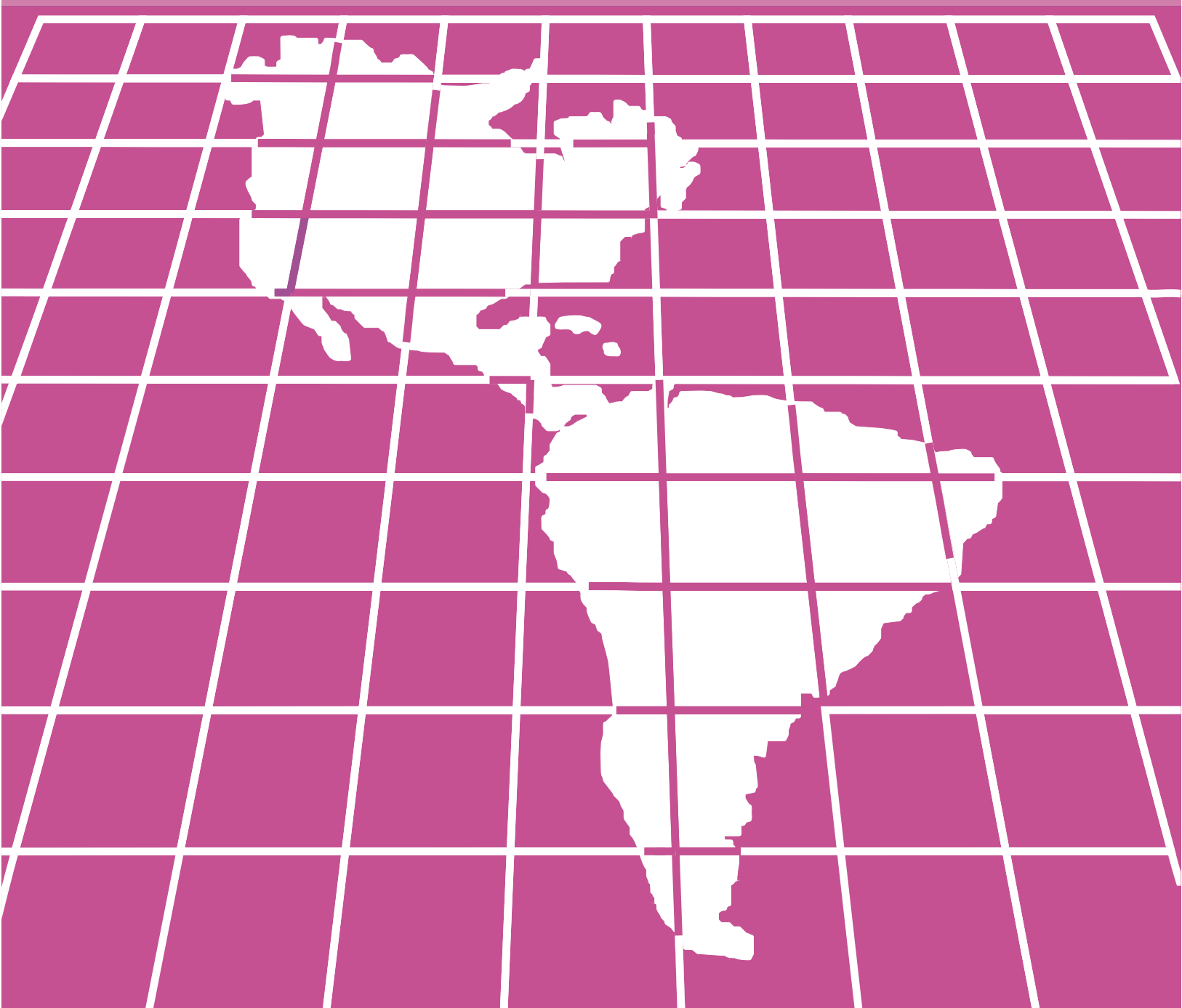
PANAMERICAN JOURNAL OF TRAUMA

ISSN 0121 - 5396

SOCIEDAD PANAMERICANA DE TRAUMA
SOCIEDADE PANAMERICANA DE TRAUMA
PANAMERICAN TRAUMA SOCIETY

Vol. 14 N° 1 2007



PANAMERICAN JOURNAL OF TRAUMA

INSTRUCTIONS FOR AUTHORS

Manuscripts and related correspondence should be sent to either Dr. Kimball Maull MD or Dr. Ricardo Ferrada MD to the following addresses:
Kimball Maull, M.D. FACS, Carraway Medical Center, 1600 Carraway Boulevard, Birmingham, Alabama USA.

1. ***Manuscript.*** The original typescript and two high-quality copies of all illustrations, legends, tables and references must be submitted. All copy, including references, must be typed double-spaced on 21 x 27 cm, heavy-duty white bond paper. Margins must be at least 1 inch. A computer diskette or CD containing a file of the article must be included. Files in Word either for IBM-compatible or Apple are preferred. The diskette should be labeled with the author's names, the title of the article, the type of computer, and the word processing software used.
2. ***Title***. The title must be short, specific and clear. It cannot exceed 45 characters per line, and is limited to two lines. The title page should include the full names, and academic affiliations of all author. Foot notes indicating where the works was done, where orders for reprints should be addressed and those contributing grants for the work should be given at the bottom of the second page. If the manuscript was presented at a meeting, indicate the name of the organization, the place and the date on which it was read.
3. ***Illustrations.*** Please send three complete sets of high contrast glossy prints. Figure number, name of senior author, and arrow indicating top should be typed on a gummed label and affixed to the back of each illustration. Cost of color figures, where used, is borne by authors.
4. ***Summary.*** A summary of 150 words or less should be submitted in English and Spanish. The summary must include a statement of the problem, methods of study, results and conclusions. A list of key words to be used for indexing should appear at the end of the summary.
5. ***References.*** References should be listed in consecutive numerical order as they are cited in the text. Once a reference is cited, all subsequent citations should be to the original number. All references must be cited in the text or tables. References to journal articles should include: authors, title, journal name as abbreviated in Index Medicus, year, volume number, and inclusive page numbers in that order. References to books should include: authors, chapter title, if any; editor in any; title of book; year; city and publisher. Volume and edition numbers, specific pages, and name of translator should be included when appropriate. The author is responsible for the accuracy and completeness of the references and for their correct text citation.
6. ***Originality & copyright.*** Manuscripts and illustrations submitted for consideration should not have been published elsewhere except for such preliminary material presented to the Panamerican Trauma Society.

