motion therapy and timing of splint immobilization are important considerations throughout the early and late post-injury period. An experienced burn hand therapist is an essential member of the burn team. Aggressive range of motion should be started soon after admission to the burn center for most partial and full thickness hand burns. For patients who are unable to actively participate due to extent of injury or other factors, therapy staff should perform regular passive range of motion.

Long-term hand outcome is typically influenced by a number of factors including formation of hypertrophic scar, joint contracture, lack of compliance with therapy regimen, pain and neuropathy. There have been few studies which have provided a longitudinal assessment of hand function following burn injury and most of the literature on long-term outcome following hand burns focuses on techniques for correction of scar contractures. In addition, there have been few studies examining the best methods for assessing hand function. In Johnson's review of hand function following deep burn injury, she recommends using the total active motion measurement to assess outcomes.⁹ The classification system for this tool is: poor <180 degrees, good 180-219, excellent 220-259, and normal 260 degrees. The technique is discussed but no actual patient data is given. In addition, there are a number of range of motion and strength measurements which are routinely obtained, yet it is not clear which are the most useful for assessing functional status. A number of the outcome tools utilized have not been validated for burn injury and it is unclear whether they are sensitive to the issues burn patients have and whether they are responsive to progress in hand function over time.

What is not Known

Despite being such a common injury, there is much that still needs to be known about hand burns. Hand burn management encompasses a number of overlapping issues including surgical management, splinting, pain management, scarring and digit/hand salvage. Within each domain of hand burn management there are several important questions that remain unanswered.

Initial Treatment and Surgical Management

There are many critical considerations in the early management of hand burns. The indications and timing for carpal tunnel release following electrical injury still has yet to be determined. In cases of deep digital burns the relative benefits of digital escharotomy have yet to be clearly defined. While early excision and grafting have become the standard management for burns that will not heal in a timely fashion, there are still many unanswered questions about the details of surgical management. For example, the best type of skin graft coverage (i.e. split vs. full thickness grafts; sheet vs. mesh grafts) and how to position the hand for grafting are not clear. In addition, the indications and optimal use for skin substitutes such as Integra needs to be determined.

Deep Hand Burns

The improved survival of patients with severe burn injury has resulted in an increased number of patients who have deep hand burns with exposed tendon and/or bone. These injuries present a number of challenges to the burn team. The overall goal of hand burn management is to optimize hand function, but there are few studies and little information to help guide management decisions in cases of deep hand burns. Clearly, there is a need to know how the exposed tendon and/or joint should be treated. During the period prior to grafting, the ideal dressings for keeping exposed tendons viable needs to be known. In addition, the ideal splinting position and range of motion protocol for hands with exposed tendons and joints needs to be known. There are also many unanswered questions related to the surgical management of deep hand burns. For example, should early arthrodesis be performed on all exposed joints? Should treatment vary if only one joint is exposed as opposed to all joints on all digits? The answers to these questions require an understanding of the relative functional impairment associated with arthrodesis as compared to Boutinierre and swan neck deformities. The potential role of skin substitutes and flaps in providing coverage for traditionally bones and tendons traditionally considered to be non-graftable also needs to be examined. The decision between hand/digit salvage and amputation also warrants further study. Clearly, the decision for amputation will be influenced by a number of other patient and injury characteristics including age, hand dominance and extent of burn injury, however, the need to define the optimal timing for amputation and the impact of proximal elbow and hand wrist function on the decision to amputate remains. Finally, the role of prosthetics in the management of deep hand burns needs to be evaluated.

Pain and Neuropathy

Hand pain and neuropathy will significantly impact hand function both in the early post-injury period as well as during the rehabilitation phase of care. The pathophysiology of chronic hand pain and neuropathy following burn injury are not clear. While the causes are multifactorial, the ability to identify patients at risk for neuropathy and the development of strategies to mitigate modifiable risk factors would clearly be beneficial. In addition, research is needed to determine the best methods for management of neuropathy, chronic pain, and complex regional pain syndrome. Since these complications occur relatively rarely, there are few studies examining the management of these issues.

Exercise and Range of Motion Therapy

Most agree that consideration of hand positioning and range of motion exercises is required early in the post-injury period. However, there is little data on the optimal timing and frequency of hand exercises and the balance between immobilization to maintain optimal hand positioning and range of motion to prevent stiffness. In addition, many different approaches to splinting (*i.e.* dynamic splinting, casts) have been described but few have been rigorously evaluated.

Other Long-term Sequelae

The management of hand burn complications can continue for years following the initial injury. Scar contractures—both those isolated to the skin and those involving tendons and joints—can be the source of hand impairment. There have been few studies examining the optimal management of these secondary deformities. In addition, nail deformities occur quite commonly in the setting of hand burns and can be a source of both pain and disfigurement. Very little is known about these deformities and the best methods for managing them.

Outcome Measurements for Hand Function

There are a number of important logistical considerations that need to be addressed in order to effectively study many of the issues discussed above. The development of rigorous studies that will provide meaningful results is contingent on having well defined outcome parameters and tools that can effectively capture them. There is an overwhelming volume of data that can be collected including individual joint active and passive motion, hand strength, nerve conduction studies, and sensation thresholds, yet the correlation between results of these tests and hand function has not been defined. There is a clear need to develop a set of functional assessment tools that is valid for persons with hand burns.

Conclusion:

In 2000, Salisbury outlined the most common deformities seen following hand burns: webspace contractures, dorsal skin contractures, fifth finger abduction deformity, MP joint extension deformities, extensor tendon adhesions, Boutonniere deformity, PIP flexion deformities, neuropathy, amputation, and proximal influences. These common deformities persist and many remain without well-described solutions. Given the critical importance of the hand to overall functional status, hypothesis driven, high quality research studies are needed evaluate the effects of different surgical and therapeutic approaches. The five priority topics for hand research are:

- 1) Determining the best approach to management of the deep hand burn with exposed tendon.
- 2) Determining the role and benefit of skin substitutes in the management of hand burns
- 3) Determining the optimal surgical approach to prevent and treat web space contractures;
- 4) Determining the optimal timing and components of burn hand therapy—including exercises and modalities.
- 5) Examining the factors that influence the outcome of partial thickness hand burns.

Successful conduct of these studies will likely require a cooperative group set up to perform multi-center trials and the dedication of appropriate resources to cover the infrastructure costs of performing such studies.

Referemnces:

1. Anzarut A, Chen M, Shankowsky H, Tredget EE. Quality-of-life and outcome predictors following massive burn injury. *Plastic Recon Surg* 2005;116(3):791-7.
2. Maslauskas K, Rimdeika R, Rapolienė J, Ramanauskas T. Analysis of burned hand function (early versus delayed treatment). *Medicina (Kaunas)* 2005;41(10):846-51.
3. Sheridan RL, Hurley J, Smith MA, Ryan CM, Bondoc CC, Quinby WC, et al. The acutely burned hand: Management and outcome based on a ten-year experience with 1047 acute hand burns. *Journal of Trauma, Infection and Critical Care* 1995;38:406-11.
4. van Zuijlen PPM, Kreis RW, Vloemans AFPM, Groenevelt F, Mackie DP. The prognostic factors regarding long-term functional outcome of full thickness hand burns. *Burns* 1999;25:709-714.
5. Cartotto R. The burned hand: Optimizing long-term outcomes with a standardized approach to acute and subacute care. *Clin Plastic Surg* 2005;32:515-27.
6. Salisbury RE. Soft tissue injuries of the hand. *Hand Clinics* 1986;2:25-32.
7. Salisbury RE. Reconstruction of the burned hand. *Clin Plastic Surg* 2000;27:65-9.
8. Holavanahali RK, Helm PA, Gorman AR, Kowalske KJ. Outcomes following deep full thickness hand burns. Submitted to *J Burn Care Rehab*.
9. Johnson C, Engrav LH, Heimbach DM, Marvin JA. Evaluating functional hand results after deep dermal burns with total active motion measurements. *J Burn Care Rehab* 1980;1:19-21.

Table 1: Research Priorities for the Hand

- Determining the best approach to management of the deep hand burn with exposed tendon.
- Determining the role and benefit of skin substitutes in the management of hand burns
- Determining the optimal surgical approach to prevent and treat web space contractures;
- Determining the optimal timing and components of burn hand therapy—including exercises and modalities.
- Examining the factors that influence the outcome of partial thickness hand burns.

Scar

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Key Words

hypertrophic scar; porcine; swine; pig; contraction, hyperpigmentation, hypopigmentation; burns; thermal injury;

Topic

Hypertrophic scar, contraction and pigment abnormalities have altered the future for decades for children and adults after thermal injury. The hard, raised, red and itchy scars; shrunk wounds, and hyper- and hypo-pigmented scars are devastating to physical and psychosocial outcomes. The specific causes remain essentially unknown and, at present, prevention and treatment are symptomatic and marginal at best.

Background

Hypertrophic scarring is the major significant negative outcome after survival from of a thermal injury. Hypertrophic scars are hard, raised, red, itchy, tender, and contracted.^{1, 2} These scars are ugly, disfiguring and uncomfortable and may diminish, but never totally go away.

Hypertrophic scarring after deep partial-thickness wounds is common. We have reviewed the English literature on the prevalence of hypertrophic scarring³ and found that children, young adults and people with darker, more pigmented skin are particularly vulnerable and, in this subpopulation, the prevalence is up to 75%.⁴⁻⁶

Hypertrophic scarring is devastating and can result in disfigurement and scarring that affects quality of life which, in turn, can lead to lowered self esteem, social isolation, prejudicial societal reactions and job discrimination.⁷⁻¹² Scarring also has profound rehabilitation consequences including loss of function, impairment, disability, and difficulties pursuing recreational and vocational pursuits.^{10, 13, 14}

Essentially the same can be said about wound contraction and hyper- and hypopigmentation after thermal injury. They are significant negative outcomes, common and devastating.^{15, 16}

What is not Known

Problems with the Current State of Clinical Science

The current understanding of post-burn scarring is deficient in many aspects. There are no useful, objective definitions that consistently distinguish between atrophic, wide, normotrophic and hypertrophic scars and keloids.¹⁷ This means that, in research studies, scars are grouped on a clinical basis, which undoubtedly varies from provider to provider. The result is confusing results and incomplete answers.

We have neither a standardized method to measure the severity of hypertrophic scar nor an objective reproducible method to measure the response to treatment. Several methods have been suggested including clinical observation, Vancouver Burn Scar Scale, scar volume, photography, vascularity, pliability, and ultrasound thickness.¹⁸⁻²⁵ None of these methods cover the entire problem and none has been accepted as the standard.

Our knowledge of incidence and socioeconomic impact of hypertrophic scar is minimal. We do not know the answers to the following questions.^{3-6, 26}

- What is the frequency following thermal injury?
- How large is the socioeconomic impact?
- Who is more likely to develop hypertrophic scar given similar severity of initial injury?
- How does age, sex, and race/origin affect the development of hypertrophic scar?
- What is the psychological impact to the surviving burn patient?

We are unable to determine which scars will become hypertrophic.²⁷ Our understanding of the pathophysiology of hypertrophic scarring is limited, both locally and systemic. Hundreds of studies of human hypertrophic scar have been done over the past decades, but the pathophysiology of hypertrophic scarring is still only partially understood.²⁸⁻³⁷

- What is the role of burn depth in the development of hypertrophic scarring?
- How does the treatment affect the development of hypertrophic scar?
- How does the timing of wound closure affect the subsequent development of hypertrophic scarring?

There is essentially no known completely effective method of prevention and/or treatment of hypertrophic scarring. Pressure garments, silicone sheeting, steroid injections and

various other treatments have been tried but none prevent and/or solves the problem.^{33, 38-43} This leaves reconstructive plastic surgery as the sole option, which is usually done months after the appearance of hypertrophic scars exposing the patient to a long period of discomfort and misery and imposing upon the patient and society the resultant financial and social burden.

The same general statements can be made regarding contraction and pigment alterations.

Problems with the Current State of Laboratory Science

Our current understanding of the cause of hypertrophic scarring is very incomplete. For example, although the abnormalities in ultrastructure and cellular and extracellular matrix in hypertrophic scar are partially understood, the factors that drive the development of these lesions remain elusive. One reason that the etiology of human hypertrophic scar is unknown is the absence of a useful animal model.^{36, 44-47} Despite numerous attempts by multiple investigators, mice, rats, rabbits, dogs and cats have all failed to produce scars analogous to human hypertrophic scars. Repetitive literature searches have yielded few references to animal models of hypertrophic scar. Morris⁴⁵ reported a scar model in the rabbit ear. We found only a limited number of studies from other investigators utilizing this model to study scar³⁹ and it is a small, full-thickness wound, which is quite different from the large, partial-thickness burn wounds in which the deep dermis remains that leads to the development of hypertrophic scar. Human hypertrophic scar tissue has also been implanted into athymic rats and mice.^{46, 48-54} These models have been used in two studies by other groups^{55, 56} but seem very dissimilar to the clinical situation and the tissue implanted is established scar so any early changes are missed. Aksoy³⁶ described a hypertrophic scar model in the albino, male guinea pig after excision of the panniculus carnosus and development of flaps, application of thermal injury, and treatment with coal tar. We could find no further use of this model. The Duroc/Yorkshire animal model of fibroproliferative scarring has received some recent attention as has burn wounds in the Large White pig.^{37, 57-71}

Without a representative animal model of human hypertrophic scar, scar tissue for study is usually obtained from humans undergoing scar revision that is done many months after the scar first developed. Time is an important variable in wound repair³⁴, and it is known that gene expression may be early and transient during wound repair.⁷² This early expression, which likely determines the pathology of hypertrophic scar weeks and months later, may be missed by our current strategies that include biopsies of established hypertrophic scar. Earlier investigation of the developing scar is likely to be essential to understanding the fibrotic process.

A second reason for our lack of knowledge regarding hypertrophic scar may be that scars of varying ages are often aggregated into a few large categories, e.g. less than 12 months, 12 to 24 months, greater than 24 months. As mentioned above, time is an important variable in wound repair and collapsing the time axis into large calendar blocks may hide the biologic events.

A third reason for our lack of understanding of the etiology of hypertrophic scarring is that, in the past, most human hypertrophic scar tissue for study has been minced and homogenized. This action destroys skin anatomy and homogenizes all cell populations. This seems inappropriate since signaling in the epidermis may be differentially regulated compared to the deep dermis. Mesenchymal-epithelial cell interactions and potential signaling cues that may regulate scarring may be masked. Laser microdissection is now possible and can be used to study different anatomic portions of scar such as the deep residual uninjured dermis and the more superficial scar mass. It can also be used to separate the collagen mass from the skin appendages, cone structures and other intrinsic structures of the skin.^{57, 58, 73}

Conclusion: Proposed Research Priorities

We propose 5 priorities to move our understanding of hypertrophic scarring, contraction and pigment alteration after thermal injury forward.

Priority #1 - Early and Serial Biopsies

Typically studies are done with samples obtained during scar revision, which means they are obtained months/years after the process began. We need samples of normal skin and shallow and deep wounds obtained in the first days and weeks after injury. Ideally, these should be in the same individual to reduce the variability in wound healing that exists between individuals. Therefore we need a standardized animal model of this process and patient and human subjects permission to biopsy burn wounds early and serially after injury.

Priority #2 - Microdissected Samples

Studies are usually done with homogenized samples. This means that any hypodermis and dermis are ground up with the scar and any differences are lost. Future studies need to separate and differentiate between residual hypodermis and dermis and the superficial scar mass and the new epidermis. Laser microdissection may permit this procedure.

Priority #3 - Studies of Wounds That Healed Spontaneously

Hypertrophic scarring often follows spontaneous healing and is likely significantly altered by excision and grafting. Therefore, the studies should include wounds that were not excised and grafted and consequently some small deep partial-thickness and full-thickness wounds may need to be permitted to heal over time and not excised and grafted.

Priority #4 - Definition of Atrophic, Wide, Normotrophic and Hypertrophic Scars

At present the definition of each of these is basically clinical. We need to characterize each of these with objective, biologic markers, which may be determined by Priorities 1-3.

Priority #5 - Incidence and Socioeconomic Impact

The incidence of these problems is not known with accuracy nor is it stratified by age, sex and race/origin. As a result, we cannot estimate the socioeconomic impact. We need this data to obtain funding for the study of these problems.

References

1. Ehrlich HP, Kelley SF. Hypertrophic scar: an interruption in the remodeling of repair—a laser Doppler blood flow study. *Plast Reconstr Surg*. 1992;90(6):993-998.
2. Rudolph R. Wide spread scars, hypertrophic scars, and keloids. *Clin Plast Surg*. 1987;14(2):253-260.
3. Bombaro KM, Engrav LH, Carrougner GJ, Wiechman SA, Faucher L, Costa BA, Heimbach DM, Rivara FP, Honari S. What is the prevalence of hypertrophic scarring following burns? *Burns*. Jun 2003;29(4):299-302.
4. Deitch EA, Wheelahan TM, Rose MP, Clothier J, Cotter J. Hypertrophic burn scars: Analysis of variables. *J Trauma*. 1983;23(10):895-898.
5. McDonald WS, Deitch EA. Hypertrophic skin grafts in burned patients: a prospective analysis of variables. *J Trauma*. Feb 1987;27(2):147-150.
6. Spurr ED, Shakespeare PG. Incidence of hypertrophic scarring in burn-injured children. *Burns*. Jun 1990;16(3):179-181.
7. Engrav LH, Heimbach DM, Reus JL, Harnar TJ, Marvin JA. Early excision and grafting vs. nonoperative treatment of burns of indeterminate depth: A randomized prospective study. *J Trauma*. 1983;23(11):1001-1004.
8. Abdullah A, Blakeney P, Hunt R, Broemeling L, Phillips L, Herndon DN, Robson MC. Visible scars and self-esteem in pediatric patients with burns. *J Burn Care Rehabil*. Mar-Apr 1994;15(2):164-168.
9. Fauerbach JA, Heinberg LJ, Lawrence JW, Munster AM, Palombo DA, Richter D, Spence RJ, Stevens SS, Ware L, Muehlberger T. Effect of early body image dissatisfaction on subsequent psychological and physical adjustment after disfiguring injury. *Psychosom Med*. Jul-Aug 2000;62(4):576-582.
10. Brych SB, Engrav LH, Rivara FP, Ptacek JT, Lezotte DC, Esselman PC, Kowalske KJ, Gibran NS. Time off work and return to work rates after burns: systematic review of the literature and a large two-center series. *J Burn Care Rehabil*. Nov-Dec 2001;22(6):401-405.
11. Fauerbach JA, Heinberg LJ, Lawrence JW, Bryant AG, Richter L, Spence RJ. Coping with body image changes following a disfiguring burn injury. *Health Psychol*. Mar 2002;21(2):115-121.
12. Van Loey NE, Van Son MJ. Psychopathology and psychological problems in patients with burn scars: epidemiology and management. *Am J Clin Dermatol*. 2003;4(4):245-272.
13. Herndon DN, LeMaster J, Beard S, Bernstein N, Lewis SR, Rutan TC, Winkler JB, Cole M, Bjarnason D, Gore D. The quality of life after major thermal injury in children: an analysis of 12 survivors with greater than or equal to 80% total body, 70% third-degree burns. *J Trauma*. Jul 1986;26(7):609-619.
14. Engrav LH, Covey MH, Dutcher KD, Heimbach DM, Walkinshaw MD, Marvin JA. Impairment, time out of school, and time off from work after burns. *Plast Reconstr Surg*. Jun 1987;79(6):927-934.
15. Stoner ML, Wood FM. The treatment of hypopigmented lesions with cultured epithelial autograft. *J Burn Care Rehabil*. Jan-Feb 2000;21(1 Pt 1):50-54.
16. Richard R, Ward RS. Splinting strategies and controversies. *J Burn Care Rehabil*. Sep-Oct 2005;26(5):392-396.
17. Lee JY, Yang CC, Chao SC, Wong TW. Histopathological Differential Diagnosis of Keloid and Hypertrophic Scar. *Am J Dermatopathol*. Oct 2004;26(5):379-384.
18. Baryza MJ, Baryza GA. The Vancouver Scar Scale: an administration tool and its interrater reliability. *J Burn Care Rehabil*. Sep-Oct 1995;16(5):535-538.
19. Davey RB, Sprod RT, Neild TO. Computerised colour: a technique for the assessment of burn scar hypertrophy. A preliminary report. *Burns*. May 1999;25(3):207-213.
20. Draaijers LJ, Tempelman FR, Botman YA, Tuinebreijer WE, Middelkoop E, Kreis RW, van Zuijlen PP. The patient and observer scar assessment scale: a reliable and feasible