INSTRUCCIONES PARA LOS AUTORES

Los manuscritos y la correspondencia se deben enviar a Ricardo Ferrada MD o Kimball Maull MD a las siguientes direcciones:**Ricardo Ferrada, M.D., FACS Departamento de Cirugía, Hospital Universitario del Valle, Calle 5 # 36-08, Cali, Colombia, S.A.**

1. ***Manuscritos.*** Se debe enviar un original del manuscrito y dos copias de todas las ilustraciones, leyendas, cuadros y referencias. Todas las copias, incluso las referencias, deben ser escritas a doble espacio en papel blanco de 21 x 27 cm. Los márgenes deben ser amplios. Se debe incluir un diskette o CD que contenga el artículo. Son preferibles los archivos en Word IBM compatibles o Apple. El diskette debe ser marcado con el nombre del artículo y de los autores, el tipo de sistema operativo y el procesador de palabras utilizado.
2. ***Título.*** El título debe ser corto, claro y específico. No puede exceder de 45 caracteres por línea y está limitado a dos líneas. La página del título incluye el nombre completo y la posición académica de los autores. En la parte inferior de la segunda página se debe indicar dónde se llevó a cabo el trabajo, la dirección para los reimpresos y las donaciones recibidas para su realización. Si el manuscrito se presentó en una reunión científica, indicar el nombre de la organización, el lugar y la fecha de presentación.
3. ***Ilustraciones.*** Por favor enviar tres copias completas de las ilustraciones en alto contraste en papel brillante. En la parte posterior de cada ilustración anote el número de la figura, el autor principal y una flecha con la punta hacia el borde superior. Si existen figuras a color, el costo será cubierto por los autores.
4. ***Resumen.*** No debe tener más de 150 palabras y debe ser enviado en español y en inglés. El resumen incluye una definición del problema, los métodos de estudio, los resultados y las conclusiones. Al final del resumen se debe adjuntar una lista de palabras claves para efectos de índice.
5. ***Referencias.*** Las referencias se citan en orden numérico consecutivo, tal como aparecen en el texto, e incluyen el siguiente ordenamiento: autores, título en el idioma original, nombre de la revista en su forma abreviada según el Index Medicus, año de publicación, volumen de la revista y páginas iniciales y finales. Se recomienda citar hasta cuatro autores en forma completa. Si hay más de cuatro autores, después del tercero, seguido por una coma, se colocan las palabras latinas et al. Las citas de libros incluyen: autores o editor y así se debe identificar (ed.), título del libro, edición, ciudad de publicación, la empresa editorial y año. Las referencias deben ser verificadas por los autores y ésta es una de sus responsabilidades.
6. ***Originalidad y derechos de autor.*** Los manuscritos deben ser inéditos y no haber sido publicados en otra parte, excepto como material presentado a la Sociedad Panamericana de Trauma.

PANAMERICAN JOURNAL OF TRAUMA

DISTRIBUNA Editorial
Colombia www.libreriamedica.com

Coordinación Editorial:
DISTRIBUNA
Editorial y Librería Médica
Autopista Norte 123 - 93
Fax: (57) 2132379
Tel: (57) 213-2379 ◆ (57) 620-2294
Bogotá - Colombia
www.libreriamedica.com
Impreso por: Gente Nueva editorial

PANAMERICAN JOURNAL OF TRAUMA

CONTENT CONTENIDO

Panamerican Journal of Trauma Vol. 14 No. 1 2007 Pages 07 - 13

ANTIMICROBIAL THERAPY – SEPARATING FACT FROM FICTION

Ajai K Malhotra, MD

As a group, antimicrobials are the second most common drug prescribed in the intensive care unit (ICU). Like any therapy, antimicrobial use has risks that need to be taken into account, and the benefits of therapy weighed carefully against these risks. Unfortunately, physicians have a tendency to prescribe antimicrobials as 'candy' oftentimes without carefully analyzing the risks and benefits. Secondly, when a patient is not doing well, there is an understandable desire on the part of the physician to do 'something' (anything) to try and help the patient, and changing or broadening the spectrum of antimicrobials very often ends up being that 'something'. In such situation however it is the physician who is getting the therapy often at the cost of the individual patient and society at large.

In very broad terms, antimicrobials are utilized for three reasons: 1. prevention of infection – prophylactic use, 2. therapy of known pathogen and site of infection – therapeutic use, and 3. therapy for presumed infection – empiric use.

PROPHYLACTIC USE OF ANTIMICROBIALS

The aim of prophylactic use of antimicrobials in the surgical patient is primarily to prevent surgical site infections (SSI). SSIs are the third most common serious nosocomial infections overall and the most common nosocomial infection among surgical patients. SSIs add to the morbidity and mortality of the surgical procedure and significantly add to the overall cost of care and length of stay. [1] For these reasons prevention of SSI is one of the six interventions of the "Saving 100,000 lives" campaign initiated by the Institute for Healthcare Improvement. [2]

Within a few years of the discovery of Penicillin, the possibility of preventing or reducing the incidence of SSI by prophylactic use of antimicrobials at the time of surgery was suggested. Some early trials published in the 1950s led to heated debates and more questions than answers. This was due to flaws in methodology including, non-randomization, lack of blinding, incorrect timing, prolonged usage, and inappropriate choices of agents. [3] Subsequent, better designed studies performed in the 1960s helped answer many of the questions. One landmark experimental study was by Burke in 1961 showing that to be effective in preventing S aureus infections the agent had to be in the skin before or at the time of exposure. [4] Subsequently two randomized placebo controlled clinical studies of patients undergoing gastrointestinal operations showed that when the appropriate antimicrobial was given just before the time of surgery, there was a significant reduction in SSIs. [5,6] In 1976 Stone et al demonstrated the lowest rates of SSIs with antimicrobials given within one hour before incision. In addition that study also showed that when the prophylactic antimicrobial was started postoperatively, the infection rates were nearly identical to those seen in patients who had received no prophylaxis. [7] Studies in the 1980s and later examined the duration of antimicrobial prophylaxis. Those studies demonstrated that prolonging therapy beyond the time of exposure ie after the incision was closed offered no additional benefit. Longer courses may actually be harmful by breeding resistant organisms, so the patients that do get infected, despite prophylaxis, oftentimes got infected with these more resistant organisms. [8]