- tool for scar evaluation. *Plast Reconstr Surg.* Jun 2004;113(7):1960-1965; discussion 1966-1967.
21. Martin D, Umraw N, Gomez M, Cartotto R. Changes in subjective vs objective burn scar assessment over time: does the patient agree with what we think? *J Burn Care Rehabil.* Jul-Aug 2003;24(4):239-244; discussion 238.
22. Nedelec B, Shankowsky HA, Tredget EE. Rating the resolving hypertrophic scar: comparison of the Vancouver Scar Scale and scar volume. *J Burn Care Rehabil.* May-Jun 2000;21(3):205-212.
23. Cheng W, Saing H, Zhou H, Han Y, Peh W, Tam PK. Ultrasound assessment of scald scars in Asian children receiving pressure garment therapy. *J Pediatr Surg.* Mar 2001;36(3):466-469.
24. Li-Tsang CW, Lau JC, Liu SK. Validation of an objective scar pigmentation measurement by using a spectrophotometer. *Burns.* Dec 2003;29(8):779-784.
25. Sullivan T, Smith J, Kermode J, Mclver E, Courtemanche DJ. Rating the burn scar. *J Burn Care Rehabil.* May-Jun 1990;11(3):256-260.
26. Dedovic Z, Koupilová I, Brychta P. Time trends in incidence of hypertrophic scarring in children treated for burns. *Acta Chir Plast.* 1999;41(3):87-90.
27. Riordan CL, McDonough M, Davidson JM, Corley R, Perlov C, Barton R, Guy J, Nanney LB. Noncontact laser Doppler imaging in burn depth analysis of the extremities. *J Burn Care Rehabil.* Jul-Aug 2003;24(4):177-186.
28. Linares HA. From wound to scar. *Burns.* 1996;22(5):339-352.
29. Rockwell WB, Cohen IK, Ehrlich HP. Keloids and hypertrophic scars: A comprehensive review. *Plast Reconstr Surg.* 1989;84(5):827-837.
30. Murray JC. Keloids and hypertrophic scars. *Clin Dermatol.* 1994;12(1):27-37.
31. Su CW, Alizadeh K, Boddie A, Lee RC. The problem scar. *Clin Plast Surg.* 1998;25(3):451-465.
32. Dasu MR, Hawkins HK, Barrow RE, Xue H, Herndon DN. Gene expression profiles from hypertrophic scar fibroblasts before and after IL-6 stimulation. *J Pathol.* Apr 2004;202(4):476-485.
33. Rahban SR, Garner WL. Fibroproliferative scars. *Clin Plast Surg.* Jan 2003;30(1):77-89.
34. Robson MC, Steed DL, Franz MG. Wound healing: biologic features and approaches to maximize healing trajectories. *Curr Probl Surg.* Feb 2001;38(2):72-140.
35. Robson MC. Proliferative scarring. *Surg Clin North Am.* Jun 2003;83(3):557-569.
36. Aksoy MH, Vargel I, Canter IH, Erk Y, Sargon M, Pinar A, Tezel GG. A new experimental hypertrophic scar model in guinea pigs. *Aesthetic Plast Surg.* Sep-Oct 2002;26(5):388-396.
37. Gallant CL, Olson ME, Hart DA. Molecular, histologic, and gross phenotype of skin wound healing in red Duroc pigs reveals an abnormal healing phenotype of hypercontracted, hyperpigmented scarring. *Wound Repair Regen.* May-Jun 2004;12(3):305-319.
38. Mustoe TA, Cooter RD, Gold MH, Hobbs FD, Ramelet AA, Shakespeare PG, Stella M, Teot L, Wood FM, Ziegler UE. International clinical recommendations on scar management. *Plast Reconstr Surg.* Aug 2002;110(2):560-571.
39. Ha X, Li Y, Lao M, Yuan B, Wu CT. Effect of human hepatocyte growth factor on promoting wound healing and preventing scar formation by adenovirus-mediated gene transfer. *Chin Med J (Engl).* Jul 2003;116(7):1029-1033.
40. Chang P, Laubenthal KN, Lewis RW, 2nd, Rosenquist MD, Lindley-Smith P, Kealey GP. Prospective, randomized study of the efficacy of pressure garment therapy in patients with burns. *J Burn Care Rehabil.* Sep-Oct 1995;16(5):473-475.
41. Costa AM, Peyrol S, Porto LC, Comparin JP, Foyatier JL, Desmouliere A. Mechanical forces induce scar remodeling. Study in non-pressure-treated versus pressure-treated hypertrophic scars. *Am J Pathol.* 1999;155(5):1671-1679.
42. Kealey GP, Jensen KL, Laubenthal KN, Lewis RW. Prospective randomized comparison of two types of pressure therapy garments. *J Burn Care Rehabil.* Jul-Aug 1990;11(4):334-336.

43. Patino O, Novick C, Merlo A, Benaim F. Massage in hypertrophic scars. *J Burn Care Rehabil.* May-Jun 1999;20(3):268-271; discussion 267.
44. Mast BA. The skin. In: Cohen IK, Diegelmann RF, Lindblad WJ, eds. *Wound healing: biochemical & clinical aspects.* Philadelphia: W.B. Saunders Co.; 1992:353.
45. Morris DE, Wu L, Zhao LL, Bolton L, Roth SI, Ladin DA, Mustoe TA. Acute and chronic animal models for excessive dermal scarring: quantitative studies. *Plast Reconstr Surg.* 1997;100(3):674-681.
46. Polo M, Kim YJ, Kucukcelebi A, Hayward PG, Ko F, Robson MC. An in vivo model of human proliferative scar. *J Surg Res.* Feb 1 1998;74(2):187-195.
47. Hillmer MP, MacLeod SM. Experimental keloid scar models: a review of methodological issues. *J Cutan Med Surg.* Jul-Aug 2002;6(4):354-359.
48. Kischer CW, Pindur J, Shetlar MR, Shetlar CL. Implants of hypertrophic scars and keloids into the nude (athymic) mouse: viability and morphology. *J Trauma.* May 1989;29(5):672-677.
49. Kischer CW, Sheridan D, Pindur J. Use of nude (athymic) mice for the study of hypertrophic scars and keloids: vascular continuity between mouse and implants. *Anat Rec.* Nov 1989;225(3):189-196.
50. Wang X, Smith P, Pu LL, Kim YJ, Ko F, Robson MC. Exogenous transforming growth factor beta(2) modulates collagen I and collagen III synthesis in proliferative scar xenografts in nude rats. *J Surg Res.* Dec 1999;87(2):194-200.
51. Polo M, Smith PD, Kim YJ, Wang X, Ko F, Robson MC. Effect of TGF-beta2 on proliferative scar fibroblast cell kinetics. *Ann Plast Surg.* Aug 1999;43(2):185-190.
52. Shetlar MR, Shetlar CL, Kischer CW, Pindur J. Implants of keloid and hypertrophic scars into the athymic nude mouse: changes in the glycosaminoglycans of the implants. *Connect Tissue Res.* 1991;26(1-2):23-36.
53. Shetlar MR, Shetlar CL, Hendricks L, Kischer CW. The use of athymic nude mice for the study of human keloids. *Proc Soc Exp Biol Med.* Sep 1985;179(4):549-552.
54. Robb EC, Waymack JP, Warden GD, Nathan P, Alexander JW. A new model for studying the development of human hypertrophic burn scar formation. *J Burn Care Rehabil.* 1987;8(5):371-375.
55. Reiken SR, Wolfort SF, Berthiaume F, Compton C, Tompkins RG, Yarmush ML. Control of hypertrophic scar growth using selective photothermolysis. *Lasers Surg Med.* 1997;21(1):7-12.
56. Wolfort SF, Reiken SR, Berthiaume F, Tompkins RG, Yarmush ML. Control of hypertrophic scar growth using antibody-targeted photolysis. *J Surg Res.* Apr 1996;62(1):17-22.
57. Matsumura H, Engrav LH, Reichenbach D, Gibran NS, Maser B. Cones, fat domes and hypertrophic scarring in the female, red, Duroc pig. Paper presented at: Plastic Surgery Research Council, 1998; Loma Linda.
58. Matsumura H, Engrav LH, Yunusov MD, Reichenbach D, Gibran NS, Maser B. Cones, fat domes, and hypertrophic scarring in the female, red Duroc pig. Paper presented at: American Burn Association, 1999; Lake Buena Vista, FL.
59. Gallant CL, Wright JB, Olson ME, Hart DA. The red Duroc pig model of hypertrophic wound healing. Paper presented at: Wound Healing Society, 2001; Albuquerque, NM.
60. Gallant CL, Hart DA, Olson ME. Skin wound healing in red Duroc pigs: Potential role of growth factors and cytokines in scar formation. Paper presented at: Wound Healing Society, 2002; Baltimore, MD.
61. Gallant CL, Olson ME, Hart DA. Full- and partial-thickness skin wounds in red Duroc pigs leads to hypercontracted, hyperpigmented scars. Paper presented at: Wound Healing Society, 2002; Baltimore, MD.
62. Zhu KQ, Engrav LH, Gibran NS, Cole JK, Matsumura H, Piepkorn M, Isik FF, Carrougner GJ, Muangman P, Yunusov MY, Yang T. The female, red Duroc pig as an animal model of hypertrophic scarring and the potential role of the cones of skin. *Burns.* 2003;29(7):649-664.

63. Zhu KQ, Engrav LH, Tamura RN, Cole JK, Muangman P, Carrougner GJ, Gibran NS. Further similarities between cutaneous scarring in the female, red Duroc pig and human hypertrophic scarring. *Burns*. 2004;30(6):518-530.
64. Liang Z, Engrav LH, Muangman P, Muffley LA, Zhu KQ, Carrougner GJ, Underwood RA, Gibran NS. Nerve quantification in female red Duroc pig (FRDP) scar compared to human hypertrophic scar. *Burns*. Feb 2004;30(1):57-64.
65. Zhu KQ, Engrav LH, Armendariz RT, Muangman P, Klein MB, Carrougner GJ, Deubner H, Gibran NS. Changes in VEGF and nitric oxide after deep dermal injury in the female, red Duroc pig-further similarities between female, Duroc scar and human hypertrophic scar. *Burns*. Feb 2005;31(1):5-10.
66. Harunari N, Zhu KQ, Armendariz RT, Deubner H, Muangman P, Carrougner GJ, Isik FF, Gibran NS, Engrav LH. Histology of the thick scar on the female, red Duroc pig: Final similarities to human hypertrophic scar. *Burns*. 2006;32(6):669-677.
67. Gallant-Behm CL, Hart DA. Genetic analysis of skin wound healing and scarring in a porcine model. *Wound Repair Regen*. Jan-Feb 2006;14(1):46-54.
68. Gallant-Behm CL, Olson ME, Hart DA. Cytokine and Growth Factor mRNA Expression Patterns Associated with the Hypercontracted, Hyperpigmented Healing Phenotype of Red Duroc Pigs: A Model of Abnormal Human Scar Development? *J Cutan Med Surg*. Mar 2 2006.
69. Gallant-Behm CL, Tsao H, Reno C, Olson ME, Hart DA. Skin wound healing in the first generation (F1) offspring of Yorkshire and red Duroc pigs: evidence for genetic inheritance of wound phenotype. *Burns*. Mar 2006;32(2):180-193.
70. Liang Z, Xie CY, Lin HB, Guo ZD, Yang WG. [Pathomorphological observation of the hypertrophic scar induced by injury to conical structure in female red Duroc pig]. *Zhonghua Shao Shang Za Zhi*. Feb 2006;22(1):29-32.
71. Cuttle L, Kempf M, Phillips GE, Mill J, Hayes MT, Fraser JF, Wang XQ, Kimble RM. A porcine deep dermal partial thickness burn model with hypertrophic scarring. *Burns*. Jul 31 2006.
72. Cole J, Tsou R, Wallace K, Gibran NS, Isik FF. Early gene expression profile of human skin to injury using high-density cDNA microarrays. *Wound Repair Regen*. Sep-Oct 2001;9(5):360-370.
73. Matsumura H, Engrav LH, Gibran NS, Yang TM, Grant JH, Yunusov MY, Fang P, Reichenbach DD, Heimbach DM, Isik FF. Cones of skin occur where hypertrophic scar occurs. *Wound Repair Regen*. Jul-Aug 2001;9(4):269-277.

Table 1: Priorities for Research in Scar

- Study of early and serial scar biopsies
- Study of microdissected scar samples that separate and differentiate hypodermis, dermis, superficial scar and epidermis
- Studies of wounds that healed spontaneously
- Definition of atrophic, wide, normotrophic and hypertrophic scars
- Studies on the incidence and socioeconomic impact of scar

Reconstructive Surgery

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Topic:

Reconstructive surgery is defined as surgery that takes something that is abnormal and tries to make it as normal as possible; this is in contrast to aesthetic surgery in which one takes something “normal” and tries to make it improve upon it. Burn reconstruction addresses the deformities and dysfunction resulting from burn injury. These pathologic conditions typically develop from hypertrophic scars, contractures, disorders of pigment and loss of anatomic parts. While the purpose of burn reconstruction is to attempt to make the burn survivor appear and function as normal as possible, the current state of the art is that we can only approach normalcy. There is a clear need to identify novel approaches and management strategies for burn deformities so that we can achieve better results. As Dr. Glenn Warden stated in his American Burn Association presidential address, burn reconstruction is the “last frontier” in burn treatment.¹

Background:

The unprecedented survival following severe burn injury has emphasized the importance of reconstructive surgery in the ultimate outcome of the burn patient. In addition, burn patients today are surviving more extensive and severe burn injuries, and, consequently, have more severe sequelae that require management over time. While acute post-injury patient care efforts focus on survival, wound closure and abrogating the negative effects of the hypermetabolic response, the long-term care provided by the reconstructive surgeon seeks to optimize the aesthetic and functional outcomes of each patient. Despite the greatest attention to matters of function and appearance during the period of acute burn management, the healing process—including scar deposition and contraction—as well as individual patient motivation and other psychosocial factors may conspire to compromise outcome.

Appearance and function are truly inextricably linked when dealing with burn reconstruction. As one approaches a patient seeking burn reconstructive surgery appropriate weight is given to both issues. Quite often correction of an unsightly scar is required to also improve function. The converse is also true. The correction of lip ectropion that interferes with saliva and food management will also undoubtedly improve appearance. The correction of a lower eyelid ectropion will not only improve epiphora and risk of corneal ulceration but will improve the often unsightly appearance of scleral show.

Table 1 lists the common reconstructive options available to reconstructive surgeons. The reconstructive ladder has long provided the conceptual framework for the practice of reconstructive surgery. Following appropriate diagnosis of a particular problem, the reconstructive surgeon must take inventory of the available tissue and the appropriate procedure to perform. These procedures can range from the most technically basic such as scar excision and primary closure to the quite complex such as microsurgical tissue transfer. The selection of an appropriate procedure requires a thorough assessment of the patient and precise definition of the cause of a given deformity. For example, burn contractures typically result from tissue deficiency; accordingly, the best treatment for this condition would be contracture release and addition of tissue.

Reconstructive procedures in burn survivors often prove quite challenging. In the case of extensive burn injury, there may be limited availability of healthy, non-scarred donor tissue. In addition there is often a need to address deformities of the skin, bone, tendon, joint and cartilage when addressing complex deformities of the face and extremities. Accordingly, the reconstructive surgeon must also take inventory of available tissue for reconstruction—this includes skin, muscle, cartilage and bone. This inventory needs to be considered in light of the reconstructive ladder in planning of surgical procedures.

Burn patients commonly require multiple procedures staged over months to years in order to address post-burn deformities adequately. Therefore, reconstructive surgery requires meticulous planning and allocation of the scarce available resources. Often it is possible to group reconstructive procedures to minimize the overall number of times a patient has to stop work, reenter the hospital and undergo an anesthetic and operation. Clearly, if procedures are to be grouped, thought must be given to which are performed concomitantly, and in which order the groups are addressed. For example, simultaneously performing procedures requiring

prolonged immobilization of both upper extremities will severely limit an individual's independence and ability to carry out activities of daily living. Similarly, one should not perform a procedure on the hand such as capsulectomy that requires immediate range of motion to obtain an optimal result with a skin graft contracture release which requires immobilization to heal properly.

It is critical to note that burn reconstruction is much more than the selection and performance of a surgical procedure or group of procedures. Just as acute burn care relies on a multidisciplinary model of care, burn reconstruction also requires a multidisciplinary approach. The requisite psychological preparedness of the patient and his or her support system to undergo a surgical procedure, post-operative therapy, splinting and potentially pressure garment therapy cannot be underestimated. The finest reconstructive procedure can be undone by poor post-operative compliance. Similarly, participation of occupational and physical therapists, nutritionists and social workers may also be crucial to the success of a reconstructive endeavor. In addition, successful reconstructive surgery requires clear communication and understanding between the patient and surgeon. The surgeon and patient must both be realistic in terms of what can be gained from a reconstructive surgery. The more closely surgical expectations and reality are aligned, the more satisfied both the patient and the surgeon will be following any procedure. Very little research has been performed on the importance and impact of patient and surgeon expectations to outcomes following burn reconstruction. The importance of non-operative and multidisciplinary approach is best expressed by Dr. Bruce Achauer in his book, Burn Reconstruction, where he states, "a beautiful reconstruction of a patient who [remains] withdrawn from society is a hollow victory."²

What is Not Known

Research in a number of areas including basic science, clinical outcomes and technology development may improve the quality of reconstructive surgery results obtained in the future. Despite all the advances in burn care—both medical and surgical—hypertrophic scar remains the Achilles' heel of burn surgeons and a source of persistent discomfort, distress and misery amongst burn survivors. The issue of scar is addressed in more complete detail in the section on scar, but it is important to note that it is the effective management of scar and its sequelae that remains the priority in reconstructive burn surgery. Below we discuss several areas where increased knowledge may significantly improve the management of burn deformities.

Tissue Engineering

The lack of available donor sites in extensive injuries requires the recropping of available donor sites in order to achieve wound closure. This results in the use of thin grafts which are more prone to contraction and scarring and donor sites which also may be slow to heal and prone to scarring. While there have been a number of products developed for use in burn care, there remains no permanent, off-the-shelf skin substitute that provides both epidermal and dermal replacement. While epidermal replacement can be achieved by culture expansion of keratinocytes, dermal replacement has provided a more formidable challenge. The complex acellular structure of dermis and the importance of other cellular and acellular components have prohibited dermal culture expansion from becoming a reality. Clearly, additional research defining the critical elements of dermis will be required prior to the development of a substitute that can recapitulate the complex biologic and functional behavior of human dermis. Future research may also identify a role for stem cells in the development of soft tissue constructs.

An effective tissue engineered soft tissue construct could provide a powerful tool not only in the acute management of burn wounds but also in the management of secondary burn deformities. The currently available off-the-shelf dermal substitute which requires a split thickness all graft to provide an epidermal cover has some utility in contracture release but the appearance of the reconstructed skin is not normal and very similar to burn scar. Furthermore, the need for a split thickness skin graft with this dermal construct does not address the potential donor site deficiency discussed above.

In addition to artificial skin, tissue engineered substitutes for tendon, joints and bone could also be very useful in burn reconstruction. Deep burns to the face and extremities often result in destruction of not only skin but also the cartilage framework of the nose and ears, articular cartilage and the bone.. The potential utility of soft tissue fillers such as restylene and collagen which have been used in cosmetic surgery also warrants further investigation for the management of contour deformities resulting from scarring or from the replacement of lost skin and subcutaneous tissue with a split thickness skin graft.

Pigment

Little is known about the causes of hyper- and hypopigmentation following burn injury. Pigment disorders can occur both in wounds that have healed spontaneously and in skin grafts, and are a source of great distress to the patient. Traditionally bleaching agents have been used for areas of hyperpigmentation and cosmetics have been used to achieve better color balance for areas of both hyper and hypopigmentation. More recently, there has been increasing interest in the use of lasers in the management of pigment problems. The use of lasers has become quite common in the treatment of both congenital deformities and the aging face and there is recent evidence to suggest that certain types of lasers may be useful in the management of the redness associated with immature scars.³ Pulse dye lasers which supplies light at a wavelength preferentially absorbed by pigment has been used to improve the rubor associated with immature scar. The selective photoabsorption in the red wavelength minimizes the risk of thermal injury to an already injured area. Studies examining the efficacy and safety of the pulsed dye laser are clearly needed and are underway. In addition, the potential utility and safety of laser treatment in the management of other scar-associated pigment disorders requires further study.

Prosthetics

Strategies for the replacement of anatomic parts also require further development and evaluation. Currently, replacement of anatomic parts can be done either by reconstructive surgery utilizing the patient's own tissues or with the use of prosthetics. While there are many autologous reconstructive options to address facial parts lost to injury, the paucity of useable local tissue or distant tissue may make the use of prosthetic ears or noses, for example, a better option. In addition, the development of osteointegrated implants has made use of prosthesis a lot more convenient. Decisions regarding digit, hand and limb salvage can also be quite challenging. Further research is needed to help guide decisions on functional outcome with an amputation and a prosthesis as opposed to an elaborate reconstructive procedure for limb salvage. How have newer prosthetics impacted this decision? Which patients do better with myoelectric prosthetics as opposed to purely mechanical prosthetics? These are questions that will become increasingly relevant to the practice of reconstructive burn surgery as more and more patients with deep extremity burns survive their injury, and the paramount importance of functional outcome receives increasing focus. In addition, even with the use of prosthetics, there remains challenges in terms of expense in manufacturing them, the need for long-term maintenance and potentially replacement. In addition, the psychological impact of prosthetic use as compared with autologous tissues is not well understood.