Based on these studies the following principles of antimicrobial prophylaxis have been established:

1. **Indications:** Indicated for all surgical procedures where a) a significant decrease in SSI (≥10% absolute reduction) has been shown to occur with prophylaxis, or b) where, even though the reduction in incidence is much smaller, the consequences of SSI are so catastrophic that antimicrobial prophylaxis is justified. Based on this the specific guidelines include: a) all clean contaminated procedures; b) clean procedures that involve implantation of a foreign body; and c)

Asst. Prof. of Surgery, Medical Coll. of Virginia, Virginia Commonwealth Univ.
Associate Director, Level-I Trauma Center, VCU Health System
Richmond, VA

clean procedures involving the central nervous or cardiovascular systems, and all orthopedic procedures. [3]

2. **Agent of choice:** The specific antimicrobial used should be one that is inexpensive, safe and that covers the likely pathogens. For most patients coming from the community and undergoing elective clean procedures or clean contaminated procedures involving the respiratory tract, the likely pathogens are the gram positive organisms from the patients' own skin and upper airways. In view of that the most commonly utilized agent is a I-generation cephalosporin eg Cefazolin. Patients undergoing elective clean contaminated procedures involving the gastrointestinal or genitourinary tracts can develop SSI due to gram positive organisms from the skin or gram negative and anaerobic organisms from the lumen of these tracts. In such patients a II-generation cephalosporin (eg Cefoxitin) that has activity against all three classes of organism (gram positive, gram negative and anaerobes) should be utilized. The ideal antimicrobial agent that should be used for patients that are likely colonized with resistant organisms – those that have been in the hospital or other health care facility within the previous three months – remains unclear. The most common organism of concern in such patients is MRSA. Based on expert opinion the Hospital Infection Control Practices Advisory Committee guideline suggests that 'high' frequency of MRSA infection in an institution should influence the use of Vancomycin for prophylaxis. [9] However the frequency at which the level should be considered 'high' and thus justify the use of Vancomycin prophylaxis was left undefined. The only firm recommendation at this time is that if the hospital surveillance program detects a sudden increase in SSI due to MRSA, then it may be justified to temporarily use Vancomycin as the prophylactic agent till the incidence falls again. [9] In a study at an institution perceived as having a high rate of MRSA, 885 patients undergoing cardiac surgery were randomized to receive either Vancomycin or Cefazolin. The rates of SSI in the two groups were nearly identical (~9%). However the organisms responsible for the SSI were different with the Cefazolin group developing more infections with MRSA, and the Vancomycin group developing more infections with MSSA. [10] In another study it was shown that preoperative antimicrobial use of >1day and preoperative hospital stay of >5days was associated with higher incidence of MRSA SSI, but lack of Vancomycin prophylaxis did not influence the rate of MRSA SSI. [11]
3. Dose: The antimicrobial should be administered in the appropriate dose based on patient weight, adjusted dosing weight or body mass index. In a study of morbidly obese patients undergoing gastroplasty, the blood and tissue concentrations of the antimicrobial were consistently below the MIC in patients receiving only one gram of Cefazolin as compared to those receiving two grams. In parallel with that, the incidence of SSI was lower in patients receiving two grams of Cefazolin as compared to those receiving one gram. [12]
4. **Timing of administration:** As mentioned above a number of studies have shown that the agent should be timed so that it has achieved peak levels at the time of exposure ie skin incision, and LD_{90} levels are maintained till the time of exposure has passed ie the skin has been closed. [13] For most agents this means intravenous administration approximately half an hour before incision. However the timing should be tailored according to the pharmacodynamics of the agent being used. For example Vancomycin takes a longer period to achieve peak levels, and hence should be administered one hour prior to incision. To maintain blood and tissue levels at the LD_{90} for the duration of the procedure, the agent may need to be redosed for prolonged procedures. In a study performed on patients undergoing cardiac surgery and receiving Cefazolin prophylaxis, the incidence of SSI was higher in patients whose operation was >400minutes and who did not receive any additional dose after the first one as compared to other similar patients that were redosed at appropriate intervals. [14] Other studies, performed on patients undergoing various clean contaminated procedures have shown similar results. In view of this the current recommendation is to redose if the procedure is still in progress after two half lives of the prophylactic agent used. [15]
5. **Duration:** Numerous studies have demonstrated that continuing prophylactic antimicrobials beyond 24 hours offers no additional benefit in terms of reduction in incidence of SSI. [15] Many studies comparing a single perioperative dose to multiple doses continued postoperatively have likewise shown no benefit of multiple doses. [15] In addition studies have demonstrated that when antimicrobials are continued beyond 24 hours the patients that do get infected develop SSI by more resistant organisms. [8] At the current time the strongest evidence supports the use of single dose that maybe continued for upto 24 hours. [15]

While the above principals of prophylactic use of antimicrobials are well known, the compliance with these recommendations is oftentimes poor. The issue of compliance was examined in a large study of 34,133 Medicare patients undergoing coronary artery bypass grafting. The results showed that the agent was administered within one hour of

incision 55% of the time, the agent was appropriate 93% of time and was appropriately discontinued within 24 hours only 41% of the time. [16]

THERAPEUTIC USE OF ANTIMICROBIALS

Strictly speaking, therapeutic use of antimicrobials is when the site of infection is known and the causative pathogen and its sensitivity profile are available through culture results. One would think that in such situations therapy should be, in the large majority of patients, accurate and appropriate. Unfortunately there are many a slips between the cup and the lip. The problems in such patients usually revolve around the following factors: 1. unnecessary therapy; 2. inappropriate dosing; 3. nonrecognition of failure of therapy; and 4. inappropriate duration of therapy.