Psychological Impact of Reconstructive Surgery

In addition to research for the development of new techniques and technologies for reconstructive surgical applications, research is needed to increase our understanding of the psychological ramifications of reconstructive surgery. As discussed above, the deleterious impact of burn injury on appearance and function are clearly stigmatizing and can impact feelings of self-esteem, capacity for community integration and functional capacity. This dynamic interplay between appearance, psychological health and surgery is fascinating and a better understanding of the interplay may allow us to establish more realistic patient expectations of surgical results and improve overall patient outcome.

Heterotopic Ossification, Ulcers, Alopecia

There are many other problems which confront the burn patient and the reconstructive surgeon about which little is known. For example, heterotopic ossification can significantly compromise the function of an extremity. A better understanding of the molecular basis of this abnormal bone formation may lead to the development of effective pharmacologic

agents or surgical techniques which can combat HO. Chronic ulcers also remain an unsolved problem for many burn patients. A better understanding of ulcer etiology may yield more effective surgical and non-surgical treatment modalities. Alopecia of the scalp and eyebrows can significantly impact a burn patient's appearance. Development of new techniques or refinement of current techniques for hair replacement is clearly needed. In addition, further research into hair biology may lead to novel approaches to the management of alopecia.

Allotransplantation

Interest in tissue allotransplantation has increased significantly over the past several years. The reports of successful hand allotransplantation in the 1990s, and the recent report of a partial face allotransplantation in France have raised the interest in the potential use of facial allotransplantation for burn patients. In many ways, burn patients could be an ideal target population for facial allotransplantation. Burn survivors with extensive scarring and minimal available donor sites could potentially benefit from an allogeneic source of soft tissue. However, facial allotransplantation is fraught with a number of practical and ethical considerations. Facial appearance is a combination of both the soft tissue and the underlying bony structure. Therefore, the appearance of a transplanted face may be highly unpredictable. In addition, a number of potential dangerous side effects of the immunosuppressive regimens required for successful allograft take remain. The skin is among one of the most potent immunogenic stimuli and a facial allotransplant of mainly skin and soft tissue may require prolonged periods of powerful immunosuppressive regimens. There are a number of prominent investigators exploring the potential for immune tolerance induction and, in the future, this may make soft tissue allotransplantation a more favorable option. In addition to research into the complex biological basis of tolerance, additional research is needed to better define the indications for and ethical issues surrounding facial allotransplantation.

Outcomes Research

Finally, the field of burn outcomes research needs to mature from its current embryonic stage. Reconstructive surgery is focused on optimizing the outcome of burn patients. Therefore, the evaluation of indications for and impact of reconstructive surgery requires measurement tools that are valid for burn patients. There is clearly a need for the development of patient reported outcome tools (PROs) which are specific to burn injury and sensitive to changes that may occur with reconstructive procedures. In addition, as new techniques and technologies are developed, there needs to be larger scale studies organized so that these tools and technologies can be adequately assessed. The number of burn reconstruction surgeries done at any one center is quite small. Therefore, most published studies are descriptions of new techniques or a single center's experience with a novel technology. Improvements in burn outcome research will require the organization of multicenter studies with standardized definitions and measurements for assessment of baseline aesthetic and functional status and the use of PROs valid for persons with burn injury as described above.

Conclusions

With increasing survival following severe burn injury, the importance of reconstructive surgery to the achievement of optimal injury outcome will continue to increase. While the use of reconstructive surgical procedures to address post-injury deformities has been described for centuries, the field is still in many ways in its infancy. In order to improve the state of the science in reconstructive surgery we propose the following five research priorities:

- 1) Development of tissue engineered skin substitutes that recapitulate the structure and function of native human tissue. An off the shelf skin replacement would be a powerful tool in the management of acute burn injuries but also in the management of secondary deformities when there is a deficiency of available virgin tissue. The off the shelf substitute must look like normal skin. This is the only way to resurface large anatomic areas after burned scarred skin has been excised.
- 2) Increased understanding of the pathophysiology of scar. Scar contraction, pruritis and abnormal appearance remain the most significant challenges to optimal outcome following both burn injury and reconstructive surgery.

- 3) Scar-less surgery so that scars can be excised and tissue rearranged surgically without leaving scars from the reconstructive procedure. This may be possible with the greater understanding of scar physiology and tissue regeneration. Stem cell research may well be applicable in this area.
- 4) Control of pigmentation: Hyper- and hypopigmented grafts and healed wounds significantly impact appearance and there are few strategies that can reliably and safely improve pigment disorders.
- 5) Development of / validation of patient reported outcome tools that are relevant to burn patients and reconstructive burn surgery. Meaningful evaluation of surgical results and novel technologies is contingent on the availability of appropriate outcome assessment tools.

References:

- 1) Warden GD. Burn Patients Coming of Age: the 1993 presidential address to the American Burn Association. J Burn Care Rehabil 1993;14:581-8.
- 2) "Getting Started: Dealing with Scars," in Burn Reconstruction, 1st ed., Achauer, B.M., Thieme Medical Publishers, Inc, New York, p. 1.
- 3) Personal correspondence with Mathias Donelan, M.D.

Table 1: Reconstructive Options

- Scar excision and primary closure
- Split Thickness Skin Grafts
- Full Thickness Skin Grafts
- Composite tissue grafts
- Local Flap/Tissue Rearrangement (i.e. Z-plasty, Y-V-plasty)
- Tissue Expansion
- Skin/dermal substitutes
- Free Tissue Transfer
- Prosthetics
- Implants
- Lasers
- Cosmetics

Table 2: Research Priorities for Reconstructive Surgery

- Development of tissue engineered skin substitutes that recapitulate the structure and function of native human tissue.
- Increased understanding of the pathophysiology of scar.
- Development of scar-less surgery so that scars can be excised and tissue rearranged surgically without leaving scars from the reconstructive procedure
- Control of pigmentation.
- Development of / validation of patient reported outcome tools that are relevant to burn patients and reconstructive burn surgery

Psychological Health and Function Following Burn Injury:
Setting Research Priorities

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Topic

There are many sources of threat to the psychological health of an individual who has sustained an acute burn injury. These include the immediate experience of intense, excruciating pain that continues at least until wound closure, and, as is now becoming clear, becomes chronic in a substantial portion of survivors.¹ This pain is most severe during the frequent and unavoidable dressing changes and rehabilitation procedures, but is often quite intense even at rest. The injury and pain are accompanied by many other challenges to psychological equilibrium such as the many secondary complications that may arise.^{2,3} The traumatic event itself often includes additional threat from perceived loss of control, horror, or hopelessness and may lead to intense symptoms of distress. The burn wound results in immediate changes and may lead to scarring and long term alterations in one's pre-injury appearance and level of physical functioning. Separation from loved ones and others in the social support system is another source of stress (either through dislocation or death), as is disruption of one's roles and daily routines.

This article describes some of the research challenges and opportunities related to the psychological issues that can follow a burn injury. Psychological responses to burn injury may take the form of psychopathology (e.g., depression, Posttraumatic Stress Disorder: PTSD),⁴ post-traumatic growth (e.g. finding new meaning, enhanced hope and confidence),⁵ or a combination of behavioral, cognitive, and emotional responses that comprise an adaptive process of psychosocial rehabilitation (e.g., resilience, active coping). Many survivors, whether experiencing psychopathology, post-traumatic growth, or adaptive psychosocial rehabilitation, are in need of assistance. For example, substantial evidence indicates that, following major burn injury, severe psychological distress is among the most prevalent, enduring and impairing of secondary complications,⁶ and may manifest as sleep disturbance⁷, depression⁸⁻¹⁰, body image dissatisfaction¹¹⁻¹² or posttraumatic distress.¹³⁻¹⁷ Severe distress is present in 33% of adults and PTSD in more than 25% of adults¹⁸⁻²⁰ and children.²¹ There is good evidence that psychological health concerns in the acute care setting have long term consequences.²² The prevalence, severity and enduring nature of psychological distress following burn injury makes it a priority in rehabilitation efforts.

Background

Psychological distress, as a component of the "fight or fight" response, is of immediate concern during acute and critical care due to its influence on the immune system²³ and hypothalamic-pituitary-adrenal (HPA) axis.^{24,25} Notably, psychotherapy has been shown to optimize cortisol response to stress.²⁶ In addition, positive coping²⁷ and social support²⁸ each increased the interferon-gamma / interleukin-4 ratio, shifting the balance toward type 1 T-cell helper lymphocytes. The complex interaction of neuron-endocrine response and immune function with wound healing, infection and metabolism is being intensely studied in burns,²⁹⁻³² however, the potential modulating effect of psychological factors on such fundamental issues in burn care is largely unexplored.

Body Image and Psychosocial Adjustment

The first step towards adoption of psychosocial rehabilitation services as a standard of care is to empirically validate interventions. This need is highlighted by the consistent observation that a significant proportion of burn survivors who sustain a change in appearance experience persistent difficulty in psychological and social adjustment.^{12, 33, 34} These difficulties in adjustment are often under-recognized, and, hence, under-treated, leaving patients to cope on their own.

Barbara Kammerer-Quayle, in her chapter in *Auchauer & Sood's Burn Surgery, Reconstruction, and Rehabilitation*,³³ summarizes her decades of experience working with burn survivors by making the following points: 1) "In terms of long-term quality of life, social and psychological rehabilitation is, for the vast majority of survivors, profoundly more important than recovery of physical function;" 2) "Personally meaningful rehabilitation and recovery from significant burn injuries can be greatly facilitated by learning behavioral and image

enhancement strategies;” and 3) “Currently, there is no systematic effort to address the critical and pressing social and psychological rehabilitation needs of burn patients.”

It is important to emphasize that many of the needs we are describing are not focused on treating psychopathology. The incidence of psychopathology among burn survivors is significant and these problems must be addressed. However, many survivors who do not experience frank psychopathology nevertheless face significant challenges, for example in learning to adjust to their changed appearance and function.^{12, 34, 35} Thus, there is a very pressing and, unfortunately, unmet need to build the evidence base regarding long-term psychosocial rehabilitation of these individuals.

It is important to note the progress in our empirical understanding of the role of body image in the long-term psychosocial adjustment of burn survivors. For example, measurement of these and related problems has been enhanced with development of psychometrically sound tools such as the Perceived Stigmatization Questionnaire and the Social Comfort Questionnaire,³⁶ and the Satisfaction with Appearance Scale.³⁷ These measures have helped clarify the moderating role of the importance of appearance in the relationship between perceived scar severity and body-esteem among adult burn survivors and a clearer understanding of problematic methods that some burn survivors use in coping with body image changes following a disfiguring burn injury.^{38,39} Most recently, a longitudinal study of body image in survivors of severe burn injury found that body image satisfaction/distress was the most important predictor of overall psychosocial functioning at one year post-injury, that this was particularly true for females, and that the degree to which appearance is important to one's definition of self moderates the impact of scar severity on body image dissatisfaction.¹² The conceptualization and measurement of body image has also advanced and may help enhance understanding of the role of body image in the long-term psychosocial rehabilitation of burn survivors. For example, the Body Image Quality of Life Inventory,⁴⁰ as well as many other assessment instruments, would likely provide excellent treatment outcome measures.⁴¹

Posttraumatic Distress and Adjustment

The estimated lifetime prevalence of PTSD is 7.8% in data from a national probability sample of community dwelling adults in the U.S.⁴² Stress disorders are often reported following burn injury and acute stress disorder (ASD) and PTSD are each much more common among adults and children who have had a burn injury.^{13,43-49} ASD is reported in 18% to 32% of burn patients.^{13,15,19} PTSD is observed in approximately 23% to 33% of patients between 3 and 6 months post burn,^{13,19} and in 15% to 45% at a year or more after the burn.^{14,16,19} A well-designed study used structured diagnostic interview to evaluate the relationship between ASD and PTSD, and found that 89% of participants who met ASD while in-hospital also met criteria for PTSD over 6 months later.¹³ Acute in-hospital symptoms of posttraumatic distress have a marked detrimental impact on health and function across time.^{22,50} Recent evidence indicates that, at least among adults, only a small minority of those with clinically severe psychological distress or PTSD during the acute phase improve to a clinically significant and reliable degree for at least the next 2 years.^{18,19} Given the high prevalence rates and the chronic course, it is imperative that acute phase symptoms are identified and treatment made available across the lifespan.

Predictors of Recovery

However, we are still in the early stages of understanding the impact on long-term psychosocial adjustment from problems such as body image dissatisfaction, posttrauma distress, and depression, or, conversely, the enhancing effect of factors such as resilience and posttraumatic growth. For example, a recent review concluded: ‘The extent to which abnormalities in skin pigmentation and texture, scar visibility, amputations, and other changes in appearance affect an individual's physical image of themselves have only begun to be examined in burn patients.’² It is especially important that we better understand the long-term epidemiology of body image distress in the burn survivor so that we can more adequately address the needs that do exist. Conversely, it also would be helpful if we had a clearer understanding of resilience and post-traumatic growth: That is, what do “high coping/thriving” survivors have to teach us?

Similarly, much remains unknown regarding modifiable factors that may affect the course and severity of PTSD. The best predictors of PTSD symptoms at 1 and 6 months are in-

hospital PTSD symptoms.^{13,17,19} A personality trait characterized by unstable negative emotions (neuroticism) was the most important personality dimension in predicting PTSD, and both avoidant coping and social support mediated the relationship between neuroticism and PTSD.⁵¹ Furthermore, following the stress of a burn injury, individuals who are conflicted between approach coping and avoidance coping experience significantly greater severity of body image disturbance, posttrauma distress, depression, and pain-related distress.^{39,52-54} Importantly, there is a large and growing body of evidence demonstrating the role of positive emotions, self-efficacy, resilience, and sleep in recovery from extreme stress⁵⁵, trauma^{5,56} and adversity.⁵⁷ For example, baseline resilience significantly predicted positive PTSD treatment outcome, and successful pharmacologic treatment increased resilience (e.g., self-efficacy and active coping).^{56,58} These represent potentially rich avenues for investigation and intervention.

Treatment

There are few randomized, controlled, treatment studies for body image dissatisfaction, PTSD, depression, or sleep disturbance following burn injury.² This is despite the fact that, outside of the area of burn care, there is a significant body of empirical research demonstrating the efficacy of body image interventions in a range of clinical contexts.⁵⁹⁻⁶¹ The efficacy of cognitive-behavioral therapy (CBT) has also been demonstrated, in nonburn populations, for acute^{62,63} and chronic PTSD,^{56,64,65} major depression,⁶⁶ insomnia,⁶⁷ substance abuse,⁶⁸ and pain.⁶⁹

What needs to be Known

There is, without question, an important bridge to be built between our emerging understanding of the psychosocial needs among burn survivors and the offering of hope through intervention or prevention. There are at least five lines of research that, if pursued, could likely make a significant difference in the long-term psychosocial rehabilitation and quality of life of burn survivors.

First, there is a definite need for replication, extension, and dissemination of the social skills program evaluated by Dr. Blakeney and colleagues.³⁵ Individuals with changes in their appearance need to learn to effectively cope with the social response to their changed appearance. This is an important step in the process of psychosocial rehabilitation and is directly related to the individual's body image experience. The efficacy of these social skills interventions need to be evaluated in child, adolescent, and adult populations.

Second, studies are needed that evaluate CBT for body image distress experienced by burn survivors with permanent disfigurement. Perhaps, to enhance access, it would be especially helpful to evaluate the differences between in-person and web-based/self-help intervention formats for children, adolescents, and adults. Alyson Bessell and her colleagues at the Center for Appearance Research in the UK are in the process of exploring the use of web-based forms of CBT intervention for individuals with facial disfigurement. These web-based interventions are particularly promising in terms of reaching burn survivors who are unable or unwilling to obtain in-person psychosocial rehabilitation services. It is also essential to conduct longer-term follow-up of the efficacy of CBT interventions.

Third, it would be especially helpful to empirically evaluate the efficacy of the Behavioral Enhancement and Skills Tools (BEST) developed by Barbara Kammerer-Quayle which has been used with many burn survivors. The many strengths of the BEST program include the fact that it addresses, in a very practical and straightforward manner, the social skills challenges encountered by many burn survivors and also provides specific methods individuals can use to enhance their appearance (e.g., through the use of cosmetics and clothing). Both of these skill sets can significantly enhance body image functioning, feelings of self-efficacy, as well as overall quality of life.

Fourth, an important priority lies in clarifying the etiology of psychological distress (body image, posttrauma, depression), the mechanisms involved in its acquisition and maintenance, and the pathways by which such impairments limit activities and restrict participation. Resilience enhancement, positive coping and posttraumatic growth are new directions in CBT and represent an area where burn researchers can play a lead role. Given the prevalence and complexity of psychological impairments and the magnitude of the associated limitations, there is an urgent need to develop and test preventive and rehabilitative interventions. It is necessary

to begin with small-scale pilot studies but it is important to follow with rigorously designed, effectiveness-oriented, randomized, controlled and blinded research protocols.

Given the emphasis on intervention research, it might be useful to enumerate some factors that have been shown to affect treatment acceptability, compliance and effectiveness. The service might be provided via self-help, trained peer helper, or professional – or any combination of these. The methods to be evaluated may include psychopharmacy, psychotherapy, CBT, social skills training or other means. The setting for intervention may occur in diverse settings (e.g., bedside, office, online). Is this primary prevention? Is this an early intervention? Or, is this a form of rehabilitation or secondary prevention? Finally, alternative delivery modalities can be explored (e.g., virtual reality technology).⁷⁰ A very promising new direction for clinical care and research regarding caring for children and adolescents with acute traumatic injuries is described in detail in a recently published treatment manual.⁷¹

Fifth, the intricate interplay among stressors and cognitive, emotional, behavioral, physiological and biochemical processes remains an important and largely unexplored means for enhancing acute wound healing, infection resistance, and metabolism. Furthermore, as medical and rehabilitative procedures improve in the effective minimization of scarring, a key component to their success will be the degree of compliance. Compliance means both treatment integrity (i.e., practitioner provides intervention as supported by the evidence), and patient adherence to prescribed regimens (i.e., patient applies evidence-based methods appropriately). Clearly, as progress is made, researchers must also bear in mind the cost effectiveness of proposed assessments and interventions and the need to translate knowledge into forms that can improve public awareness and promote appropriate ways of interacting with people who have been traumatized and those with altered appearance.

In pursuing these and other important lines of research, long-term collaborations between clinicians, researchers and interested parties such as burn survivors/patient advocate, professional groups and funding agencies (e.g., Phoenix Society; American Burn Association; International Association of Firefighters; National Institute on Disability and Rehabilitation Research) may promote empirical study of accessible psychosocial rehabilitation programs. There is also much that needs to be learned about barriers to psychosocial interventions (financial, geographic, psychosocial). For example, some patients, health care providers and families seem to “resist” directly addressing the obvious suffering that some burn survivors experience, perhaps due to a fear of stigmatization.

Conclusion: Top Five Research Priorities

As discussed above, the five research priorities for psychological health are:

- 1) Replication, extension and dissemination of social skills programs in children and adults.
- 2) Studies to assess cognitive based therapy for body image distress;
- 3) Evaluation of the efficacy of the Behavioral Enhancement and Skills Tools (BEST) program;
- 4) Clarifying the etiology of psychological distress (body image, posttrauma, depression), the mechanisms involved in its acquisition and maintenance, and the pathways by which such impairments limit activities and restrict participation.
- 5) Improved understanding of the interaction between physiologic stressors and psychological/emotional stressors their synergistic effect on outcome.

In closing, it is important to underscore that there are many excellent methods already available for addressing the long-term psychosocial rehabilitation needs of burn survivors. Empirical evaluation of these and other prevention and rehabilitation methods is the key to insuring the highest quality of life for the greatest number of survivors over the long-term.

1. [Dauber A, Osgood PF, Breslau AJ, Vernon HL, Carr DB](#). Chronic persistent pain after severe burns: a survey of 358 burn survivors. *Pain Med*. 2002 Mar;3(1):6-17.
2. Esselman PC, Thombs BD, Magyar-Russell G, Fauerbach JA. Medical and psychological aspects of rehabilitation from burn injury. *American Journal of Physical Medicine and Rehabilitation* 2006 Apr;85(4):383-413.
3. Bombaro KM, Engrav LH, Carrouger GJ, Wiechman SA, Faucher L, Costa BA, Heimbach DM, Rivara FP, Honari S. What is the prevalence of hypertrophic scarring following burns? *Burns*. 2003 Jun;29(4):299-302.
4. American Psychiatric Association, American Psychiatric Association, Task Force on DSM-IV. *Diagnostic and Statistical Manual of Mental Disorders : DSM-IV*. 4th ed. Washington, DC: American Psychiatric Association; 1994.
5. Zoellner T, Maercker A. Posttraumatic growth in clinical psychology - a critical review and introduction of a two component model. *Clin Psychol Rev*. 2006 Sep;26(5):626-53.
6. Blakeney PE, Fauerbach JA, Meyer WJ, Thomas CR. Psychosocial recovery and reintegration of patients with burn injuries. In: Herndon D ed. *Total Burn Care*. 2nd ed. London, England: Elsevier; 2002:783-797.
7. Lawrence JW, Fauerbach J, Eudell E, Ware L, Munster A. The 1998 Clinical Research Award. Sleep disturbance after burn injury: a frequent yet understudied complication. *J Burn Care Rehabil*. 1998;19:480-486.
8. Ptacek JT, Patterson DR, Heimbach DM. Inpatient depression in persons with burns. *J Burn Care Rehabil*. 2002;23:1-9.
9. Wiechman SA, Ptacek JT, Patterson DR, Gibran NS, Engrav LE, Heimbach DM. Rates, trends, and severity of depression after burn injuries. *J Burn Care Rehabil*. 2001;22:417-424.
10. [Thombs BD, Bresnick MG, Magyar-Russell G](#). Depression in survivors of burn injury: a systematic review. *Gen Hosp Psychiatry*. 2006 Nov-Dec;28(6):494-502.
11. Lawrence JW, Heinberg LJ, Roca R, Munster A, Spence R, Fauerbach JA. Development and validation of the satisfaction with appearance scale: Assessing body image among burn-injured patients. *Psychol Assess*. 1998;10:64-70.
12. Thombs BD, Notes LD, Lawrence JW, Magyar-Russell M, Bresnick MG, Fauerbach JA. From Survival to Socialization: A Longitudinal Study of Body Image in Survivors of Severe Burn Injury. (In Review/2007).
13. Difede J, Ptacek JT, Roberts J, et al. Acute stress disorder after burn injury: A predictor of posttraumatic stress disorder? *Psychosom Med*. 2002;64:826-834.
14. Fauerbach JA, Lawrence J, Haythornthwaite J, Richter D, McGuire M, Schmidt C, Munster A. Psychiatric history affects post trauma morbidity in a burn injured adult sample. *Psychosomatics*. 1997;38:374-385.
15. Ehde DM, Patterson DR, Wiechman SA, Wilson LG. Post-traumatic stress symptoms and distress following acute burn injury. *Burns*. 1999;25:587-592.
16. Ehde DM, Patterson DR, Wiechman SA, Wilson LG. Post-traumatic stress symptoms and distress 1 year after burn injury. *J Burn Care Rehabil*. 2000;21:105-111.
17. Van Loey NE, Maas CJM, Faber AW, Taal LA. Predictors of chronic posttraumatic stress symptoms following burn injury: Results of a longitudinal study. *J Trauma Stress*. 2003;16:361-369.
18. Fauerbach JA, McKibben J, Bienvenu OJ, Magyar-Russell GM, Smith MT, Holavanahalli R, Patterson DR, Wiechman SA, Blakeney P, Lezotte D. Psychological distress following acute burn injury. (In Review).
19. McKibben J, Bienvenu OJ, Bresnick MG, Fauerbach JA. Acute stress disorder and posttraumatic stress disorder following major burn injury. *Proceedings of the American Burn Association* 2007b: San Diego, CA.
20. Powers PS, Cruse CW, Daniels S, Stevens B. Posttraumatic stress disorder in patients with burns. *Journal of Burn Care and Rehabilitation*. 1994;15:147-153.
21. Tarnowski KJ, Rasnake LK, Gavaghan-Jones MP, Smith L. Psychosocial sequelae of pediatric burn injuries: A review. *Clinical Psychology Review*. 1991;11:371-398.

22. Fauerbach JA, Lezotte D, Cromes GF, Kowalske K, de Lateur BJ, Goodwin CW, Blakeney P, Herndon DN, Wiechman S, Engrav LH, Patterson DR. 2004 American Burn Association Clinical Research Award. Burden of Burn: A Norm-Based Inquiry into the Influence of Burn Size and Distress on Recovery of Physical and Psychosocial Function. *Journal of Burn Care & Rehabilitation*. 2005 Jan-Feb;26(1):21-32.
23. Miller GE, Segerstrom SC. Psychological stress and the human immune system: A meta-analytic study of 30 years of inquiry. *Psychol Bull*. 2004 July; 130(4):601 - 630.
24. Gaab J, Rohleder N, Nater UM, Ehlert U. Psychological determinants of the cortisol stress response: the role of anticipatory cognitive appraisal. *Psychoneuroendocrinology*. 2005 Jul;30(6):599-610.
25. Seeman TE, McEwen BS. Impact of social environment characteristics on neuroendocrine regulation. *Psychosom Med*. 1996 Sep-Oct;58(5):459-71. Review.
26. Gaab J, Sonderegger L, Scherrer S, Ehlert U. Psychoneuroendocrine effects of cognitive-behavioral stress management in a naturalistic setting--a randomized controlled trial. *Psychoneuroendocrinology*. 2006 May;31(4):428-38.
27. Sakami, Shotaro, Maeda, Masaharu, Maruoka, Takayuki, Nakata, Akinori, Komaki, Gen, Kawamura, Noriyuki. Positive Coping Up- and Down-Regulates in vitro Cytokine Productions from T Cells Dependent on Stress Levels. *Psychotherapy and Psychosomatics*, Vol 73(4), Jul-Aug 2004. pp. 243-251.
28. Miyazaki T, Ishikawa T, Nakata A, Sakurai T, Miki A, Fujita O, Kobayashi F, Haratani T, Imori H, Sakami S, Fujioka Y, Kawamura N. Association between perceived social support and Th1 dominance. *Biol Psychol*. 2005 Sep;70(1):30-7.
29. Klein MB, Silver G, Gamelli RL, Gibran NS, Herndon DN, Hunt JL, Tompkins RG; Inflammation and the Host Response to Injury Investigators. Inflammation and the host response to injury: an overview of the multicenter study of the genomic and proteomic response to burn injury. *J Burn Care Res*. 2006 Jul-Aug;27(4):448-51.
30. Ipaktchi K, Mattar A, Niederbichler AD, Hoesel LM, Vollmannshäuser S, Hemmila MR, Su GL, Remick DG, Wang SC, Arbabi S. Attenuating burn wound inflammatory signaling reduces systemic inflammation and acute lung injury. *J Immunol*. 2006 Dec 1;177(11):8065-71.
31. Smith JW, Gamelli RL, Jones SB, Shankar R. Immunologic responses to critical injury and sepsis. *J Intensive Care Med* 2006; 21:160-172.
32. Madhally SV, Toner M, Yarmush ML, Mitchell RN. Interferon gamma modulates trauma-induced muscle wasting and immune dysfunction. *Ann Surg*. 2002 Nov;236(5):649-57.
33. Kammerer-Quayle, B. Behavioral skills and image enhancement training for burn survivors: Essential interventions for improving quality of life and community integration. In: Auchauer & Sood's *Burn Surgery, Reconstruction, and Rehabilitation*. Edited by Sood, R. Saunders, 2006.
34. Rose M, Blakeney P. [Pediatric Burn Injury](#). In: *Psychological aspects of reconstructive and cosmetic plastic surgery: Clinical, empirical, and ethical perspectives*. Sarwer, David B.; Pruzinsky, Thomas; Cash, Thomas F.; Goldwyn, Robert M.; Persing, John A.; Philadelphia, PA, US: Lippincott Williams & Wilkins Publishers, 2006. pp. 83-103.
35. [Blakeney P](#), [Thomas C](#), [Holzer C 3rd](#), [Rose M](#), [Berniger F](#), [Meyer WJ 3rd](#). Efficacy of a short-term, intensive social skills training program for burned adolescents. [J Burn Care Rehabil](#). 2005 Nov-Dec;26(6):546-55.
36. Lawrence JW, Fauerbach JA, Heinberg LJ, Doctor M, Thombs BD. The Reliability and Validity of the Perceived Stigmatization Questionnaire (PSQ) and the Social Comfort Questionnaire (SCQ) in an Adult Burn Survivor Sample. *Psychological Assessment*. 2006 Mar;18(1):106-111.
37. Lawrence JW, Heinberg LJ, Roca R, Munster A, Spence R, Fauerbach JA. Development and validation of the satisfaction with appearance scale: Assessing body image among burn-injured patients. *Psychol Assess*. 1998;10:64-70.
38. Lawrence JW, Fauerbach JA, Thombs BD. A test of the moderating role of importance of appearance in the relationship between perceived scar severity and body-esteem among adult burn survivors. *Body Image* 2006; 3:101-111.
39. Fauerbach JA, Heinberg L, Lawrence JW, Bryant AG, Richter L, Spence RJ. Coping with body image changes following a disfiguring burn injury. *Health Psychology* 2002; 21:115 – 121
40. Cash TF, Jakatdar TA, Williams EF. [The Body Image Quality of Life Inventory: Further validation](#)

- [with college men and women](#). *Body Image* 2004(Sept); 1(3):279-287.
41. Cash TF, Grasso K. [The norms and stability of new measures of the multidimensional body image construct](#). *Body Image* 2005 (Jun); 2(2):199-203.
 42. [Kessler RC, Sonnega A, Bromet E, Hughes M, Nelson CB](#). Posttraumatic stress disorder in the National Comorbidity Survey. [Arch Gen Psychiatry](#). 1995 Dec;52(12):1048-60.
 43. Armstrong, F. D., Gay, C., & Levy, J. D. (1994). Acute reactions. In K. J. Tarnowski (Ed.), *Behavioral Aspects of Pediatric Burns* (pp. 55–75). New York: Plenum Press.
 44. Saxe G, Stoddard FJ, Markey C, Taft C, King D, King L, & Sheridan RL. Acute stress symptoms in burned children. Paper presented at the 29th Annual Meeting of the American Burn Association; 1994; New York, NY.
 45. Stoddard FJ, Norman DK, Murphy JM, Beardslee WR. Psychiatric outcome of burned children and adolescents. *J Am Acad Child Adolesc Psychiatry*. 1989;28:589-595.
 46. Fleming MP, Difede J. Effects of varying scoring rules of the clinician administered PTSD scale (CAPS) for the diagnosis of PTSD after acute burn injury. *J Trauma Stress*. 1999;12:535-542.
 47. Madianos MG, Papaghelis M, Ioannovich J, Dafni R. Psychiatric disorders in burn patients: A follow-up study. *Psychother Psychosom*. 2001;70:30-37.
 48. El hamaoui Y, Yaalaoui S, Chihabeddine K, Boukind E, Moussaoui D. Post-traumatic stress disorder in burned patients. *Burns*. 2002;28:647-650.
 49. Difede J, Barocas D. Acute intrusive and avoidant PTSD symptoms as predictors of chronic PTSD following burn injury. *J Trauma Stress*. 1999;12:363-369.
 50. Fauerbach JA, Lawrence JW, Munster A, Palombo D, Richter D. Prolonged adjustment difficulties among those with acute post trauma distress following burn injury. *Behavioral Medicine*. 1999;22:359-378.
 51. Lawrence JW, Fauerbach JA.. Personality, coping, chronic stress, social support and PTSD symptoms: A path analysis. *Journal of Burn Care & Rehabilitation* 2003; 24: 63-72.
 52. Fauerbach JA, Richter L, Lawrence JW. Regulating acute posttrauma distress. *Journal of Burn Care & Rehabilitation* 2002; 23: 249-257.
 53. Fauerbach JA, Lawrence JW, Bryant AG, Smith JH. The relationship of ambivalent coping to depression symptoms and adjustment. *Rehabilitation Psychology* 2002; 47: 387 - 401.
 54. Fauerbach JA, Lawrence JW, Haythornthwaite JA, Richter L. Coping with the stress of a painful medical procedure. *Behavior Research and Therapy* 2002; 40: 1003 - 1015.
 55. Charney DS. Psychobiological mechanisms of resilience and vulnerability: implications for successful adaptation to extreme stress. *Am J Psychiatry*. 2004;161:195-216.
 56. Davidson JR, Payne VM, Connor KM, Foa EB, Rothbaum BO, Hertzberg MA, Weisler RH. Trauma, resilience and saliostasis: effects of treatment in post-traumatic stress disorder. *Int Clin Psychopharmacol*. 2005 Jan;20(1):43-48.
 57. [Linley PA, Joseph S](#). Positive change following trauma and adversity: a review. *J Trauma Stress*. 2004 Feb;17(1):11-21.
 58. Connor KM, Davidson JR. Development of a new resilience scale: the Connor-Davidson Resilience Scale (CD-RISC). *Depress Anxiety*. 2003;18(2):76-82.
 59. Strachan MD, Cash TF. [Self-help for a negative body image: A comparison of components of a cognitive-behavioral program](#). *Behavior Therapy* 2002(Spring); 33(2):235-251.
 60. Jarry JL, Ip K. The effectiveness of cognitive behavioural therapy for body image: A meta-analysis. *Body Image: An Inter J Research*, 2005;2, 317-331.
 61. [Winzelberg AJ, Eppstein D, Eldredge KL, Wilfley D, Dasmahapatra R, Dev P, Taylor CB](#). Effectiveness of an Internet-based program for reducing risk factors for eating disorders. *J Consult Clin Psychol*. 2000 Apr;68(2):346-50.
 62. Bryant RA, Moulds ML, Guthrie RM, Nixon RDV. The additive benefit of hypnosis and cognitive-behavioral therapy in treating acute stress disorder. *J Con Clin Psychol* 2007;73(2):334-340.
 63. Bisson JI, Shepherd JP, Joy D, Probert R, Newcombe RG. Early cognitive-behavioural therapy for post-traumatic stress symptoms after physical injury. *British Journal of Psychiatry*. 2004;184:63-69.
 64. Bisson J, Andrews M. Psychological treatment of post-traumatic stress disorder (PTSD). The Cochrane Database of Systematic Reviews 2005, Issue 3. Art No: CD003388.pub2.

65. Ehlers A, Clark DM. Early psychological interventions for adult survivors of trauma: a review. *Biol Psychiatry*. 2003;53:817-26.
66. March J, Silva S, Petrycki S, Curry J, Wells K, Fairbank J, Burns B, Domino M, McNulty S, Vitiello B, Severe J; Treatment for Adolescents With Depression Study (TADS; Team. Fluoxetine, cognitive-behavioral therapy, and their combination for adolescents with depression: Treatment for Adolescents With Depression Study (TADS) randomized controlled trial. [JAMA](#). 2004 Aug 18;292(7):807-20.
67. Smith MT, Perlis ML, Park A, Smith MS, Pennington JY, Giles DE, Buysee DJ. Comparative meta-analysis of pharmacotherapy and behavior therapy for persistent insomnia. *Am J Psychiatry*. 2002;159:5-11.
68. Carroll KM, Nich C, Ball SA. Practice makes progress? Homework assignments and outcome in treatment of cocaine dependence. *J Consult Clin Psychol*. 2005 Aug;73(4):749-55.
69. [Holzman AD](#), [Rudy TE](#), [Gerber KE](#), [Turk DC](#), [Sanders SH](#), [Zimmerman J](#), [Kerns RD](#). Chronic pain: a multiple-setting comparison of patient characteristics. *J Behav Med*. 1985 Dec;8(4):411-22.
70. Wiederhold BK, Wiederhold MD. Virtual reality therapy for anxiety disorders: Advances in evaluation and treatment. Washington DC; American Psychological Association: 2005.
71. [Saxe GN](#), [Ellis BH](#), [Kaplow JB](#). Collaborative Treatment of Traumatized Children and Teens: The Trauma Systems Therapy Approach. 2007; Guilford Press: New York, NY.

Table 1: Research Priorities for Psychological Health

- Replication, extension and dissemination of social skills programs in children and adults.
- Studies to assess cognitive based therapy for body image distress;
- Evaluation of the efficacy of the Behavioral Enhancement and Skills Tools (BEST) program;
- Clarifying the etiology of psychological distress (body image, posttrauma, depression), the mechanisms involved in its acquisition and maintenance, and the pathways by which such impairments limit activities and restrict participation.
- Improved understanding of the interaction between physiologic stressors and psychological/emotional stressors their synergistic effect on outcome.

Community Integration

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Topic: Burn survivors tell us that community integration with its accompanying social anxiety and social strain is arguably the single most important issue for burn survivors. Their overall sense of well-being and satisfaction with life are contingent on the ease with which they interact with the non-burned community. Their long-term psychosocial adaptation depends in large part on their successful integration into community life.

Background: Integration implies transition; for the burn survivor, it means leaving the protection of the hospital and the role of 'patient' where one's life is managed by health care professionals and now having to interact with a multitude of non-burned people who are unfamiliar with the aftermath of burn injury. It means that the burn survivor and the family of the burn survivor must re-assume the responsibility of managing their own lives without those hospital based professionals to guide them. Burn survivors¹ say they feel very self-conscious and anxious about relating to other people. They themselves are unaccustomed to their changed physical appearance, and feel sad and angry about how they look. They feel protective of their families, and they are not necessarily helped by non-specific suggestions that their situation will improve with time. Families of burn survivors (particularly siblings) report distress¹ and feel that they bear an additional load; outpatient visits represent an additional burden, yet they miss the support of the in-patient burn team.

¹ The statements reporting concerns of burn survivors and their families are based on actual statements made by clients of *Changing Faces*, a UK organization that provides advocacy, consultation, and research for persons with disfigurement.

Survivors in general find little assistance from burn care professionals in their struggle to live their lives with burn scar disfigurement beyond discharge from their acute hospitalizations, though those who access the support of burn survivor organisations like the Phoenix Society applaud the empowerment they receive. Survivors say that everyday social interactions represent a real challenge. Going shopping, being in public places and on public transport means being stared at and dealing with curiosity. The responses of others contribute to difficulties in re-defining their self-image and self-worth. They would like assistance in learning how to deal with these situations and they would like the public to be better educated about burns and disfigurement.

Although school re-entry programs receive a generally positive press from both survivors and schools, the desire for ongoing support (rather than a one-time school visit) has been expressed; adult survivors express frustration at having little or no assistance in obtaining and maintaining employment.

What we do Know

The knowledge about integration among burn professionals exists on two levels: first, what we think we know because we have heard it repeatedly (examples are offered above), and second, what we can glean from systematic research studies. The latter knowledge is far more limited than the former.

Most research in this area has focused on “psychosocial adjustment” rather than specifically on integration. Many studies have reported that most burn survivors eventually adjust well based on performance on standardized self-report measures.²⁻⁷ However, 20-30% of adult burn survivors demonstrate moderate to severe psychological and/or social difficulties.^{1,2} The incidence of psychopathology among children is approximately the same as that for adults, but about 50% have diminished competence, especially social competence.^{7,8} A significant minority of adult burn survivors report a diminished quality of life, including dissatisfaction with appearance and social or occupational difficulties.⁹⁻¹³ Burn injury often leads to at least transient difficulties in social involvement¹¹⁻¹³ and vocational activity, with 50-60% of individuals requiring a change in employment status.⁹ Decreased sexual satisfaction, particularly for women, may also occur and appears to relate to physical changes and body image more than burn size or location.¹⁰

Researchers have yet to determine a “best model” for assessing adjustment. Many factors seem to contribute to or predict adjustment. Certainly pre-burn mental status predicts adjustment post-injury,^{14, 15} but other factors that have been indicated as predictors are functional limitations, the valence or salience of appearance concerns and functional limitations, temperament, family environment, social support, other stressors, and time post-injury.¹⁵

Burn researchers are only beginning to tease out specific problems that impede community integration and are commonly experienced by burn survivors. Data¹⁶ support that 13-65% of an adult sample report significant emotional problems in the first 12 months after discharge, and that 30-40% think they would benefit from professional support. As many as 40% need specialist support at 2 years post-discharge. There is some evidence of greater distress just prior to discharge, during the first months after hospital discharge, and at about 18-24 months as the survivors become aware of the permanence of their burn scars. About 30-50% of burned adults complain of chronic and pervasive “social strain”, i.e. difficulties coping with the behavior of others or with their own behavior in social situations¹⁵. As many as 50% burned children lack adaptive strategies for social reintegration.

Data also support a need for assistance for families. We have data from studies of resilience in burned children that indicate the quality of family environment to be of prime importance for positive adjustment, but we do not know how best to help families achieve that environment.¹⁷ We do know there are pre-existing problems in as many as 30% of the families of burn survivors and dysfunctional family dynamics post-burn in up to 36%.¹⁶

What is not Known

There are no true longitudinal studies of psychosocial aspects of burn recovery and rehabilitation. Without such studies we are limited in being able to tell survivors how long it may take for them to experience a stable sense of identity, self-worth, and well-being. We also have scant information on lifespan issues for burn survivors or on ethnic differences. In terms of

initial steps toward integration, we don't know how best to assist patients and/or offer support as they leave the acute hospitalization. Few studies have elucidated the needs of families, either acutely or long-term. We need to know their needs and to develop and evaluate interventions to assist them.