1. **Unnecessary therapy:** The most common causes of unnecessary therapeutic antimicrobial therapy are related to physicians not distinguishing between: a. colonization versus true infection; and b. positive cultures due to contamination versus true infection.
   a. **Colonization versus true infection:** The hospital environment, particularly the ICU, and the multiple invasive devices used on patients lead to rapid colonization of the patient with multiple potentially pathogenic organisms. Routine culture of these areas of the body will invariably show the presence of these organisms. It is important to be able to differentiate mere non-pathogenic colonization that does not require therapy, and true invasive infection that does require therapy. Failing to do that leads to unnecessary use of antimicrobial agents with potential harm to the patient and promotion of resistance in society. In addition it also leads to a false sense of security that if the patient is febrile, the source has been found – positive culture from colonized area – and is being treated appropriately, while in reality the true source of fever is not being looked for and remains untreated. One of the most common sources of positive cultures due to mere colonization is the upper respiratory tract of mechanically ventilated patients. Tracheal aspirates almost invariably reveal the presence of colonized organisms within five days of mechanical ventilation. [17] These do not represent true invasive infection. One of the methods used to differentiate ventilator associated pneumonia (VAP) from mere colonization is by quantitative culture of bronchoscopically obtained deep respiratory specimen. [17] A multi-institutional study involving 413 patients in 31 ICUs comparing the two techniques demonstrated significantly lower antimicrobial usage in the bronchoscopic group versus the non-bronchoscopic group. Even more importantly, the all cause 28-day mortality was significantly lower in the bronchoscopic group as compared to the other group. [18]
   b. **Contamination of culture specimen:** the reliability of culture result is dependent upon how meticulously the specimen was obtained, transported to the laboratory and processed. Studies performed on 497,134 blood cultures drawn at 640 institutions showed a significant contamination rate. [19] Another study examining the predictive value of blood cultures drawn from peripheral sites and central venous catheters showed that the positive predictive value of centrally drawn cultures was only 63%. [20]

2. **Inappropriate dosing:** To achieve the desired result ie eradication of infection, the antimicrobial has to be effective against the pathogen being treated, has to reach the area of the body where the pathogen is causing the infection, and the levels at the site of infection have to be adequate to achieve killing of the pathogen. The manner in which most hospital microbiology laboratories report sensitivity profiles maybe too simplistic and at times unreliable for certain organisms. [21] Different antimicrobials have different requirements to achieve adequate killing. Some antimicrobials are time dependent and concentration independent. For those agents it is not the level of the drug as much as the time the levels of the drug are above the MIC for the pathogen being treated. Other antibiotics on the other hand are concentration dependent and time independent. In such situations the agent has to have high concentrations relative to MIC. [22] In general beta-lactams, carbepenems, and monobactams are time dependent, and fluoroquinolones, glycopeptides and oxazolidinones are concentration dependent. Aminoglycocides, extremely useful for some difficult gram-negative organisms, have a narrow therapeutic window and the peak level to MIC ratio should be utilized. [23] Finally some antimicrobials have poor penetration in some tissues and hence the dosing has to take that into account for adequate therapy. A good example of the later is Vancomycin for the treatment of MRSA VAP. Vancomycin has poor penetration into lung tissue and hence significantly higher serum levels (trough levels of ~20µgm/ml) need to be aimed for to achieve the tissue levels in the lung required for therapy. A recent drug – Linezolid – has been shown to have at least equivalent activity against MRSA, but

achieves better tissue levels in the lung. Initial studies suggest that it may replace Vancomycin as the drug of choice for MRSA VAP. [24] These results are to be confirmed by an ongoing multi-institutional study.

3. **Nonrecognition of failure:** An extremely important concept in treatment of infections where the antimicrobials are the mainstay of therapy is ongoing evaluation to detect nonresponse to or failure of therapy early. If the patient does not have the expected response to therapy within 48-72 hours – objective evidence of abatement of infection and its systemic effects – a systemic review should be performed to detect the reason(s). The reasons of failure maybe: 1. inappropriate antimicrobial therapy – wrong choice of agent, wrong dose etc; 2. emergence of resistance; and 3. another source of infection not being adequately treated.

   To adequately address this there has to be a systematic approach and the urge to blindly change the antimicrobial or broaden the coverage should be resisted. Careful thought needs to be given to the choice and administration of the antimicrobial agent particularly in reference to the organisms being treated and the site of infection. The advice of a pharmacist, microbiologist or an infectious disease specialist can be extremely helpful. Rapid emergence of resistance is a well recognized phenomenon. In a study on patients being treated for VAP, despite a good response to adequate therapy, the investigators showed colonization by resistant gram-negative organisms by day six of therapy. Patients who then went on to develop a second infection were often infected by these resistant organisms. [25] Lastly in patients with non response to antimicrobial therapy, a thorough evaluation for any additional source of infection should be initiated.

4. **Inappropriate duration of therapy:** The duration of antimicrobial therapy for various sites of infection and various organisms is an area of intense study. By and large the previously accepted durations for various infections were arbitrary and based on expert opinion rather than firm data from trials. In recent years some studies have been initiated to review this. In a well designed multi-institutional study, Chastre et al evaluated the hypothesis that 8-day course of appropriate antimicrobial therapy is non-inferior to the traditional 15-day course of therapy in patients with bronchoscopically obtained culture proven VAP when the therapy was initiated within 24 hours. The results from 401 patients from 51 centers showed that the 8-day therapy was as effective in treatment as the 15-day therapy. In addition the study showed that although the recurrence rate for pulmonary infections was similar in both groups, of the patients that did develop recurrence, resistant organisms were more common in the longer therapy group than the 8-day therapy group. The majority of the recurrences however involved patients whose initial infection was caused by non-fermenting gram-negative bacilli. [26] As more such studies are performed and more objective data becomes available it is possible that the duration of therapy will be determined by not only the site of infection but also by the causative organism.

EMPIRIC USE OF ANTIMICROBIALS

Empiric antimicrobial therapy generates the most heated of debates. The clinician is caught between two opposing yet equally valid concerns. Multiple studies have shown that early appropriate antimicrobial therapy improves outcomes and decreases overall cost of care. In view of that there has to be a low threshold of initiating antimicrobial therapy in any patients suspected of having an infection, and to maximize the chance of the therapy being appropriate (effective against the causative organism) the therapy should have as broad a spectrum as possible. Yet on the other hand liberal use of broad spectrum antimicrobials is the principal cause of the development of resistant organisms that may worsen outcome in the individual patient being treated and be harmful in the long run for society. To reconcile these two opposing concerns, a reasonable compromise that takes into account the clinicians duty to the individual patient and the concern for the future is probably to have a reasonably low threshold for initiating relatively broad spectrum antimicrobial therapy for suspected infection, but be ready and willing to stop or de-escalate therapy when more information becomes available from the culture results and other tests. The temptation to 'not rock the boat' when the patient is improving by empiric broad spectrum antimicrobials should be stringently resisted. The following principals of empiric therapy should be followed.