Although burn survivors frequently report difficulties in social situations, more studies of social anxiety or social comfort among burn survivors are needed. We need to study the prevalence of these difficulties and the contributory factors, as they seem to be precursors to other forms of psychopathology¹⁸ such as the anxiety disorders reported by long-term (more than 2 years post injury) adolescent and adult burn survivors.^{19,20} If, as burn survivors tell us, these are common and debilitating, we need to develop and evaluate treatment interventions to address the problems. There have been some positive developments in our knowledge about body image satisfaction²¹⁻²⁴, but most of this literature is based on findings in other populations; little has been published about these issues in burn survivors. We do now have a validated scale to assist us in the studies of stigma.²⁵

Few interventions to help with issues of integration or self-perception or social comfort have been reported in the burn literature. Those that have been reported are rarely evaluated to determine efficacy. Cognitive Behavioral Therapy, often used, has been assessed in other settings. Social Interaction Skills Training has been assessed with adolescents and adults.^{9,26} Camps for burned children have been evaluated for contributions to self esteem on a limited basis.^{27,28} Although many school re-entry programs have been reported, none have been truly evaluated to know if and how they may help. Work re-entry programs have rarely been reported, much less evaluated.

In short, we are just beginning to understand the detail of the difficulties involved in the community integration of burn survivors and what kind of interventions are important to assist the process. We need to know how best to deliver the interventions; e.g. via web sites, literature, support groups, self-help manuals, etc have all been suggested.

Conclusion: The five areas of research to be nominated for high priority in the field of community integration for burn survivors are:

1. Refine the model of adjustment for burn survivors and identify the key contributory factors in adjustment for most survivors. Only with more precise definition of adjustment and identification of salient aspects (e.g. social anxiety, perceived stigma, body image) can we address need most effectively.
2. Complete longitudinal studies (5-10 years post-burn) of both adult and children who survive burns. Recovery occurs over many years and issues become more or less salient with changes in the life span. We need to determine recovery curves for different age groups, sizes of burns, ethnic groups, psychological profiles, etc. Knowing the pattern of needs and recovery for both adults and children would assist both health care professionals and survivors to prepare for integration.
3. Evaluate and refine existing interventions, and as we determine need, we must develop, evaluate and refine new interventions.
4. Evaluate methods of delivery of our interventions.
5. In addition, we need to better understand why the public react negatively or with curiosity to seeing people with burn scar disfigurement. And then...we need to develop and evaluate public education initiatives.

Burn survivors can and many do eventually lead happy lives, but often with considerable effort and with many obstacles to overcome; and not all reach that state of contentment that we would hope for. There is much that needs to be known in order to change this situation.

Lastly, research on the psychosocial aspects of burn care has been funded at levels far lower than many other areas of burn research. Funding for re-integration programs has been poor historically in all countries. Thus—and finally—we need to address yet another area of research—and perhaps this actually should become a top priority—i.e. to examine and model the macro-economic costs and benefits of assisting (or not assisting) burn survivors to integrate productively into their communities.

References:

1. Phillips C, Rumsey N. Considerations for the provision of psychosocial services for families following paediatric burn injury – a quantitative study. Burns (in press 2007).
2. Patterson DR, Everett JJ, Burns GL, Marvin JA. Hypnosis for the treatment of burn pain. J Consult Clin Psychol 1992; 60: 713-17.
3. Faber A, Klasen H, Sauer E, & Vuister F. Psychological and social problems in burn patients after discharge: a follow-up study. Scand J Plast Recon Surg 1987; 21(3): 307–9.
4. Tarnowski K, Rasnake L, Linscheid T, & Mulick J. Behavioral adjustment of pediatric burn victims. J Pedia Psychol 1989; 14: 607–15.
5. Blakeney P, Meyer W, Robert R, Desai M, Wolf S, & Herndon D. Long-Term Psychosocial adaptation of children of children who survive burns involving 80% or greater total body surface area. J Trauma Injury: Infection & Critical Care 1998; 44(4): 625-634.
6. Sheridan RL, Hinson MI, Liang MH, Nackel AF, Schoenfeld DA, Ryan CM, Mulligan JL, Tompkins RG. Long-term outcome of children surviving massive burns. JAMA 2000; 283(1): 69 - 73.
7. Meyer, III, WJ, Blakeney, P, Russell W, Thomas, C, Robert, R, Berniger, F, Holzer, III, C. Psychological problems reported by young adults who were burned as children J Burn Care & Rehab 2004; 25: 98-106.
8. Blakeney P, Meyer W, Moore P, Broemeling L, Hunt R, Robson M, & Herndon D. Social competence and behavioral problems of pediatric survivors of burns. J Burn Care & Rehab 1993; 14: 65–72.
9. Blakeney P, Thomas C, Holzer C, Rose M, Berniger F, Meyer WJ. Efficacy of a short-term social skills training program for burned adolescents. J of Burn Care and Research, 2005; 26(6):546-555.
10. Korloff B. Social and economic consequences of deep burns, in Wallace AB, Wilkinson AW (eds): Research in burns: Transactions of the 2nd International Congress on Research in Burns. Edinburgh, Scotland, Livingstone, 1996.
11. Tudahl LA, Blades BC, Munster AM: Sexual satisfaction in burn patients. J Burn Care & Rehab 1987; 8: 292-293
12. Bernstein NR. Objective bodily damage: Disfigurement and dignity, in Cash TF, Pruzinsky T (eds): Body Images: Development, deviance, and change. New York, Guilford, 1990.
13. Rosenberg M, Blakeney P, Robert R, Thomas C, Holzer III, C, Meyer III, W. Quality of life of young adults who survived pediatric burns. J of Burn Care & Research, 2006,27(6):773-778.
14. Patterson, David R. PhD; Finch, Carmel P.; Wiechman, Shelley A. PhD; Bonsack, Rhonda PhD; Gibran, Nicole MD; Heimbach, David MD Premorbid Mental Health Status of Adult Burn Patients: Comparison with a Normative Sample. J of Burn Care & Research, 2003, 24(5): 347-350.
15. Fauerbach JA, Lawrence JW, Haythornthwaite J, McGuire M, & Munster A. (1996). Preinjury psychiatric illness and postinjury adjustment in adult burn survivors. Psychosom 1996; 37(6): 547-555.
16. National Burn Care Group, UK Results of national study of burn care in the UK. Results found at <http://www.nationalburncaregroup.nhs.uk>
17. Blakeney, P., Portman, S., Rutan, R. (1990). "Familial values as factors influencing long-term psychological adjustment of children following severe burn injury". J Burn Care & Rehab. 11(5):472-475.
18. Ginsburg, G. S., La Greca, A. M., and Silverman, W. K. Social anxiety in children with anxiety disorders: relation with social and emotional functioning. J Abnorm Child Psychol. 1998;26(3):175-85.
19. Meyer, W. J., Russell, W., Blakeney, P., Thomas, C., Robert, R., Holzer, C. Incidence of Major Psychiatric Illness in Young Adults who were Burned as Children. Proceedings of the 35th Annual Meeting for the American Burn Association, Vol. 24, Miami, FL, 2003.
20. Blakeney P, Thomas C, Berniger F, Holzer CE, Meyer W. Long term psychiatric disorder in adolescent burn survivors. Proceedings of the ABA 33rd Annual Meeting, Vol. 22, Abstract #99, Boston, 2001.

21. Pruzinsky, T.; Doctor, M. E. Body images and pediatric burn injury. Tarnowski, K. Behavioral aspects of pediatric burns. New York: Plenum Press; 1994. pp.169-91.
22. Fauerbach J, Heinberg L, Lawrence J, Munster A, Palombo D, & Richter D. The effect of early body image dissatisfaction on subsequent psychological and physical adjustment following disfiguring injury. Psychoso Med 2000; 62: 576 - 582.
23. Fauerbach JA, Heinberg LJ, Lawrence JW, Bryant AG, Richter L, Spence RJ. Coping with body image changes following a disfiguring burn injury. Health Psychol. 2002, 21(2):115-21.
24. Lawrence JW, Fauerbach JA, Heinberg L, Doctor M. Visible vs hidden scars and their relation to body esteem. J Burn Care Rehabil. 2004, 25(1):25-32.
25. Lawrence JW, Fauerbach JA, Heinberg LJ, Doctor M, Thombs BD. The reliability and validity of the Perceived Stigmatization Questionnaire (PSQ) and the Social Comfort Questionnaire (SCQ) among an adult burn survivor sample. Psychol Assess. 2006, 18(1):106-11.
26. Robinson E, Rumsey N, Partridge J. An evaluation of the impact of social interaction skills training for facially disfigured people. Br J Plastic Surg. 1996; 49: 281-289.
27. R Rimmer, GM Fornaciari, DM Caruso, KN Foster, RC Bay, JT Critt. The impact of a pediatric residential burn camp experience on burn survivor's perceptions toward self and attitudes regarding the camp community. Abstract presented at the 9th Cong Eurpoean Burns Assoc (EBA), Leon, France, 2001.
28. SL Gaskell. The impact of a burn camp on children's psychological well-being: a quantitative evaluation. European Burns Assoc, Leon, France, Abstract 2001.

Table 1: Research Priorities for Community Integration

- Refine the model of adjustment for burn survivors and identify the key contributory factors in adjustment for most survivors.
- Complete longitudinal studies (5-10 years post-burn) of both adult and children who survive burns.
- Evaluate and refine existing interventions, and as we determine need, we must develop, evaluate and refine new interventions.
- Evaluate methods of delivery of our interventions.
- Improve understanding of why the public react negatively or with curiosity to seeing people with burn scar disfigurement and then develop and evaluate public education initiatives.

Restoration of Function

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Topic

Restoration of function is crucial to the performance of activities of daily living, vocational and recreational activities as well as to community integration and psychosocial aptitude. Strategies to optimize restoration of function include both physical considerations as well as metabolic considerations that can significantly impact physical capacity. Given the breadth of this topic, Drs. Herndon and deLateur focused on two of the most critical facets of restoration of function: metabolic support of the burn patient and exercise/fitness.

Background

Advances in knowledge about effective means of providing early support for the hypermetabolic response to trauma have contributed significantly to the dramatic decrease in burn mortality during the past 20 years as well as benefiting early restoration of function for the individual with large burn injury. The hypermetabolic response that occurs in response to burn injury $\geq 40\%$ TBSA¹ and lasts for about 1 year post-burn² is characterized by a number of events that are life-threatening to the patient, e.g. tachycardia and cardiac dysfunction, increased cardiac output, increased resting energy expenditure, increased protein catabolism and peripheral protein wasting, hyperpyrexia, and increased lipolysis. The erosion of body mass that occurs with catabolism can lead to impaired immune function, decreased wound healing, pneumonia, pressure sores, and eventually death. Children with large burns suffer arrested vertical growth³. Bone formation is slowed, and bones are weakened⁴. Even when the patient survives, the debilitating effects of hypermetabolism delay and limit restoration of function for the patient.

What is Known About Restoration of Function

Acute and long-term (1 year post-burn) administration of certain anabolic agents has successfully modulated the effects of the hypermetabolic response. Recombinant Human Growth Hormone⁵, oxandrolone⁶, and propranolol⁷ have been shown to decrease resting energy expenditure, improve skeletal muscle protein metabolism, attenuate the erosion of lean body mass, attenuate increase in liver size, and decrease prevalence of infection. Additionally, bone mineral content has increased with the use of anabolic agents⁸ as has vertical growth in burned children⁴.

A recent study afforded by participation in a large multisite study⁹ allowed identification of 6 genes up-regulated and 2 genes down regulated with the administration of propranolol to burned children, suggesting the eventual possibility of targeting our interventions with greater specificity¹⁰.

Burn injury also results in severe deconditioning and fatigue that can significantly impact functional aptitude. A three-year outcome study at Harborview Medical Center in Seattle, Washington revealed an almost universal complaint of fatigue as a major barrier to return to work and other daily activities. This study examined energy expended by patients with major burns for given, progressive, submaximal external work loads, and found that they did not differ from the energy expended for those same loads by healthy, age- and sex-matched controls. In addition, strength of various upper and lower body muscles, such as the quadriceps, and the endurance index (ratio of the magnitude of the last of ten contractions to the first in a series of ten attempted maximal isokinetic contractions) were measured. However, this study did not measure the maximal aerobic capacity (VO₂max) of these burned patients or the controls so the overall fitness levels were not assessed. On average, with an endurance index of about 0.7, the burn patients did not differ from the controls, and thus did not demonstrate early fatigue of isolated muscles or muscle groups. What they did demonstrate was notable muscular weakness at discharge, 3, 6, 9, 12, and 18 months post-burn; they approached, as a limit, the strength of the age- and sex-matched controls only at 24 months. The study also found that patients with a major burn were "pulse-responders" in that, for any given external load, or for any given level of rate of oxygen consumption, burn patients had a higher heart rate than the controls. The pulse response to progressive, submaximal, external loads was linear within the range studied. The steepest line was for burned smokers. The lowest line was for nonburned nonsmokers. The lines for nonburned smokers and burned nonsmokers were identical, and fell between the extremes. The conclusion was that smoking results in the same, excessive pulse

response as does a major burn; the interaction between smoking and having a major burn was so striking that it seems likely that smoking is a contributor to the fatigue symptoms of those with major burns.¹¹

Exercise programs which seek to restore function lost through post-injury deconditioning have been found to be effective strategies to enhance recovery and rehabilitation in both children and adults. A 3 month in-hospital aerobic and strengthening exercise program designed for burned children ages 7-18 also has been shown to mitigate the effects of the hypermetabolic response¹². The children participating in this program had significant increases in endurance and muscle strength as compared to those children who received their prescribed rehabilitation program at home. They also required significantly fewer surgical releases than did the home exercise group¹³.

The results of this program were so convincing that a similar program with exercises incorporated into movement to music has been developed for children under the age of 7; thus far, the program is promising with the participants having significantly greater range of motion than the non-participating children. All children in both programs continue to receive standard of care rehabilitation exercises throughout the 3 months of the more intensive exercise program.

Exercise intervention programs in adults have similarly found to be effective in helping to achieve restoration of function. An exercise intervention, consisting of the addition of a 3-month, thrice-weekly session of treadmill walking, up to 30 minutes in duration, with a target heart rate of 60% of the heart rate reserve ($0.6 \text{ of the quantity } [HR_{\text{max}} - HR_{\text{resting}}], \text{ plus } HR_{\text{resting}}$), will be reported in the forthcoming supplement of the Archives of Physical Medicine and Rehabilitation, devoted to the topic of burn rehabilitation¹³. This study revealed that such an addition of exercise to usual care, which is tailored to the specific needs of the individual patient, had a large and robust favorable effect on the aerobic capacity of the recipients, and that it did not matter whether the intensity and duration of the exercise were on a work-to-tolerance basis or a work-to-quota (quota set by investigative protocol) basis.

However, the impact of exercise on recovery may be influenced by both patient and injury characteristics. For example, recent evidence suggests that women and men generally differ in their metabolic responses to incremental exercise¹⁴ and that gender differences in pulmonary function and exercise capacity serve to limit aerobic capacity and exercise tolerance among women¹⁵.

In summary, it has been shown that early intervention, begun during the acute treatment phase, has long-term implications for restoration of function. Treatment with anabolic agents and intensive exercise programs, alone and together, can successfully mitigate the effects of the hypermetabolic response to result in faster recoveries for patients with large burns. Patients so treated not only can leave the hospital sooner, but they are physically stronger; they can participate in their rehabilitation earlier, improve function more quickly, and begin the reintegration process as stronger individuals. There is early evidence that we can identify specific genes to be targeted for modification to enhance efforts to counter the debilitating effects of the hypermetabolic response.

What We Don't Know:

Pharmacologic Interventions: We have limited information about which patients will most benefit from which pharmacologic therapy. For some patients use of one anabolic agent may be preferential; for some, a specific anabolic agent may not be useful. Although we have thus far experienced no ill side effects, for some patients, an anabolic agent may even be harmful. We have little evidence to guide us in differentiating and choosing treatments. We need to know which patient characteristics, e.g. age, gender, or pre-existing conditions, indicate efficacy of one approach over others. Gene analysis suggests that other agents or techniques might be developed that would target with specificity certain genes for modulation, affording yet more efficiency in recovery.

Maintenance of Intervention Benefits: We need to know how to prolong the positive effects of treatment beyond the time the treatment is being applied. How can we help the individual who has done very well in the 3 month in-house program continue to exercise to maintain the advantages of strength and endurance? Exercise programs can be designed for specific

groups to assist them in continued participation; just as the movement to music seems to be effective in providing fun for young children, programs that provide more pleasure might be designed to motivate other groups who find no enjoyment in the standard aerobic and strengthening exercises. Finally, we yet have little evidence about the long term benefits of these early interventions. We hypothesize, but do not know, that such improvements help the survivor of large burn injury to better reintegrate into the community, i.e. to succeed in school, to pursue their chosen field of work, and to achieve a satisfactory quality of life.

Design of Exercise Programs:

While the benefits of exercise programs are clear, the optimal content of these programs requires further investigation. Could aerobic training, somewhat easier to quantify, actually result in strength development of individual muscles (based upon the principle of initial condition)? In addition, the optimal timing for initiation of an exercise program and the impact of age, gender and injury severity on patient compliance and program effectiveness all warrant additional study. Finally, the potential synergy of exercise programs and pharmacologic intervention (*i.e. beta blockade and/or growth hormone*) needs to be explored.

Specific Benefits and Mechanisms of Exercise Effects:

The relationship between patient fatigue and muscle weakness is not well understood. For example, could an exercise program that increased patient strength result in decreased fatigue/increased overall patient endurance (as opposed to the relative endurance of isolated muscle contractions)? Will patients with improved aerobic capacity be more likely to return to work? Is there a linear relationship (or, at least, a linear transient) between aerobic fitness and return to work? Is there a threshold level of fitness for return to work? Is the relationship between absolute fitness or improvement in fitness?

Conclusions: Top Five Priorities for Research in Restoration of Function

- 1) Design of Multicenter Studies to Determine Optimum Pharmacologic Therapies for Modulation of Hypermetabolic Response:** There are a number of pharmacologic agents with known benefits in restoration of function, yet better defining the optimal age and gender appropriate regimens remains a research priority. This information would likely be best gathered in the setting of a multi-armed prospective randomized trial. Likely, more than one trial would be needed to satisfactorily answer these questions
- 2) Prospective Studies to Better Define Optimum Exercise Regimens:** The benefits of exercise programs are quite clear, however more research is needed to define the duration and content that will best provide restoration of function. Again, there will likely need to be age, gender and injury severity specific considerations which will have to be defined over time.
- 3) Better understanding of the interaction between genetic and injury characteristics on hypermetabolic response and recovery potential:** The increasing sophistication of gene analysis technologies can increase our understanding of the impact of an individual's genome on their hypermetabolic response and injury recovery pattern. Better understanding of these interactions can allow for development of interventional strategies to try and optimize restoration of function.
- 4) Increased understanding of the interaction between functional restoration and community integration and psychological health:** Functional status clearly impacts work capacity and ability to achieve independence in daily activities—two important factors in community integration. Capacity for community integration, fatigue and energy level are all inextricably linked with psychological health.
- 5) Assess the successful translation and application of these in-hospital based exercise rehabilitation programs into community based (fitness centers, YMCA's) exercise rehabilitation programs.**

These questions, of course, only scratch the surface of what we don't know (but need to know) about the rehabilitation of patients with major burns.

REFERENCES

1. Hart, D.W., Wolf, S.E., Chinkes, D.L., Gore, D.C et al. Determinants of skeletal muscle catabolism after severe burn. *Ann Surg* 2000;455-465.
2. Hart DW, SE Wolf, R Mlcak, DL Chinkes, et al. Persistence of muscle catabolism after severe burn. *Surgery* 2000;128:312-319.
3. Low JFA, Herndon DN, Barrow RE. Growth hormone ameliorates growth delay in burned children: a 3-year follow up study. *Lancet* 1999; 354:1789.
4. Klein GL, Herndon DN, Goodman WG, et al. Histomorphometric and biochemical characterization of bone following acute severe burns in children. *Bone* 1995;17:455-60.
5. Przkora, R, Herndon, DN, Suman, OE, Jeschke, et al. Beneficial effects of extended growth hormone treatment after hospital discharge in pediatric burn patients. *Ann Surg* 2006;243:796–803.
6. Murphy, KD, Thomas S, Mlcak RP, Chinkes, DL, et al. Effects of long-term oxandrolone administration in severely burned children. *Surgery* 2004;136:219-224.
7. Herndon DN. Hart DW. Wolf SE. Chinkes DL. Wolfe RR. Reversal of catabolism by beta-blockade after severe burns. *NEJM* 2001;345:1223-9.
8. Hart DW, Herndon DN, Klein GL, Lee SB, et al. Attenuation of muscle catabolism and osteopenia with growth hormone therapy after severe burn. *Ann Surg* 2001; 233:827-834.
9. Cobb, JP, Mindrinos, M N, Miller-Graziano, C, Calvano, SE, Baker, HV, et al. Application of genome-wide expression analysis to human health and disease. *Proc Natl Acad Sci U S A.* 2005;102:4801.
10. Herndon DN. Dasu MR. Wolfe RR. Barrow RE. Gene expression profiles and protein balance in skeletal muscle of burned children after beta-adrenergic blockade. *Am J Phys - Endocrinology & Metabolism.* 285(4):E783-9, 2003.
11. deLateur BJ, Giaconii RM, Alquist AD; Fatigue and performance: data from normal adults and from patients with neuromuscular and musculoskeletal syndromes; response to training. *Proceedings of the AAEE diagnostic program, Thirty-fifth Annual Meeting,* 1988.
12. Suman OE, Thomas SJ, Wilkins JP, Mlcak RP and Herndon DN. Effect of exogenous growth hormone and exercise on lean mass and muscle function in children with burns. *J Appl Physiol* 2004;94: 2273-2281.
13. Celis, MM, Suman, OE, Huang, TT, Yen, P, Herndon, DN. Effect of a Supervised Exercise and Physiotherapy Program on Surgical Interventions in Children with Thermal Injury. *J Burn Care Rehabil* 2003;24:57-61.
14. deLateur BJ, Magyar-Russell G, Bresnick MG, Bernier F, Ober MS, Krabak BJ, Ware L, Hayes MP, Fauerbach JA. Augmented exercise in treatment of deconditioning from major burn injury. Submitted and in review. *Arch Phys Med & Rehabil Supplement (in press).*
15. Kang, J, Hoffman, JR, Chaloupka, EC, Ratamess, NA, and Weiser, PC. Gender differences in the progression of metabolic responses during incremental exercise. *J Sports Med Phys Fitness* 2006;46:71-8.
16. Harms, CA. Does gender affect pulmonary function and exercise capacity? *Respir Physiol Neurobiol* 2006;151: 124-131.

Table 1: Priorities for Research in Restoration of Function

- **Design of Multicenter Studies to Determine Optimum Pharmacologic Therapies for Modulation of Hypermetabolic Response**
- **Prospective Studies to Better Define Optimum Exercise Regimens**
- **Better understanding of the interaction between genetic and injury characteristics on hypermetabolic response and recovery potential**
- **Increased understanding of the interaction between functional restoration and community integration and psychological health**
- **Assess the successful translation and application of these in-hospital based exercise rehabilitation programs into community based (fitness centers, YMCA's) exercise rehabilitation programs**

The Burn Survivor Perspective

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Introduction

The burn survivor's perspective is critical in helping focus the priorities for burn research over the next ten years. The goal of medical science is to improve outcomes and the lives of those we serve. As individuals who have experienced a burn injury, burn survivors can provide an important and unique perspective. There have been numerous advances in burn care and as was discussed in the first two days of this State of the Science conference, yet there is a lot of work yet to be done. Each of us survivors has tremendous respect and gratitude toward the burn team, and the following comments are made with the goal of improving care for current and future burn survivors. Real progress can happen if we work together to develop the goals, knowledge base, and then ultimately implement the available and proven interventions as a standard of care.

The purpose of the burn survivor panel discussion was to provide a personal perspective of the priorities in burn care research. The collective burn survivor community is a wealth of information---if we listen. Both Erin Mounsey and Chris Gilyard are burn survivors with a point of view that will help demonstrate some common themes we hear across the country at the Phoenix Society for Burn Survivors. They are two individuals burned some 20 plus years apart and both believe that psychosocial rehabilitation of patients should be the priority in patient care and thus the priority for research.

The first thing I must tell you is that I am not a researcher, but I do value the importance of a scientific approach to the care we provide. I will share my perspective from several vantage points to demonstrate some of the themes that are common for many people that I speak to regarding burn recovery. First, as someone who has been in the bed as a patient receiving burn care I learned that the burn team helps to lay a strong foundation for the healing necessary both physically and emotionally. Not only were compassionate care givers key to the progress physically, but they helped to create a safe place for emotional healing to start. I only wish I could have taken the burn team with me out into the world as I transitioned back into my community and my peer group. It is there that I stumbled and lacked the necessary information, tools (to manage stares and questions) and support. The psychosocial reentry was the most difficult part of my personal recovery.

I also spent seven years at the bedside as a burn nurse working to meet the needs of patients and families. At times I felt very inadequate as patients and families asked the tough questions about their future and how to handle the reality of their disfigurement. The easy part for me was providing the "physical care". I did not receive specific training during my orientation nor was I prepared for the psychosocial issues that the burn patient and family may experience. As a caregiver I lacked the tools to support this part of recovery beyond what I learned in my nursing program. Because I had "been there" I was able to offer some hope and examples of how I handled life after a burn injury though it was just one perspective. It was interesting to me that the patient and family would receive this information from me in a different way (than from other staff members). It was my first experience of the power of peer support.

One of the most dynamic educational experiences for me as a new nurse was attending World Burn Congress. I learned there is not one way to do this thing called "burn recovery" and that many types of resources are needed at different times in the recovery process. I realized that my own personal biases of what was needed for successful burn recovery could get in the way of what I provided for the patients I cared for. An example of this was the belief that corrective cosmetics were just a way to hide and not deal with the reality of the burn. That was my perspective. After attending World Burn Congress, I met Barbara Kammerer Quayle and many others who shared that for them it was a necessary tool to take that first step – it was a tool to help them gain confidence to get back out there socially. Shortly after that experience, we trained several staff on the burn center to assist

in this area of psychosocial rehabilitation.

I transitioned to the manager of the burn center and fought the battles to keep the burn program and used tools such as verification to improve the quality of care on our center. We were able to incorporate several programs to assist with social reentry. We had burn camp, burn survivor reunions, monthly support groups, image enhancement, a social skills program, and sent a group each year to World Burn Congress. From this perspective it appeared like we were meeting the needs of the patients and families. Like many units these psychosocial rehabilitation programs were a “add on” to staff roles above and beyond their hours. No one was ultimately accountable for the success, evaluation or the succession of these programs. If the staff who took this on left the unit, so did the support programs. The programs were not embraced by the whole team and often were not offered.

Then I took the role as the Executive Director of the Phoenix Society for Burn Survivors. Despite tremendous progress in the medical care of burn survivors, I quickly realized there are a substantial number of individuals who experience significant long-term psychosocial adjustment difficulties, particularly those individuals who have changes in appearance. Though these adjustment difficulties (e.g., coping with staring and teasing when out in public, body image changes, relationship issues) do not necessarily meet diagnostic criteria for psychopathology, they do significantly affect quality of life.

With the reality of decreasing length of stays and the limit of human resources, it is clear that the burn center is just the starting line and that much of the recovery happens out in the community and long after our contact with patients and families. When I started answering the 800 line and email requests at the society, a whole new perspective of the long term issues (beyond two years) of survivors was realized. The other thing I found as I worked with numbers of organizations around the country - efforts are being made in the area of psychosocial support within burn centers, non-profits and rehabilitation centers, but often they occur in isolation and without the support of research. At this time there seems to be a disconnection between those who are doing research in this area and those who ultimately provide the services and interventions to assist in the psychosocial rehabilitation.

SOAR (Survivors Offering Assistance in Recovery) program was developed to increase the access of peer support to the burn survivors and their families. This type of support is not offered consistently in the rehabilitation of those with burn injuries. For nearly 30 years our organization has been providing peer support based programming. In my 25 years in burn care, I have been sold on the power of peer support. Do we have the research to support the efficacy of these efforts? The answer is no. We need to partner with the research community, and are willing to do so as we move forward to set goals for research in the next ten years. The SOAR program is now in the process of implementation in over 30 burn centers, and it provides a standardized model to study. What we need is to work together to complete the research on this program. We need to know if it has a positive impact on the psychosocial rehabilitation, when is it best to offer peer support and a whole host of other questions.

A resource that we are about to launch is another significant opportunity for multi-center research. The Journey Back is a school reentry resource that was developed based on an identified need. Parents, teachers and burn care professionals all have contacted us for information and resources to assist in the important transition back to school after a burn injury. School Reentry is not a new concept. Is it a standard of care offered to all burned children? It is not.

Many burn centers and foundations have been providing school reentry for years, yet there is not a well documented, accepted program out there for general use. We approached many of our partners in burn care to try and identify a tool we could provide to

our members. When we could not find one packaged and ready to use, we worked to develop a resource based on agreed best practice. The content has been reviewed by over 20 burn care professionals, mental health care providers, parents and teachers. Would it be beneficial to have a standardized approach within burn care based on research? Definitely. Again we hope to partner with those who are experts in the research area as we implement this program. It will only improve the resource and the justification for school reentry as a standard of care offered for burn injured children. Like many of you, I assumed that this was offered to most of the children who are treated in burn centers in our country. The reality is that it is not

Social challenges, the impact of changed appearance as well as the effect trauma has on relationships are critical areas for research in the next 10 years. There are a number of high quality interventions out there. We need to accomplish a collaborative approach to research the psychosocial rehabilitation interventions already available. Only then can we make progress toward making psychosocial rehabilitation a standard of our care. If we move beyond our own organizational boundaries and explore the most practical and efficient way to deliver these types of interventions we will have a tremendous impact on the quality of life of those we serve.

Below the personal perspectives and experiences of two burn survivors are presented. The purpose of their stories is to articulate current limitations in burn care and identify areas for future research which may positively impact the life of burn survivors.

Erin Mounsey

My story is presented as an example of the harsh reality that can exist for some burn survivors after hospitalization and highlights several areas which could truly benefit from research and program development. It is imperative that more research be conducted in the fields of psychosocial rehabilitation, recovery from facial disfigurement and the effects of intervention programs. The importance of conducting this research is exemplified by how disastrous my recovery became when these tools were not applied. It is also interesting to note how significantly my recovery improved as I became exposed to the burn community and some of the psychosocial skills and programs available at events like World Burn Congress.

Seven years ago, on a beautiful, sunny tuesday in late October, I awoke with every intention of changing things in my life. Little did I know what an absolutely devastating and life altering change was in store for me. Throughout that summer I had been working on a home remodeling project that had begun to stagnate as other priorities took precedence. That day I was focusing on refinishing the oak hardwood floors in the living room.

After sanding the floors, my partner and I started using lacquer thinner to remove any remaining varnish and to tack the floor before applying polyurethane. We properly ventilated the house, wore respirators and took precautions to dissipate the fumes. When I was just about finished with the process I poured out the last of the thinner that was left in the can, making a larger puddle than previously. The puddle crept across the floor and towards a wall mounted gas heater. The fumes that roiled off the front of the puddle ignited off the pilot light and instantly the interior of the house was engulfed in flames. The air itself was on fire. The air was fire.

The experience of being burned alive was truly surreal. So surreal that I almost laughed as I tried to wrap my mind around the life threatening situation that had instantaneously appeared all around me. The empty can of lacquer thinner exploded. The compression from the explosion tossed my partner through the glass paned front door. Even though I was peripherally able to comprehend her exit I, reacting to my flight response, darted to the back door. When I grasped the brass door knob, it was already far

too hot to touch and I watched as the skin of my fingers seared off.

I was trapped by the large oak door, which had a complex locking mechanism in addition to the door knob. I turned to look back to the front door, feeling the amazing heat across the left side of my face. The site of the the air throughout my house boiling with the wicked hues of orange, purple and red with such an intense area of concentration directly between me and the front door, has been a long standing image of emotional trauma. The utter desolation and desperation that accompanied that sense of being completely trapped by certain death, with no one to save me but myself, resonated in flashbacks for years to follow.

I snapped from my desolation and doubled back into a bathroom to my left. Knocking out the high window and boosting myself up off the rim of the toilet, I made a hasty and harried escape. As I dangled, straddling the glass sharded sill, I screamed out to the world that I needed help. My bellowing caught the attention of some neighbors. I fell to the ground. And as I rolled out the remnants of my fire torn clothes across the lawn, paramedics were called and neighbors came to the aid of my partner and I.

Just like that my world was turned upside down, inside out and spun all around. I was unable to even imagine at that point the depths of change and uncertainty that had consumed my reality. In a moments time, I had suffered severe burns over 80% of my body, mostly full-thickness.

My experience with what was modern burn care, was for the most part positive. At least that is the way I seemed to perceive it at the time and the way I continue to consider it today. The pain management and amnesiac medications made what must have been a horrifically difficult seven months of severe burn recovery seem like a surmountable challenge without precedence. I just simply awoke each day, after the medically induced coma, to the unknown and did as I was told. Or, at least submitted to what I was instructed would be happening to me.

It was an experience filled with excellent pain management techniques, amazing burn care, exceptional therapy and superb management of infections and collateral reactions. Over the years, I have had the opportunity to go back and review medical records from those months with family members that were there. In my reflections I am consistently amazed that all of the varied and multiple life threatening obstacles were managed in such a way as to provide me, once again, with an opportunity at life.

While still in the hospital, there was an excellent timing and environmental set-up to the advent of me seeing my facial scarring for the first time. The response to my adverse reaction to that experience was also exceptional. There was a trained mental health professional in my ear for about a week afterwards until I had sufficient opportunities to grieve and begin to accept this new reality.

My hospitalization went as well as could be expected under the circumstances and I learned to cope with my facial disfigurements while there. But, the hospital was a safe zone where artificial forms of acceptance and untried coping skills were relied upon.

With the loss of my face I felt as though I had lost my identity and suffered a sincere disconnect with my sense of self. This was one of the most difficult losses to grieve and accept. I suffered a tremendous amount of long-term psychosocial adjustment difficulties as I struggled to overcome this loss.

Seven months later when I was healthy enough to leave the hospital I felt that everything was going to be just fine. Just fine considering I was recovering from a severe burn from head to toe. I was too medicated and my family was too worn out from the trial of the preceding months to comprehend what we were in for. There were struggles as I

assimilated into the urban community around the hospital, but nothing that I was not able to overcome.

It was then time to return to the small rural town in southern Colorado that was my home. I had goals of returning to operating my business, rebuilding my house and dreams of a happy reunion with my fiancée, friends and family. This was not to be the case. My goals and dreams quickly dissolved into a bottomless nightmare.

While I was still in the hospital my fiancée had fallen out of love with me when faced with the prospect of disfigurements and disabilities. By the time I returned home, bandaged and still healing in so many different ways, she had already begun taking steps to sever ties. Everything in my world, once again, fell apart and I began a spiraling descent into that nightmare. Far from the safety and security of the burn care team and my hospitalization, I slipped away.

Post Traumatic Stress Disorder became more and more a part of my reality as it slowly entered my psyche under the guise of “a normal reaction to a series of unfortunate life events”. A year after my burn, when I moved into an apartment of my own, the severe trauma, tremendous loss and subsequent isolation became too much. It was more than my limited set of coping skills could handle. I suffered a form of insanity. It is possible that PTSD was identified, but there was no effective intervention. All the right conditions for PTSD were present for quite some time, but when it was identified that my psychosocial reaction was not a positive one, it was too late.

By January, I was in the County Jail facing a four year sentence in State Prison. It was too late. Psychosocial interventions or behavioral enhancement programs that may have been an option to help treat the PTSD and my difficult psychosocial adjustments had not been tried.

Within a couple months of the start of my incarceration, the Phoenix Society sent me a package containing information on; the burn recovery process, PTSD, the path of other survivors' recovery and other burn resources. Prior to that point I was convinced that I had suffered the worst burn ever and I was suffering on a level never experienced before. My eyes had been opened to a whole world of burn survivors. I was able to read about survivors that had suffered in ways that I could relate to. The tools that they had used in their recovery were right there for me to glean. Finally the resources that I needed to help me through my grief and recovery process were available to me. Over the next three years I studied the resources that I was able to find through this organization and I made great strides in my recovery.

When I started my reintegration process after leaving prison some of the same psychosocial problems began to resurface. Things were much more manageable with some of the new coping skills that I had developed, but I was still struggling.

One of the areas that was causing the greatest distress was intimacy. I had learned to love myself as a burn survivor and I was rejoicing in some of the amazing personal gifts that were a byproduct of this tragedy. Yet, I was feeling an emptiness from experiencing this life alone. The scarring and severe changes allowed so many doubts to alter my body image. I had no idea how to even approach the possibility of developing a relationship. I had met some people that I would have liked to ask out but I recoiled in fear. I was genuinely concerned that someone might be insulted to be asked out by someone like me.

I began attending World Burn Congress that year. That first experience was absolutely revolutionary and life changing. Within a five day conference I had been transformed. I was sent away with so many new tools and a sense of such utter self confidence. Break-out sessions on relationships and intimacy provided some of the simplest but absolutely necessary tips, techniques and messages on overcoming my

struggles.

Today life is so different than the devastation and desolation that overwhelmed me after leaving the hospital. I know from many acquaintances in the burn community that my psychosocial rehabilitation difficulties are not isolated. This is commonplace in the lives of burn survivors. These struggles don't often manifest themselves with the extremes that occurred in my life, but the difficulties and the pains are just as profound.

I share my story to help illustrate that the struggle to survive a burn injury continues long into the post-hospitalization stage. It is not enough that the burn care profession researches to improve the survival rate for severe burns or to minimize scarring. There must be some collaboration with the burn community to improve research into the fields of psychosocial rehabilitation, recovery from facial disfigurement and the effects of intervention programs.

Chris Gilyard:

I am a burn survivor of 28 years and have worked as a burn care professional for the past 6 years. I want to mention a few things about my burn experience, primarily as a reference point for the progress that burn care has made in the past 30 years.

Soren Kierkegaard said, "Life is lived forward, but understood backward." It is looking back to the past that we understand the impact of education and research on the future of burn care. 28 years ago burn care was, from a patient's perspective, archaic. I was 17 years old when I was burned & had deep 2nd & 3rd burns to 21 % of my body, primarily to my back & face. Here are a few notable examples of progress:

- 28 years ago, drug therapy was relatively conservative. I can still recall vividly the pain and trauma of the tub room. Today we are much more proactive, liberal and understanding with pain medication and pain management.

- 28 years ago, grafting was performed weeks & months out from the initial burn injury. My face was grafted after 3 ½ weeks and my back was grafted two weeks later. Today, with the same burns, I would probably be totally grafted by two weeks out.

- 28 years ago, I was an inpatient for two months. Today, I could easily be discharged before the end of a month. It's easy to see that in the past 28 years, the science of burn care has progressed by leaps and bounds.

But while the physical pain my burn caused was unbelievable, the emotional pain was equally devastating. I remember the first two times I saw myself. The first time, a nurse asked me if I wanted to see myself before I was grafted. She caught me as my knees buckled and I almost fainted. The second time was a week after I was grafted. I looked at myself and thought, "who is ever going to love me?"

A few days later the Occupational Therapists came in carrying a transparent face mask and said this is what we use to keep facial scarring to a minimum. They told me I would have to wear it for one to two years. I laughed at them. I knew how people were treated who had any cosmetic difference; they were laughed at, teased and stared at. But, I was afraid to not wear it. So they made me a mask and I went home.

Everything I was afraid of happened. No one prepared me for what I would experience. No one talked to me about being stared at, teased, laughed at. I didn't meet another person who wore a face mask, or even had a facial burn close to what I had, for over a year.

Today, 28 years later, when people go home with facial or other visible burns, they often times are still NOT prepared for what to expect or how to deal with it.

Twenty-eight years ago, there were no school or social re-entry programs, there were few support groups, newsletters or camps. Websites and chat rooms were unheard of. Conferences for adults were a dream. I truly believe that if I had had those resources available to me then, ten years after my burns I would not have started having flashbacks of the burn unit, suicidal thoughts and panic attacks for fear of getting burned again. But, as previously quoted, “Life is lived forward, but understood backward,” and by looking back, I was able to address the issues that needed addressing and I was able to begin looking forward and utilizing my experience to make a difference for others.

Today I work as a Burn Support Representative at the Regions Hospital Burn Center offering support, education and coaching for our survivors and families, as well as implementing programs which promote positive psychosocial re-integration:

- Burn Support Representative: Offering consistent support, education and coaching for our burn survivors and families. Implementing numerous psychosocial rehabilitation programs, such as 3 support groups (burn, electrical injury & necrotizing fasciitis), the BEST program, and SOAR.

- The BEST program (Behavioral and Enhancement Skills Training), dealing with social re-entry, staring, questions and teasing. The program offered a formatted way to address these problems. It is an tool invaluable when working with survivors who are struggling with some of these psychosocial adjustment issues. As burn professionals, knowing what we know today, we have no excuse to not offer this material to our patients.

- The SOAR program (Survivors Offering Assistance in Recovery). Though I try to visit with as many of our inpatients as I can, I am only one part-time representative. Additionally, there are just times when a man would rather meet with a man, or someone from a house fire would rather visit with someone burned in a similar manner. That's the beauty of this program; we can match people up.

- The SCIN program (Sexual Considerations and Intimacy Needs). Our goal in this program is to address patient patient sexuality and intimacy issues, as well as train staff to evaluate their own values and beliefs and find their comfort zone with the subject.

These programs provide support and education for patients and their families, including specific training for school reentry, dealing with teasing/staring and dealing with issues surrounding intimacy. These programs involve all members of the burn team in one way or another—including occupational and physical therapy, pastoral care, child life therapists and nurses.

While these programs have been successful in establishing better patient education programs, support systems and improved rehabilitation programs, there have also been many challenges including staff reluctance to having a burn survivor as part of the burn team, difficulty for burn survivors making the transition from patient to burn team member and getting “buy-in” from the entire staff for these programs.