1. **Initiation:** The decision to initiate empiric antimicrobial therapy in a patient who may have an infection should be taken with care. Therapy should not be initiated without a careful evaluation and by going through a process to try to answer the following questions: 1. what are the chances of an infection being present? 2. if an infection is present, how serious is the likely infection? and 3. if a relatively innocuous infection is present, can antimicrobial therapy be safely withheld till the results of tests to confirm or rule out an infective process are available ie the type of infection suspected has a very low likelihood of systemic or local spread?

To answer these question a thorough history and physical examination should be initiated. Since the suspicion of an infection usually starts with the development of new onset fever, the process starts by going through an algorithm of evaluation of a new onset fever. Excellent algorithms are available through the societies of critical care medicine and infectious diseases.

Once the initial evaluation, including simple blood and radiological tests, has been performed the decision to initiate antimicrobials is to be made. When the chances of an infection being present are low, the nature infection if present is not serious, the patient is not systemically ill, and the suspected infection has low likelihood of spread, empiric antimicrobials can be safely withheld till the final culture results become available. In the large majority of instances however, the answer to one or more of these questions is 'yes' and hence empiric antimicrobial therapy needs to be initiated. Prior to initiation it is imperative that all cultures are drawn and sent to the laboratory.

2. **Choice of empiric agent:** The choice of agent is dependent upon many factors. The most important of which are 1. Identity of the likely pathogen(s) – relatively susceptible community acquired or the more resistant hospital acquired – and 2. Their likely susceptibilities. Once a likely site of the infection has been identified, a reasonable guess of the likely pathogen(s) can be made. The organisms are likely to be resistant in patients that have been in the hospital or other health care facility in the previous three months, and those that have received antimicrobials, for any reason, within the previous two weeks. Finally when the likely pathogen(s) have been thought of, the antimicrobial agent or combination most likely to be effective against those organisms should be initiated. Of the available drugs that have good activity against the likely organisms, the drug with the narrowest of spectrum should be chosen. In some instances, the site of infection and the likely pathogen(s) may be impossible to even guess upon. In such situations it maybe justified to initiate a broad spectrum single antimicrobial or combination. However, even in such situations if the infection is likely to be community acquired I-line agents can be utilized keeping the more potent II- and III-line agents for the patients more likely to have the more resistant hospital acquired organisms. One specific agent of concern is Vancomycin. Till recently it was the only effective agent against MRSA. As the incidence of MRSA has increased in the hospital and now even in the community, Vancomycin usage, both therapeutic and empiric, has risen too. In parallel with the increasing use of Vancomycin has been the rise of Vancomycin resistant enterococcus (VRE) and some strains of Vancomycin-intermediate SA (VISA). [27] When infection with MRSA is a serious concern, empiric Vancomycin is justified, however extra care needs to be exercised when making that decision.

While these guidelines should be kept in mind, it should also be remembered that the choice of agent utilized by physicians is often inappropriate in that it is not effective against the organism finally cultured. In a study by Kollef et al, the initial antimicrobial did not target the organism identified by culture in 17% of the community acquired infections, 34% of the hospital acquired infections and 45% of infections initially acquired in the community with super-infection while in the hospital. [28] Since multiple studies have demonstrated poorer outcome in patients receiving inappropriate antimicrobials initially, [28] strategies are being developed to minimize the use of inappropriate therapy. Two strategies that have been shown to be effective are: 1. Use of local antibiogram; and 2. Computer assisted antimicrobial management.

   a. **Antibiogram:** These are periodic reports by the local microbiology laboratory about the sensitivity profiles of the common organisms cultured from patients within the hospital. Once the decision to initiate empiric antimicrobial therapy has been made and the likely pathogen(s) guessed at, the appropriate agent can be chosen based on the sensitivity profile of the local strain of that organism shown in the antibiogram. When the sensitivity profile of the organisms changes locally, this will be reflected in the next antibiogram, and the choice of empiric agent too can be modified. Such a strategy of rotating antiimicrobials according to changing sensitivity profile seen on antibiograms, has been shown to be effective in promoting appropriate empiric therapy, and at the same time limiting the development of resistance. However to be an effective tool, these antibiograms have to be hospital area eg ICU specific. Hospital wide antibiograms are of little help. [29]

   b. **Computer assisted antimicrobial management:** Optimal decisions about antimicrobial therapy require access and processing of a large amount of complex information. Computers are perfectly suited to this task. Such a program was developed and tested by Evans et al and the results reported in the *New England Journal of Medicine*. The program assimilates epidemiological data, patient specific microbiological data, patient's diagnosis and current status and recommends an antibiotic regimen. The program was prospectively evalu-

ated in a twelve bed ICU. Patient outcomes were examined for a period of one year after introduction of the program, and compared to outcomes over the preceding two years, prior to introduction. There was a significant decrease in patient length of stay, inappropriate antimicrobial usage, and cost of therapy. [30]

3. **De-escalation of therapy:** Whatever strategy of choosing the initial empiric antimicrobial agent(s) is followed, it is paramount that once the culture results from specimen sent prior to initiation of the empiric therapy are available (usually in 48-72 hours), the empiric therapy be modified. This modification of therapy, usually by narrowing the spectrum to target only cultured organism based on its individual sensitivity profile, is termed de-escalation of therapy. Of all sources of overuse and abuse of antimicrobials, the initiation of overly broad spectrum empiric therapy and not de-escalating the therapy once the culture results are available probably contributes the most. The area where this strategy has been tested the most is in patients with VAP. Studies have been able to demonstrate improved outcomes in the form of reduced frequency of secondary infection, reduction in antimicrobial resistance, and improved mortality. [31] Studies to expand the strategy to different infections are needed.

CONCLUSIONS

Antimicrobials are utilized to prevent infection, treat known infection, and to treat presumed infections. Each of these broad reasons to prescribe antimicrobials has different set of principals to be applied for the optimum results. For prophylaxis the appropriate agent active against the likely pathogens causing SSI should be administered in the appropriate dosage based on patient habitus, within one hour of the surgical incision and discontinued within 24 hours of the procedure. For treating known infections, it is important to be sure that what is being treated is actually a true infection. If it is then the agent to be utilized should be based on its activity against the pathogen, in the appropriate dose and for the shortest possible duration. The narrowest spectrum agent should be used. The drug pharmacodynamics can be very helpful in deciding the appropriate agent for a particular infection site and pathogen. Careful re-evaluation to detect failure of therapy early should be performed and appropriate steps taken to find the cause of failure. Lastly appropriate empiric broad spectrum antimicrobial therapy is often necessary. However, as soon as the culture results become available, usually 48-72 hours, the antimicrobials should undergo de-escalation to reduce exposure and keep resistance at bay.

Today's antimicrobial agents are much more powerful than ever before. Despite that serious infections continue to take lives, increase morbidity and add to the cost of care. Also misuse, abuse and overuse of antimicrobials continue to promote the development of resistant organisms that make the available antimicrobials less useful. Fortunately after a lull in the development of newer agents, in the 1980s and early 1990s, the pace of development has again increased. While this maybe good news the newer agents are oftentimes more toxic and certainly more expensive. There are some basic science reports suggesting that we may actually run out of finding new classes of antimicrobials as there is a limit to the metabolic processes within the bacteria that the antimicrobials can act upon. To maintain the effectiveness of the current antimicrobials and to provide the best of care to our patients it behooves us to practice good evidence based antimicrobial management.

REFERENCES

1. Kirkland KB, Briggs JP, Trivette SL, et al. The impact of surgical-site infections: attributable mortality, excess length of stay, and extra costs. Infect Control Hosp Epidemiol 1999;20:725-730.
2. http://www.ihi.org/IHI/Programs/Campaign
3. Nichols RL. Preventing surgical site infections: a surgeon's perspective. Emerg Infect Dis 2001;7:220-224.
4. Burke JF. The effective period of preventive antibiotic action in experimental incision and dermal lesions. Surgery 1961;50:161-168.
5. Bernard HR, Cole WR. The prophylaxis of surgical infection: the effect of prophylactic antimicrobial drugs on the incidence of infection following potentially contaminated operations. Surgery 1964;56:151-169.
6. Polk HC, Lopez-Mayor JF. Postoperative wound infection: a prospective study of determinant factors and prevention. Surgery 1969;66:97-103
7. Stone HH, Hooper CA, Kolb LD, et al. Antibiotic prophylaxis in gastric, billiary and colonic surgery. Ann Surg 1976;184:443-452.
8. Harbarth S, Samore MH, Lichtenberg D, et al. Prolonged antibiotic prophylaxis after cardiovascular surgery and its effect on surgical site infections and antimicrobial resistance. Circulation 2000;101:2916-2921.
9. Mangram AJ, Horan TC, Pearson ML, et al. Guideline for prevention for surgical site infection, 1999. Hospital Infection Control Practices Advisory Committee. Infect Control Hosp Epidemiol 1999;20:250-278.
10. Finkelstein R, Rabino G, Mashiah T, et al. Vancomycin versus cefazolin prophylaxis for cardiac surgery in the setting

of a high prevelance of methicillin-resistant staphylococcal infections. J Thorac Cardiovasc Surg 2002;123:326-332.

11. Manian FA, Meyer PL, Setzer J, et al. Surgical site infections associated with methicillin-resistant Staphylococcus aureus: do postoperative factors play a role? Clin Infect Dis 2003;36:863-868.
12. Forse RA, Karam B, MacLean LD, et al. Antibiotic prophylaxis for surgery in morbidly obese patients. Surgery 1989;106:750-756.
13. Classen DC, Evans RS, Pestotnick SL, et al. The timing of prophylactic administration of antibiotics and the risk of surgical-wound infection. N Eng J Med 1992;326:281-286.
14. Zanetti G, Giardina R, Platt R. Intraoperative redosing of cefazolin and risk for surgical site infection in cardiac surgery. Emerg Infec Dis 2001;7:828-831.
15. Bratzler DW, Houck PM. Antimicrobial prophylaxis for surgery: an advisory statement from the National Surgical Infection Prevention Project. Clin Infect Dis 2004;38:1706-1715.
16. Bratzler DW, Houck PM, Richards C, et al. Use of antimicrobial prophylaxis for major surgery: baseline results from the National Surgical Infection Prevention Project. Arch Surg 2005;140:174-182.
17. American Thoracic Society Document; Guidelines for the management of adults with hospital-acquired, ventilator-associated, and healthcare-associated pneumonia. Am J Resp Crit Care Med 2005;171:388-416.
18. Fagon JY, Chastre J, Wolff M, et al. Invasive and noninvasive strategies for management of suspected ventilator-associated pneumonia. A randomized trial. Ann Int Med 2000;132:621-630.
19. Schifman RB, Strand CL, Meier FA, et al. Blood culture contamination: a College of American Pathologists Q-Probes study involving 640 institutions and 497134 specimens from adult patients. Arch Pathol Lab Med 1998;122:216-221.
20. DesJardin JA, Falagas ME, Ruthazer R, et al. Clinical utility of blood cultures drawn from indwelling central venous catheters in hospitalized patients with cancer. Ann Int Med 1999:131:641-647.
21. Steward CD, Wallace D, Hubert SK, et al. Ability of labotratories to detect emerging antimicrobial resistance in nosocomial pathogens: a survey of project ICARE laboratories. Diag Microbiol Infect Dis 2000;38:59-67.
22. Ibrahim KH, Gunderson B, Rotschafer JC. Intensive care unit antimicrobial resistance and the role of the pharmacist. Crit Care Med 2001;29S:N108-N113.
23. Micek ST, Heuring TJ, Hollands JM, et al. Optimizing antibiotic treatment for ventilator-associated pneumonia. Pharmacother 2006;26:204-213.
24. Lam AP, Wunderink RG. Methicillin-resistant S. aureus ventilator associated pneumonia: strategies to prevent and treat. Semin Respir Crit Care Med 2006;27:92-103.
25. Dennesen PJ, van der Ven AJ, Kessels AG, et al. Resolution of infectious parameters after antimicrobial therapy in patients with ventilator-associated pneumonia. Am J Respir Crit Care Med 2001;163:1371-1375.
26. Chastre J, Wolff M, Fagon JY, et al. Comparison of 8 vs 15 days of antibiotic therapy for ventilator-associated pneumonia in adults: a randomized trial. JAMA 2003;290:2588-2598.
27. Schentag JJ, Hyatt JM, Carr JR, et al. Genesis of methicillin-resistant Staphylococcus aureus (MRSA), how treatment of MRSA infections has selected for vancomycin-resistant enterococcus feacium, and the importance of antibiotic management and infection control. Clin Infect Dis 1998;26:1204-1214.
28. Kollef MH, Sherman G, Ward S, et al. Inadequate antimicrobial treatment of infections: a risk factor for hospital mortality among critically ill patients. Chest 1999;115:462-474.
29. Lautenbach E, Nachamkin I. Analysis and presentation of cumulative susceptibility data (antibiogram): substantial variability across medical centers in the United States. Infect Control Hosp Epidemiol 2006;27:409-412.
30. Evans RS, Pestotnik SL, Classen DC, et al. A computer-assisted management program for antibiotics and other anti-infective agents. New Engl J Med. 1998;338:232-238.
31. Relo J, Vidaur L, Sandiumenge A, et al. De-escalation therapy in ventilator-associated pneumonia. Crit Care Med 2004;32:2183-2190.