Life being lived forward, and understood backward. It is as we look to the past of burn care that we realize how these psychosocial programs truly do help people move forward in their recovery and forward in their lives.

A final saying to conclude: “Success is the child of audacity.” 28 years ago, it was an audacious group of burn professionals who worked to change the science of burn care so that it would be what it is today. They are our role models. Let us be audacious as we pursue psychosocial rehabilitation as a standard of burn care, so that we, too, can say we have

succeeded in pursuing the best that burn care has to offer. Be audacious.

Conclusion

Based on our experiences, we believe five priorities for future burn research should be:

- 1) The development of a collaborative approach to research the psychosocial rehabilitation interventions already available;
- 2) Improvements in the management of facial disfigurement;
- 3) Development of relevant metrics and conduct of studies to assess the effectiveness of burn rehabilitation programs
- 4) Development of effective programs focused on the transition from burn center to home.
- 5) Development of effective educational programs focused on psychosocial rehabilitation and social reintegration issues for the burn injured person as well as burn center staff.

Table 1: Priorities for Burn Research (Survivor's Perspective)

- Development of a collaborative approach to research the psychosocial rehabilitation interventions already available
- Improvements in the management of facial disfigurement
- Development of relevant metrics and conduct of studies to assess the effectiveness of burn rehabilitation programs
- Development of effective programs focused on the transition from burn center to home
- Development of effective educational programs focused on psychosocial rehabilitation and social reintegration issues for the burn injured person as well as burn center staff

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The first two days of the Burn State of the Science Research Conference brought together scientists, clinicians, burn survivors, and other members of the burn care team to delineate the priorities for burn research for both the acute and reconstructive phases and outline the resources needed to complete those priorities. Perhaps the biggest success of the meeting was in uniting people from different areas who want to improve the care of the burn patient and providing them with an environment in which to exchange ideas and discuss how to achieve their goals. In the process, it has become clear that burn research lacks some of the basic tools needed to conduct meaningful clinical outcomes studies such as definitions of disease states, injury severity grading systems, clinical endpoints, and common outcome measures. Consensus on these topics must be achieved and then the definitions and hypotheses should be validated. Resources necessary for the proper conduct of research need to be obtained, and the current research paradigm reexamined. The last, but perhaps most essential step in the process is the dissemination of research via publication in medical journals.

The final day of the conference was devoted to essential steps associated with research: publication, funding, and research team-building. First, the editors for the major journals publishing burn research were asked to provide information on each of their journals as well as the weaknesses and strengths of burn research publication. Second, several major sponsors of burn research were asked to give a presentation on potential funding mechanisms available to burn researchers from their agency. Finally, to conclude the conference, Dr. Herndon provided a capstone lecture on the building of research teams how the burn research paradigm may need to be evolve to accommodate new research requirements, study designs, and funding.

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Introduction

Creating, funding, and conducting a research project is an important and necessary step in improving our knowledge and treatment of burn injury. However, the research process is not complete until the findings are published in an established journal. New discoveries are of little use without transmission to others in the field. As such, the opening session of the final day of the State of the Science: Burn Research featured a discussion by the editors of major journals that publish burn research. The journals and their respective editors were: *Journal of Burn Care and Research*, Dr. Richard Gamelli; *Burns*, Dr. Steve Wolf; *Journal of Trauma*, Dr. Basel Pruitt; and *Rehabilitation Psychology*, Dr. Timothy Elliott. The editors were asked to respond to a series of questions with respect to their journal. The questions are listed in Table 1. This paper will summarize each editor's response to the questions posed for consideration; the paper was prepared from audio recordings of the presentations.

Journal of Burn Care and Research (JBCR)

Mission: The mission of JBCR is to be the preferred journal for publication of advances in burn care, research, education, prevention and rehabilitation. These goals are in concert with the mission of the American Burn Association, which owns the journal. The target audience for the journal ranges widely, and includes the following: surgeons, nurses, therapists, nutritionists, pharmacists, residents, medical students, scientists, healthcare administration, industry, government, firefighters, and patients. In essence, JBCR is targeted to all members of the burn team as well as the people the burn team serves.

Editorial Process: JBCR has taken several steps to streamline the submission and publication process. The journal has adopted an electronic submission process. The last article submitted on paper will be published later this year. Papers submitted electronically are sent within 0.3 days to the journal editor, and is sent to reviewers within 1 day. Each article is assigned to an average of three reviewers for evaluation. Once these three reviews are sent back to the editor, a decision is made to either reject, accept, accept with minor revision, or reconsider pending major revision. The time to sending out the first decision to the author averages 14 days. This is a testament to the reviewers as well as the electronic process. Authors have up to 45 days to make revisions and resubmit. Ultimately, the length of time needed for final decision rests with the author, who must make and resubmit revisions.

Articles Published: A wide variety of article types are submitted to JBCR, including case reports, invited critiques, letters to the editors, summary articles, practice guidelines, special reports, prospective trials, and original articles. Articles presented and submitted at the annual ABA meeting receive expedited review by the session moderators. The volume of articles received continues to increase with the advent of electronic submission. The final rejection rate for JBCR is approximately 34%.

JBCR is seeking the articles in multiple realms. Basic science studies, both discovery and hypothesis-driven, translational studies, and well-conducted clinical studies (especially prospective trials with class 1 data) are priorities. In essence, quality research that has a potential impact on patient care receives serious consideration.

Suggestions for Improving Burn Research: Research support needed to conduct high quality studies will require the amalgamation of multiple different funding mechanisms. Funding for discovery and basic science as well as clinical outcomes will need to be available. In addition, training grants, which engage young investigators in burn research, are needed to assure the future of quality research in burns. Randomized prospective trials are required to achieve quality science in clinical trials. The design, conduct, and monitoring of these trials requires intensive use of a variety of resources, all of which require funding.

The "Achilles Heel" of burn research is the relatively limited patient base. Studying many of the important topics in burn research will require multi-institutional collaboration, since as few as 11% of eligible patients enter into clinical trials for which they are appropriate. Funding for this type of research is limited at both the private and state institutional level. Research must compete with health care cost containment and the demands for clinical, as well as research, productivity of the investigator. Obtaining and maintaining extramural support has become an increasing challenge for burns. Finally, the research community, including burn researchers, is

aging, and the number of burn research scientists is limited. The answer may lie in the formation of research teams, rather than solo investigators, to accomplish meaningful research.

Information systems will be critical for the development of prospective studies in the future. Current initiatives, such as the National Burn Repository, are important in terms of establishing data fields, definitions, and providing a sound epidemiologic database for future studies. Cross-talk between clinicians and basic scientists will be essential to translate important basic science findings to the clinical arena. Finally, training programs for burn researchers need to be maintained and extended to help develop research scientists interested in solving problems important to the burn population.

Ultimately, JBCR will continue to seek the best data from all members of the burn team that support advances in patient care and improves the quality of care that we provide to our patients, their families, and our society. We cannot advance the quality of care that we deliver and improve the outcome of our patients and families without the knowledge provided by high-quality burn research.

Burns

Mission: The mission of Burns is to foster the exchange of information among all engaged in preventing and treating the effects of burns. Burns differs from JBCR in that it targets an international audience. Articles are sought globally to obtain the international perspective of burn care and research. Some areas of the world have limited resources, limiting them to epidemiologic studies, while others are able to conduct complicated multicenter studies. Any article that addresses burn or burn-related treatment will be considered for publication. The readership of Burns is broad and includes all professions involved in the care, treatment, or prevention of burns: surgeons, intensivists, psychology professionals, basic scientists (physiology, microbiology, biomechanical engineering), epidemiologists, public health specialists, burn therapists, and nutritionists to name but a few.

Editorial Process: The review process for Burns is completely electronic, with editorial staff in both the U.S. and England. Approximately 500-600 articles are submitted, and they are sent out to two or more referees for review. Each reviewer is given three weeks to review the manuscript. Similar to JBCR, the editor reviews the recommendations and makes a decision on publication based on the journal's mission statement. The source of the article is taken into consideration in the decision-making process. Areas with limited resources or language challenges may need additional editor input prior to publication.

The three potential decisions are accept, reject, or revise. Once a paper is accepted, it may take 7-10 months to be published in a paper form. However, it may be cited earlier due to the electronic media format. When the editor recommends revision prior to acceptance, he is offering the author the opportunity to improve the manuscript so that it can be published. Clearly addressing each of the points raised by the reviewers and amending the manuscript as requested will increase the chance for publication. Finally, remember that a rejection is not a personal attack. It merely means that the study is too small or the methodology is not appropriate at that time to make a reasonable contribution to the literature.

Articles Published: The average turn-around time from paper to submission to final decision is approximately 6 weeks. The type of article submitted will impact the time to actual publication. Original articles are published first, while case reports have the longest interval between submission and publication. Burns seeks descriptive studies on burn-induced responses and potential targets for treatment, mechanistic basic science investigations based on clinical questions, and trials answering clinical questions of interest to burns. All types of articles, ranging from descriptive studies to basic science to clinical trials and case reports are considered for publication.

The number of manuscripts and publications in burns have increased since 1980. This is probably due to a variety of factors, including the electronic submission process as well as individual investigations. The acceptance rate for Burns is approximately 50%. Revisions are required for 60%, 30% are rejected, and 10% are accepted on first submission without revision. Authors are asked to return revisions within 3 months. Because Burns is an international journal, 70% of abstracts originate outside of the U.S., 30% from the U.S. Clinical trials to define and prove what we should be doing to maximize patient outcomes is sorely needed.

Perspective on Future of Burn Research: The “Achilles heel” of burn publication and research is writing and submitting the manuscript for publication. Communication of research findings is the key to improving burn care, and publication of important results represents the best way to communicate with researchers both now and in the future. Without this, future researchers may well repeat mistakes and/or waste valuable time recreating what another person has already investigated, thus slowing down progress in the field. However, it is important to remember that it is research quality, not quantity, that is the most important. Publication of findings in a peer-reviewed journal reflects both on the journal and the author. The challenge is to present quality research in a quality fashion.

Journal of Trauma (J Trauma)

Mission: The mission of J Trauma is to receive, review, and publish manuscripts reporting clinical studies, laboratory investigations, and new developments in education and health care delivery in the field of trauma. As such, burns is a component, but not the sole, topic covered by this journal. J Trauma is owned by the American Association for the Surgery of Trauma (AAST). The majority of the subscribers are physicians and other scientists. The total print circulation is 3,400 and has been decreasing, but electronic subscriptions have concomitantly increased. In June 2006, J Trauma reached an estimated 2,000 individual institutions.

Editorial Process: Editorial processing at J Trauma tends to be much longer than cited by JBCR and Burns. AAST papers are given priority; the average time from receipt to final decision is 3.3 months. Time from receipt to publication for AAST papers is 7.3 months. Manuscripts submitted *de novo* have an average time of 1.5 years from submission to publication. Case reports have the longest interval between submission and publication. The most rapid notification (mean of 1.7 months) occurs for rejected papers. The paper review process is similar to those outlined by Dr. Gamelli and Dr. Wolf. The editor makes the final decision. Associate and section editors are used to resolve reviewer disagreements and evaluate questions of duplicate publication.

The number of submitted manuscripts submitted to J Trauma was 1700, with increasing number of submissions from third world countries. J Trauma publishes predominantly clinical papers, although 15% are laboratory studies, and orthopedic topics represent 12% of articles published. Special feature articles, such as review articles and Glue Grant standard procedures, are also published in the journal. The acceptance rate for publication varies. An article presented at the AAST or other trauma society for which J Trauma is a platform (Western Trauma Association (56%), Eastern Association for the Surgery of Trauma (66%), Trauma Association of Canada (86%)) has a higher acceptance rate than an independent submission, which has an acceptance rate of 36%. Submissions are principally from the U.S. (41.4%), followed by Taiwan, Turkey, U.K., Canada, Japan, India, China, Australia, and Korea.

Perspective on Future of Burn Research: Multiple areas of concern regarding burn research need to be addressed. First, research funding from multiple arenas, including the government, foundations, and industry, for burn research needs to be increased. Second, we need to develop infrastructure for multi-institutional trials. Peer review by the ABA Research Committee needs to be expanded, and study-specific multi-institutional study consortia focused on specific research questions need to be developed. The third area vital to the future of burn research is the development of burn research fellowships. Burn research fellowships are necessary to train the next generation of burn researchers in the proper conduct of clinical and basic science research and to cultivate new ideas and interests in burn research. The development of study-specific multi-disciplinary research teams involving clinician scientists, basic scientists, nurses, and paraprofessionals will be necessary to translate basic science and mechanistic research to patient care. Finally, burn patient management will need to be an essential component of the surgical residency. This benefits both burns and the trainee: exposing residents to burns will engender interest in the field, thus assisting burn research, and the exposure to critical care, wound healing, and multidisciplinary team leadership will improve resident knowledge and management skills.

Burn research and publications have limitations in several areas. First, the conduct of randomized trials is challenging. They require expenditure of many resources and precise

coordination as well as close supervision to be completed successfully. Quality of research is an additional concern. The preponderance of inadequately controlled trials, experiments with poor design and inappropriate statistical analysis, and unwarranted extrapolation of research findings can easily result in the adoption of inappropriate treatment methodologies. Yet at the same time, the transfer of information from bench research to clinical practice is painstakingly slow. Mechanisms for facilitating interactions between basic scientists and clinicians need to be developed, and collaborative efforts fostered. The final area that limits burn research and practice is the failure to document the efficacy of treatment guidelines in a prospective randomized fashion. Many of the “standards” of burn care are not based in science.

The research goals for burns should thus be to increase the quality and volume of multidisciplinary and multi-institutional clinical and laboratory research studies to bring new information and new technology to the bedside and improve the care of burn patients.

Rehabilitation Psychology (Rehab Psych)

Mission: The mission of Rehab Psych is to be the premier journal for the psychological study of issues germane to chronic disease and disability across the lifespan.

Articles Published: The journal is focused primarily on the behavioral and social factors that cut across all chronic health conditions that have a disability component. The journal is published by the American Psychological Association (APA), and journal editors change every 5 years. The journal addresses psychological components, including physiologic, neurologic, and policy issues that influence people who live with these conditions. Rehab Psych seeks articles on theoretical issues that can inform practice and advance the scientific literature from the behavioral and social standpoint. The subscription base is primarily composed of psychologists, half of whom are in private practice. Total subscriptions are approximately 2,000. Rehab Psych accepts submissions electronically and has a 2-3 month interval from submission to initial decision. In general, 2-3 reviewers evaluate each submission. Reviews and editorial decisions are provided to authors via electronic mail, and revisions are reviewed by the action editor and at least one of the original reviewers. The editorial board is diverse and the editors also utilize ad-hoc reviews from international experts and junior colleagues with expertise in a related area. The acceptance rate for publication is now over 70%. Depending on the editorial decision and response of authors’ to editorial feedback, a paper may now appear in print within a year of initial submission.

Rehab Psych is cited in multiple journals, including Archives of Physical Medicine and Rehabilitation. Articles in Rehab Psych frequently cite papers published in Archives of Physical Medicine and Rehabilitation, Brain Injury, Disability and Rehabilitation, American Psychologist, and Journal of Head Trauma Rehabilitation.

Rehab Psych was created as a result of the effects of World War II, and was heavily influenced by psychologists who studied the interactions between the person and environment. As such, spinal cord injury, which is a classic example of a low incidence, high impact, high cost disability has permeated much of the research. This work is often sponsored by funds from the Department of Education and the National Institute of Disability Research and Rehabilitation, with a resultant stimulation in multidisciplinary, multi-site research garnering information on a large number of patients to improve practice. The journal has a strong link to physical medicine and rehabilitation in general.

The scope of Rehab Psych has expanded due to the aging population and ongoing limitation of resources for chronic illness. Approximately 45% of the nation’s population has at least one incurable chronic health condition that requires long-term maintenance. The primary mechanisms influencing the outcomes in these conditions are behavioral and social in nature. Declines in support for services as well as shifts in emphasis of the funding agencies have resulted in an increasing emphasis to these areas of research.

Rehab Psych has seen an influx of scholarship internationally, which broadens the scope of the coverage. Rehabilitation psychology, in general, is largely based on national stated priorities, and those priorities vary by country. The ability to conduct studies also varies widely, with some countries having better long-term research capabilities than others. Different countries are also in different stages of industrialization, which influences the rehabilitation issues they face. The World Health Organization model of disablement has greatly influenced

the practice and research. Partnering with the people who are impacted by these conditions has assumed increased importance, and subsequent research should be linked to what they tell us is important. For example, control over emotional life and management of pain is a priority for people with chronic disfiguring and disabling conditions.

Rehab Psych seeks well-written papers based on sound scientific studies that follow the APA writing style format. Theory driven papers, particularly from a behavioral or social perspective, are desirable. Although randomized clinical trials are valued, there is still a place for good single case and quasi-experimental designs. Given the small number of people who agree to participate in a trial in low-incidence conditions, and the difficulty in constructing meaningful control groups (particularly in areas that have no “routine standard of care”), and the uniqueness of the problems for specific populations (such as burns), a single case design may be the only method of accruing enough patients and disease-specific data.

Topics Addressed by the Editors in Question/Answer Forum

1. Dr. Greenhalgh: Could you discuss the impact factor and how we can improve the impact factor for our journals?

The Impact Factor is a method for quantifying journal quality. The formula used to calculate a journal's impact factor is:

Impact Factor = # of articles cited in the past 2 years / # of articles published

There are several limitations to this formula. First, using the number of citations of a published article as criteria for impact is problematic, as it encourages journals to cite their own work during publication. Review articles, which have little new science, are usually cited more frequently than new studies. Hence, this methodology encourages the publication of reviews rather than innovative research. In addition, the method for determining the impact factor currently does not include the electronic submission and publication process. The future will likely have a metric for measuring how many times an article is downloaded. Of note, editorials are not counted in the total number of articles published, which can influence its value.

The best way to increase the impact factor for a specialty journal is to submit high quality research that will, due to its merits, be cited frequently by others.

2. Dr. Saffle: Should the journals carry editorials that might have an influence on public policy?

These discussions are not outside the purview of journals. However, the scope of a journal may not be broad enough to influence public policy. The readership of a journal is limited to its subscribers, who are often aware of the issue. The people who need the information are not likely to seek information from a subspecialty journal. Access to the broader community, such as the NIH roadmap increasing translational research, and unique opportunities, such as the glue grant, will be of assistance. However, each researcher needs to take an active role in promoting public policy on burns and burn research.

Table 1. Questions for Journal Editors

1. What is your mission statement?
2. What is your readership? Who is the target audience?
3. What is your average turn around time for submission and final decision?
4. What is your editorial process?
5. What types of articles do you consider for publication?
6. Which type of article receives top priority for publication?
7. What type of articles do you receive most frequently?
8. What is your acceptance rate for publication?
9. What types of research are lacking and what needs to be done to increase that type of research?
10. What are the “Achilles Heels” for burn research?
11. What should be the single most important goal for research in the next 10 years?

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Introduction

The first two days of the consensus conference identified a myriad of research topics that require analysis. However, there continues to be concern over the insufficient funds to conduct rigorous research in basic science, translational research, and clinical research in burns. The randomized prospective multicenter clinical trial is now considered to be the gold standard for clinical research, and researchers are being encouraged to conduct this type of study. However, to be conducted properly, randomized trials require a multitude of resources, including personnel, equipment, database software, and patients. Study design is essential to the success of such trials, and a solid foundation built upon the results of smaller studies, including prospective, retrospective, and basic science studies, will be essential for the development of rigorous multicenter trials. Since research is the key to delivering the best care for patients, obtaining and identifying potential sources of research funding assumes increased importance. The funding opportunities session featured program managers from three potential funding organizations: the National Institute on Disability and Rehabilitation Research, the Rehabilitation Research Development Service Department of Veteran Affairs, and the National Institute of the General Medical Sciences in the National Institutes of Health (NIH). This article will summarize the presentations of each of the speakers based on audio recordings of the presentations.

NIDRR Funding Opportunities (Theresa SanAgustin, MD)

NIDRR is one of the components of the Office of Special Education under the Department of Education. It is a separate entity from the National Institutes of Health. NIDRR's mission is to generate new knowledge and promote its effective use to improve the abilities of people with disabilities to perform activities of their choice in the community, and to expand society's capacity to provide full opportunities and accommodations for its citizens with disabilities. NIDRR operates on the policy of President Bush's New Freedom Initiative, which promotes increased access for individuals with disabilities to assistive and universally designed technologies; expanded educational opportunities for individuals with disabilities, integration of Americans with disabilities into the workforce, and full access to all aspects of community life for individuals with disabilities.

NIDRR has several funding mechanisms, including Rehabilitation Research and Training Centers, Rehabilitation Engineering Research Centers, Model Systems, Field-Initiated Projects (research and development), Disability Rehabilitation Research Projects, Advanced Rehabilitation Research Training, Fellowships, and Dissemination and Knowledge Translation grants. Additional funding is available through Small Business Innovation Research (SBIR), *Americans with Disabilities Act (ADA)* technical assistance centers, and state technology assistance projects.