Panamerican Journal of Trauma Vol. 14 No. 1 2007 Pages 14 - 16

BLOOD BANK – ¿FRIEND OR FOE? IMPLEMENTING A MASSIVE TRANSFUSION PROTOCOL IN REAL TIME

Erwin R. Thal, MD

Transfusion therapy remains one of the most common and important treatment modalities in the acute management of trauma. Hoyt et al reported that 82% of deaths in the operating room are due to bleeding. Over ten million units of blood are transfused each year in the United States. The treatment of injured patients requires a team effort and the blood bank plays a key role in that regard. It must definitely be considered a friend rather than a foe. To be a friend requires establishing a collegial relationship with the blood bank personnel and a cooperative effort to develop appropriate and effective protocols. The key to a successful program is precise pre-planning, which will allow protocols to be initiated on a moments notice with a single phone call. It is essential that all personnel be familiar with the protocols, especially those who work during off-hours and newly hired employees.

There have been major changes in blood banking over the past several years. Fresh whole blood is a precious commodity that is now rarely available due to the more efficient use of its' component parts. These components are now used to restore intravascular volume, restore oxygen carrying capacity and correct coagulopathies.

Restoration of volume is the most common indication for the administration of packed red cells in the ED. It is given to patients who remain hypotensive (SBP <90) after the administration of 2 liters of crystalloid in the absence any other source of shock. It is important for the blood bank to be part of the Level I trauma activation. When a Level I patient arrives, most hospitals deliver a cooler to the ED containing two to four units of universal donor packed cells. In the absence of an automatic delivery, the blood bank must be prepared to release universal donor blood immediately upon a properly executed request.

Restoration of oxygen carrying capacity usually occurs simultaneously with resuscitation and continues in the postoperative or post resuscitative period. A hemoglobin of 7 g/dL (Hct 20-21) is generally well tolerated in younger patients once all bleeding has been controlled. A hemoglobin of 10 g/dL (Hct 30) may be more optimal for elderly patients or those with cardiovascular disease. This must be carefully monitored by physiological parameters such as pulse rate, respiratory rate, blood pressure, base deficit, orthostasis, urine output etc.

Coagulopathies are commonly seen in trauma patients and generally occur with massive transfusions (>10 units), hypothermia, acidosis, over resuscitation with crystalloid solutions and prolonged shock. Based on certain triggers these are corrected with variations of fresh frozen plasma, platelets and cryoprecipitate. During the resuscitative period it is suggested that platelets (administered in six unit increments) be kept above 100,000, although much lower values (20,000 – 40,000) are acceptable once the patient has been stabilized and is no longer bleeding. Fresh frozen plasma is used to keep the INR, PT and PTT at or equal to 1.5 times the normal values. Vitamin K may be used as an adjunct. It is important to note that these values are not accurate in the hypothermic patient. Cryoprecipitate is indicated when the fibrinogen levels are low.

A recombinant form of activated factor VII (rVIIa) in the past has been reserved for the treatment of hemophilia. There is now growing evidence that it is very effective in controlling hemorrhage in the trauma patient. Dutton and co authors concluded in a series of 81 coagulopathic trauma patients that FVIIa therapy lead to an immediate reduction in hemorrhage in most cases. Boffard et al reported their results of a randomized, placebo-controlled, double blind clinical trial for both blunt and penetrating trauma. They found that rFVIIa resulted in a significant reduction in RBC transfusions in severe blunt trauma and a similar trend in penetrating trauma patients. In spite of the expense associated with the use of rVIIa, (approximately $4500) it is proving to be cost effective.

There are two general methods by which patients who are massively bleeding can be treated; laboratory based and empiric. Laboratory based management seems logical, how-

ever, it is impractical. The time to get the results is unacceptable, the results do not reflect what has happened since the blood specimens were drawn and the tests are done at 37^0 C and, hence do not reflect the true coagulopathy. Management based on test results will delay the transfusion as it generally takes 10-20 minutes to prepare the components.

In June 2004 a massive transfusion protocol was developed at Parkland Memorial Hospital in Dallas, Texas. This was implemented after lengthy discussions with the blood bank, trauma surgeons and specialty services. The goals were to:

1. Prevent dilutional coagulopathy.
2. To anticipate and provide the blood products in a timely manner.
3. To avoid wastage of blood products via coordination with the treatment area regarding the status of these patients.

The clinician initiates the protocol. The blood bank is notified by phone and an emergency request on a blue card is sent with massive transfusion protocol (MTP) written on it. The blood bank will contact the transfusion medicine resident for coordination if needed. (This rarely occurs)

The blood products are issued in appropriate containers. The blood bank always stays one shipment ahead of the requests. When additional blood is needed, someone goes to the blood bank and the next shipment is ready to be picked up. The products are shipped in appropriate ratios (see shipment schedule below). If the clinician wants doubling of the products in an exsanguinating patient, it will require an additional phone call to the blood bank, require a written request at the time of pick-up and will take additional time to prepare the products. The operating room will terminate the protocol by notifying the blood bank upon instructions from the surgeon.