Three model systems are currently funded by NIDRR: Spinal Cord Injury (SCI), Traumatic Brain Injury (TBI), and Burn. The burn model system was established in 1992 and is the most recently added model system; the SCI model system was established 35 years ago, and the TBI model system was added 25 years ago. The Burn Model System (BMS) funds four centers every five years at \$300,000 per year. The Burn Data Coordinating Center (BDCC) is funded at \$250,000 per year to facilitate data collection, and management as well as statistical support for the BMS. Both the BMS and the BDCC will be accepting applications for grants this year.

The BMS centers conduct studies in innovative projects for the development, delivery, demonstration, and evaluation of comprehensive services. Current areas of research by the model systems include: etiology of hypertrophic scarring, long-term outcome of burn injuries, burn-associated neuropathy, augmented deconditioning exercise, efficacy of oxandrolone treatment, effectiveness of pressure garments, effect of virtual reality on active range of motion during physical therapy, Acute Stress Disorder intervention, barriers to return to work, and social stigmatization of burn survivors.

Another potential source of funding for burn researchers from NIDRR is the Burns Rehabilitation Research and Training Center. The Advanced Rehabilitation Research Training grant is designed to train ARRT at the postdoctoral level and is funded at \$150,000 per year for five years. This award is made to educational institutions only and must be

interdisciplinary. Fellowships for individuals with less than 7 years of experience in burns or other discipline, called Merit awards, are funded for \$65,000 per year. Distinguished awards are funded for \$75,000 per year for those with more than 7 years of experience. These grants are funded for 1 year only.

The Field-Initiated Projects represent another potential funding mechanism for burns. These grants are funded for up to \$200,000/year for three years and may be either research or developmental in nature. Awards are decided by standing panels and are based on criteria set forth by NIDRR. Small Business Innovation Research (SBIR) grants, designed to assist small companies or researchers who need one or two studies prior to marketing, are also available. The award amount is determined by the phase of the study. Phase I is funded up to \$75,000 (six months), and Phase II is funded up to \$250,000 per year (two years). Further information can be obtained at <http://www.sba.gov/sbir>.

The direct link for the burn model system can be found at the following: <http://www.ed.gov/legislation/FedRegister/proprule/2006-3/091906b.html>. Further information on NIDRR programs is available from Donna Nangle, email address of donna.nangle@ed.gov, and for the BMS contact Theresa San Agustin at theresa.sanagustin@ed.gov. Investigators willing to do field work or review but are not interested in applying for a BMS grant can also contact NIDRR to offer services.

The Department of Veteran Affairs (VA) (Danielle Kerkovich, Ph.D.)

The Veteran's Administration was started by Abraham Lincoln following the Civil War. The VA follows any service-related condition that happens to a veteran during or after service. Approximately 25% of the U.S. population is eligible for VA care. The VA takes care of veterans for extended periods of time: today 5 dependents from the Civil War and 440 children and widows of the Spanish-American War are receiving benefits. Therefore, the soldiers who are sustaining burn injuries today will be cared for by the VA for the next 50-70 years.

The VA consists of more than 1000 facilities, including 157 hospitals, 862 ambulatory care centers, nursing homes, residential centers, and 207 veterans centers. These facilities are connected by the country's largest paperless medical records system and represent the largest single provider of health care in the U.S. Because of this, the VA is also one of the largest single providers of health professional training and research. The research component consists of 4 parts: Biomedical and Laboratory Research and Development (BLR&D), Clinical Science Research and Development Service (CSR&D), Health Services Research and Development (HSR&D), and Rehabilitation Research & Development Service (RR&D).

BLR&D seeks investigation into the coordination of cellular mechanisms in burn injury repair with and without drug delivery, recombinant DNA, biodegradable polymers, cellular scaffolds and approved stem cell technology using *in vitro* and *in vivo* model systems. CSR&D seeks exploration of long- and short-term systemic events following burn. HSR&D is interested in all aspects of healthcare delivery related to improved outcomes. Specifically, HSR&D is interested in delivery of healthcare as soldiers transition from Department of Defense to Veterans Health Administration, delivery of care for persons with polytrauma and long-term healthcare planning as soldiers and veterans age with disability.

The final research component, RR&D, with a budget of \$55 million, is dedicated to the restoration of function. Projects in basic science and biomedical engineering with foreseeable clinical applications and current clinical application are eligible for funding. The majority of funding is for investigator initiated studies. Burn is a priority area of interest for RR&D. Types of grants include: Career Development Programs, Investigator initiated funding (Merit Review), and Centers for Excellence Programs. Currently there are 15 Centers of Excellence in Rehabilitation Research. Two examples of this are: 1. The Providence VA Center for Rebuilding, Regenerating and Restoring Function after Limb Loss is creating "biohybrid" limbs and 2. The Cleveland Advanced Platform Technology Center is dedicated to the development of engineering technologies for clinical application and research. There are 4 Polytrauma Centers for care following brain injury, amputation, limb salvage, burn injury or combination thereof. These four centers were created specifically in

response to the current conflict. Although veterans who sustain burn injury are initially treated in a civilian burn center, the majority will be followed at the VA in the long-term. Soldiers with burn injury during the war currently go to the Institute for Surgical Research for their acute care. However, their aftercare and long-term rehabilitation will take place elsewhere, and the optimal rehabilitation regimens need to be defined.

The VA has several other unique programs, including the cooperative studies program, the technology transfer program, and the quality enhancement research initiative. The VA Cooperative Studies Program is a Division of VA ORD that is responsible for the planning and conduct of large multicenter clinical trials within the VA. The VA is the largest laboratory for multi-site studies in the United States, largely due to this program. The Technology Transfer Program translates the results of worthy discoveries made in VA into practice. The program educates inventors concerning their rights and obligations, rigorously evaluates all inventions, obtains patents, and assists in the commercialization of new products. Finally, the Quality Enhancement Research Initiative (QUERI) is responsible for the translation and implementation of best practices throughout VHA. Currently a poly-trauma QUERI is in development.

The VA has several priority areas for research. These priorities are: 1. cellular mechanisms of injury and recovery, 2. clinical investigation, 3. health services delivery (between DoD and VA), 4. assistive technology and combined therapies, 5. reintegration, including PTSD and anxiety, 6. reintegration, including caregiving, 7. reintegration with respect to family coping, and 8. reintegration and vocational rehabilitation. Reintegration is assuming increasing importance due to the increase in burn and polytrauma. Yet another program supported by the VA is the research training program. Career development programs are for clinicians and non-clinicians alike.

There are several requirements for obtaining funding from the VA. VA-funded PIs and co-PIs must have 5/8ths time VA appointments based on a 40 hour work week. Co-Investigators, however, may have smaller appointments. The majority of VA researchers hold joint appointments with their academic affiliate, thus increasing their available resources. Some trials are jointly funded by VA and others (such as the NIH), thus combining resources within each agency. An additional mechanism to increase available resources include Cooperative Research and Development Agreements with nonprofit and commercial companies. Specialized expertise can also be added to VA-funded proposals using IPAs and contract mechanisms.

The VA has a multitude of potential resources available to the burn researcher. Further information on these resources can be obtained from the VA Office of Research & Development at <http://www1.va.gov/resdev>, VA Rehabilitation Research & Development at <http://www1.va.gov/resdev/programs/rrd.cfm>, and the VA Rehab Centers of Excellence website <http://www.rehab.research.va.gov/cent/centers.htm>.

The National Institute for the General Medical Sciences (NIGMS)- Scott Somers, Ph.D

The National Institutes of Health (NIH) is a compendium of 27 different centers, offices, or institutes. Some institutes/centers have intramural programs (i.e. labs) which receive funding, while others, such as NIGMS, do not. Thus, funding from NIGMS is awarded extramurally. The majority of applications are reviewed by the Center for Scientific Review.

NIGMS began approximately 45 years ago to fund primarily basic biomedical research. It is the fourth largest institute in the NIH, surpassed only by the National Cancer Institute, the National Heart, Lung, and Blood Institute, and the National Institute of Allergy and Infectious Diseases. The bulk of NIGMS funded research is investigator initiated; thus, few Requests for Applications (RFA) or Program Announcements (PA) are issued by NIGMS. In addition, NIGMS does not set aside funding for specific topics to assure that proposals with the best science will get funded.

The topics considered by NIGMS vary widely: organic chemistry, biochemistry, genetics, developmental biology, structural biology, and pharmacology are but a few examples. NIGMS is also responsible for funding science that does not fit into any other category, including burns and trauma. NIGMS funding supported some of the early burn research in the 1960s and 70s, many of which are current standards for burn care.

NIGMS to date has funded multiple different types of studies, including basic animal research, molecular research, human-based research, and some single site clinical trials. To accommodate the wide variety of topics in NIGMS, several topics are divided among program officers: Trauma, Burn and Peri-operative Injury (Scot Somers), Sepsis (Sarah Dunsmore), Innate Immunity and Inflammation (Sara Dunsmore), Wound Healing (Richard Ikeda), and Anesthesia and Integrated Systems (Alison Cole). These program officers are interested in injury research and are an important link to obtaining funding.

The funding in NIGMS consists of primarily Investigator Initiated Research (IIR) project grant awards that are reviewed by the Center for Scientific Review. These studies can be animal, human, or a combination of the two. The success rate for these grants is 23-24%. Mentored career development awards (K08 and K23) are designed for young faculty members who have an academic appointment. Program Project Grants (P50) are multi-component complex grant applications involving multiple centers and investigators. They are reviewed by the national advisory council and staff to assure that the project is sound and meets scientific rigor worthy of funding.

NIGMS continues to support the majority of burn-related research, with the remaining projects funded by 16-17 of the other NIH institutes. NIGMS will continue to fund scientifically sound projects in burns. Investigators considering applying for NIGMS funding are encouraged to be creative and communicate with program officers to optimize their chances for funding.

Building the Research Teams of the Future: Changing the Paradigm
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Scientific knowledge about the treatment of burn injuries and the care of burn patients continues to advance, ever changing the nature of the research questions to be asked. At a meeting to review the state of the science, we look forward to meeting challenges of the next 5 years and preview the evolution that the burn research community will undergo in meeting those challenges.

As the burn research paradigm changes, the basic model of a process that melds basic science with clinical research and clinical care must not change. Integrating scientific research with clinical care has been promoted throughout the recent history of burn care. In the late 1940's, the first US burn center at the Medical College of Virginia and the US Army Surgical Research Unit, later renamed the US Army Institute of Surgical Research emphasized the importance of collaboration between clinical care and basic scientific disciplines.¹ In 1947, the freighter SS Grandcamp exploded in Texas City, Texas, killing 653 and injuring thousands. Dr. Truman Blocker cared for many of those who were burned in that disaster and then led the way to establish one of the world's first designated burn units at the University of Texas Medical Branch in Galveston, Texas. In 1966, under Dr. Blocker's continued leadership, the first Shriners Burns Hospital (SBH) opened in Galveston, affiliated with the University of Texas Medical Branch. Dr. Blocker believed in interdisciplinary research and care and that belief formed the philosophy that has continued to thrive through the 40 years since the hospital opened. In 2006, we still have interdisciplinary research teams and collaborative projects to improve the care of burn injuries. Clinicians, basic scientists, allied health specialists, and students interact to pose research questions based on clinical problems, to look for answers in the laboratories and then in the clinical setting in a perpetual positive feedback loop. The interest of the clinicians and the concerns of the patients spark excitement in the researchers. The researchers' enthusiasm elicits interest among the clinicians.

Advances in burn care attest to the value of a dedicated burn unit organized around the concept of a collegial group of basic scientists, clinical researchers, and clinical care givers, all asking questions of each other, sharing observations and information, and together seeking

solutions to improve the welfare of their patients. Much past research has been directed to solving problems that would enhance the probability of survival. Now, a significant decrease in burn mortality has been widely recognized (Table 1.). That decrease has been due to advances in knowledge stemming from that interactive, interdisciplinary process that led to changes in: resuscitation, control of infection, support of the hypermetabolic response to trauma, and early closure of the burn wound. Scientifically sound analyses of patient data have led to the development of formulae for fluid resuscitation and nutritional support. Clinical research has demonstrated the utility of topical antimicrobials in delaying onset of sepsis. Prospective randomized clinical trials have determined the efficacy of early surgical therapy in improving survival for many burned patients by decreasing blood loss and by diminishing the occurrence of sepsis. Basic science and clinical research have contributed to decreased mortality by describing pathophysiology related to inhalation injury and suggesting treatment methods which have decreased the incidence of pulmonary edema and pneumonia. Scientific investigations of the hypermetabolic response to major burn injury have led to improved management of this life-threatening phenomenon, resulting not only in diminished loss of life but also promising improved quality of life. The continued interaction of the basic and clinical scientists with each other and with other caretakers as well as patients kept the process moving. The researchers typically have worked within their own site, sharing information with colleagues in other centers through scientific meetings and published literature. Improved clinical care, decreased mortality, and new knowledge gained that could be applied elsewhere, e.g. to healing other kinds of wounds or to supporting the physiological response to other kinds of trauma, have been the laudable results.

Building the research teams of the future to address what is not known:

During the next 5 years the problems burn researchers will focus more on life and less on preventing death. Although we must continue to improve in mortality and morbidity for the very young and very old, much of our future research will address issues related to improving quality of life for the ever-increasing number of survivors of severe burn injury. Important topics for future research are: techniques to control hypertrophic scarring; methods of improving physical comfort, e.g. minimizing itching; methods such as anabolic agents to speed recovery and rehabilitation; improved psychological care promoting reintegration into society; and improved quality of life especially participation in social activities.

Although familiar types of research, i.e. basic or bench research, animal research, translational research, and single center clinical studies will continue, the emphasis on problems in living for survivors will require large scale studies with more subjects in order to increase statistical power and increase generalizability of findings. More questions will have to be answered by large, multi-center studies; research teams will not only have to interact and collaborate with each other but also with the members of research teams from other burn centers—or perhaps other burn centers and other trauma centers. Burn researchers must adopt a cooperative and collaborative stance, diminishing the competitive position that has traditionally driven ambitious professionals in our society.

Future research teams should continue to follow the model that has served so well in the past of integrated clinical care and research, promoting interdisciplinary interaction on an ongoing basis with formal meetings and patient rounds as well as informal interactions. Membership in the team should include a few people who have already proven their capabilities in terms of research, e.g. getting funding, publishing. The team should also include some young unproven but promising scientists who are ambitious and just beginning their careers. The combination of senior mentors, junior scientists, and research fellows in training, is necessary to provide education and support to more junior members and to continue to train new investigators in research methodologies.

As the issues to be addressed in burn research are more often those of living as a burn survivor, the membership of the team must become more inclusive. Burn survivors become more active in defining the problems to be studied and in setting priorities. They also will function more as members of review panels, providing their own expertise regarding how to best obtain information from burn survivors and to be sure that our research serves their best interests. Additionally, research teams must include professionals from a variety of behavioral

sciences that previously have not participated to any great extent in burn research. Sociologists, anthropologists, and social psychologists will be helpful in elucidating issues of survivor reintegration into society and will join the more familiar regime of molecular biologists, physiologists, pathologists, etc. on the research team. Traditional health care professionals more often will be joined by career counselors, cosmetologists, and educators in our efforts to devise better interventions to assist survivors in living optimally.

However, one must be very wary of the fact that gathering together a group of experts from diverse disciplines will not constitute a team. In fact, the diversity of the disciplines, in addition to individual differences of gender, ethnicity, values, professional experience and professional status render such teamwork a process fraught with opportunities for disagreements, jealousies, and confusion. Time must be devoted to a process of trust-building among the team members. It is imperative that the team communicate, openly and frequently, or the group will lose effectiveness.

The group becomes a team when they have common goals and tasks to be accomplished and when the individual members share overlapping values that will be served by accomplishing their goals.ⁱⁱ The team becomes an efficient work group through a process of establishing mechanisms of collaboration and cooperation which facilitate focusing on explicit tasks rather than on covert distractions of personal need and interpersonal conflict.^{2,iii} Work groups develop best in conditions which allow each individual to feel acknowledged as valuable to the team. A burn team has defined and shared goals with clear tasks. For the group of burn experts to become an efficient burn research team, skillful leadership that facilitates the development of shared values among team members and ensures the validation of the members of the team as they accomplish tasks is necessary. Every expert voice must be heard and acknowledged.

The leader of such a team, usually the burn surgeon, must be prepared to share leadership with one or more 'informal' leaders in such a way that all leadership functions are fulfilled. Empirical studies, with remarkable consistency, indicate that the required functions for successful leadership can be grouped into two somewhat incompatible clusters: to direct the group toward tasks and goal attainment and to facilitate the interaction of the group members.

Studies of group behavior demonstrate that high performance teams are characterized by synergy between task accomplishment and individual need fulfillment. The most effective leader is one who engages the talents of others and empowers them to utilize their abilities to further the work of the group.^{2,3,iv} Failure to empower the informal leaders limits their abilities to contribute fully. Sharing power does not mean giving up control. The physician shares leadership by seeking information and advice from other team members and empowers them by validating the importance of their expertise in the decision making process.

In conclusion, the new paradigm in burn research will incorporate the interdisciplinary model in which all researchers and clinicians participate in collaborative projects to answer questions related to improving patient care and enhancing quality of life for burn survivors. Future projects will more often address issues of quality of life and focus less on improving survivability following severe burns. These studies will best be done in large scale, multi-site collaborative studies, and will include more involvement from burn survivors themselves as well as behavioral scientists heretofore non-participatory in burn research. Thus, burn researchers will have to function well as collaborators with other researchers and clinicians within their own center or site as well as with those in diverse sites.

Table 1. Percent total body surface area (TBSA) burn for an expected mortality of 50% in 1952, 1993, and 2006

Age (years)	1953 [†] [% TBSA]	1993* [% TBSA]	2006 [°] [% TBSA]
0 – 14	49	98	99
15 – 44	46	72	88
45 – 65	27	51	75
>65	10	25	33

[†] Bull, JP and Fisher, AJ. Annals of Surgery 1954;139

*Shriners Hospital for Children and University of Texas Medical Branch, Galveston, Texas

[°]Pereira, CT et al. J Am Coll Surg 2006; 202(3): 536-48 and unpublished data

Burn State of the Science Research Conference Concluding Remarks

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The Burn State of the Science Research Conference was a success on multiple levels. First, the conference achieved its stated purpose: the identification and prioritization of burn research goals for the next decade and the delineation of the resources needed to achieve those goals. Issues ranging from acute burn care through the rehabilitative period were addressed in a single forum and brought together in this publication. Several common themes emerged during the discussions. Although much progress has been made in burn management, much remains to be learned, and several tenets of research are missing. Universal definitions and grading systems which can be applied for both clinical and basic science research are lacking. Endpoints of care, such as resuscitation, are still not clear. Consensus in these areas is vital to conducting meaningful research, but even that is not enough. Once consensus is achieved, the conclusions need to be validated via basic science and pilot studies. Ultimately, multicenter randomized trials will be necessary to define the “best” burn care. Funding for research in general is dissipating, yet adequate funding for burn research is sorely needed, and burn researchers will need to be creative in pursuing funding sources.

Perhaps the greatest achievement of the State of the Science conference was the open interaction it fostered between researchers and clinicians representing multiple medical and scientific disciplines, burn survivors, funding organizations, journal editors, military personnel, and international burn researchers. Each group participated in the discussions, adding unique and valuable perspectives to the problems being addressed. The attendees learned about not just what we know and don’t know about burns, but, just as important, how other groups view what is known and not known. The collaborations formed during the conference may well set the tone for future collaborative research.

The research paradigm for burns is shifting: burn investigators from different backgrounds will need to unite to solve the problems facing the burn patient. This conference is but the first step in achieving the goals of burn research. Future consensus conferences, basic science projects elucidating mechanisms and treatment modalities, single institution pilot studies, translational studies, and multicenter prospective randomized trials will need to be performed to fulfill the final goal of the conference: achieving the research priorities and goals for the future.

The Burn State of the Science Research Conference would not have been possible without the support of multiple sponsoring organizations, including the American Burn Association, the National Institute of Disability and Rehabilitation Research, the U.S. Army Medical Research Materiel Command, Shriners Hospitals for Children, the Veteran’s Administration, and the National Institute for the General Medical Sciences. The broad scope of interests addressed in the conference is reflected in the diversity among the sponsoring agencies. The publication of the proceedings is but the first step. Continuing the process will need the participation of all interested in advancing burn care.

References:

- i. Artz CP & Moncrief JA. The burn problem. In: Artz CP & Moncrief JA, eds. The Treatment of Burns 2nd edition. Philadelphia, PA: W B Saunders Co, 1969: 1-21.
- ii. Hughes TL & Medina-Walpole AM. Implementation of an interdisciplinary behavior management program. J Am Geriatr Soc, 2000; 48: 581-587.
- iii. Schofield RF, Amodeo M. Interdisciplinary teams in health care and human services settings: Are they effective. Health and Social Work, 1999; 24 : 210.
4. Jordan PJ & Troth AC. Managing emotions during team problem solving: emotional intelligence and conflict resolution. Human Performance, 2004; 17: 195-218.