The component shipment schedule is as follows:

Shipment	RBC	FFP	Platelets	Cryoprecipitate	rVIIa
1	5	2			
2	5	2	5 pack		
3	5	2		10 units	4.8 mg
4	5	2	5 pack		
5	5	2			
6	5	2	5 pack	10 units	2.4 mg
7	5	2			
8	5	2	5 pack		
9	5	2		10 units	
10	5	2	5 pack		

The blood products are dispensed in individual containers.

Product	Temperature	Container
5 PRBCs 2 FFP	1-6^0 C Coolant	Large Cooler
1 Platelet Pack 10 Units of Cryo	Room Temperature No Coolant	Clear Plastic Box
rFVIIa	1-6^0 C Coolant	Smaller cooler

The protocol has been well accepted by both the blood bank and the surgeons. It works well and although on the surface may seem to be expensive because of the use of rVIIa, it has many advantages. If one does not use rVIIa one can anticipate the additional use of blood products, development of coagulopathies, additional surgical procedures, longer operating room times, longer hospital stay, potential for morbidity related to blood product use and patient mortality. The goal is to aggressively treat the bleeding patient as early as possible and limit the blood loss before complications occur.

The data was reviewed after the first 54 severely injured patients of whom 27 survived.

	Issued	Transfused	Returned	Wasted
RBC	940	651	289	0
Platelet Pools	16	7	9	8
FFP	444	346	98	6
Cryoprecipitate	50	45	15	30
Novoseven	32	26	6	0

A recent analysis indicated a significant cost savings to the hospital as evidenced by the reduction of packed red cells per case from 21.4 to 13.5 and a reduction in the use of fresh frozen plasma per case from 9.1 to 6.9 both of which are statistically significant. The turn around time for all of these products was considerably shortened.

	Pre-MTP* (5-03 to 5-04)	Post MTP (6-04 to 2-06)
Number of patients	65	105
Total RBCs used	1390	1423
RBC/Case	21.4	13.5
Total FFP used	596	732
FFP/Case	9.1	6.9
RBC/FFP Ratio	2.3	1.9
Total Platelets used	88	122
Platelets/case	1.4	1.2
Total Cryo used	46	79
Cryo/case	0.7	0.7
Total Novoseven used	8	56
Novoseven/case	0.1	0.6

* MTP = Massive Transfusion Protocol

In summary the blood bank has proven to be an integral friendly partner of the trauma program at a major Level I trauma center. With cooperative pre-planning an effective massive transfusion protocol has been developed and implemented resulting in a significant reduction in the number of packed red cells and fresh frozen plasma that has been used in the first two years since its' inception.

Panamerican Journal of Trauma Vol. 14 No. 1 2007 Pages 17 - 19

BLUNT SMALL BOWEL INJURIES – JUST AS DIFFICULT, JUST AS DANGEROUS

Samir Fakhry, MD, FACS

INTRODUCTION

Blunt small bowel injury (SBI) is an unusual injury that is frequently difficult to diagnose in a timely fashion [1,2,3]. . Blunt SBI is the most common hollow viscous injury diagnosed [7]. In the era prior to widespread use of the abdominal computerized tomography (CT) scan, frequent operative intervention for intraperitoneal injury allowed timely diagnosis of most blunt SBI. Non-operative management of patients with abdominal injuries has become increasingly commonplace over the past 2 decades [4,5,6]. Driven by the widespread adoption of CT scan as the diagnostic test of choice, the majority of patients with blunt abdominal injury can now be successfully managed without operative intervention. While the management of solid organ injury has improved, clinicians have encountered significant challenges in the timely diagnosis of blunt hollow viscous injury.

Blunt SBI can be divided into two categories: perforated and non-perforated. For the purposes of this discussion, we will consider non-perforated SBI to require no surgical intervention. In fact, it is likely that non-perforated injuries (such as bowel wall hematomas and non-transmural tears) occur much more frequently than is clinically apparent. The management of blunt perforated SBI is relatively straightforward in almost all cases. It is in the diagnosis of perforated SBI that the difficulties and the challenges arise.

MULTI-INSTITUTIONAL STUDY

In 2003, we published the results of the Eastern Association for the Surgery of Trauma (EAST) Multi-Institutional study of HVI [1,7]. Ninety five Trauma Centers evaluated a total of 275,557 patients to study the incidence, diagnosis and outcomes of blunt hollow viscous injury (HVI). The study included patients managed over a two year period and was concluded in the spring of 2001. All ages were included. The study used a retrospective, descriptive, case-control design with a 1:1 match of cases to controls. Index (or primary) cases were patients with any blunt hollow viscous injury (ICD-9-CM 863.0 to 863.99, excluding isolated pancreas injuries). Matching control cases were patients who were worked up for suspected blunt intra-abdominal injury but who did not have hollow viscous injury. Patients were case matched on age (+ 5 years) and Injury Severity Score (+ 20%). Patient level data were abstracted by individual chart review at the participating institutions using a standardized data collection form with a data dictionary. Data were collected at each institution on medical history, physical examination findings (tenderness, distension, appearance, peritoneal signs, contusion, abrasion, and previous operation), transferring facility, demographics, other injuries, laboratory studies and results, diagnostic studies, operative procedures, complications, and outcome. The date and times of key events were recorded including the times of: injury, transfer, hospital arrival, performance of diagnostic and laboratory tests, diagnosis of a HVI, operations, and discharge/death.

The contributing institutions were predominately Level I and II Trauma Centers (91.6%). The majority were teaching institutions (87.2%). The institutions admitted a mean of 1450 trauma patients per institution annually (range 63-7998). The mean number of controls was 497 per institution (range 40-2603) and the mean number of blunt SBI patients seen annually was 13 per institution (range 1 to 47). Control patients outnumbered small bowel injury patients at a rate of about 34 to 1. The 95 participating centers submitted a total of 4,144 completed cases and controls for analysis. The data were entered into a secured database at the Inova Regional Trauma Center in Falls Church, Virginia, the lead institution for the study.

The study found that perforated SBI was rare (0.3 % of patients) and difficult to diagnose. The findings on CT scan are shown in Table 1. Approximately 13% of patients with perforated SBI at surgery had a normal preoperative abdominal CT scan. The presence of free fluid without solid organ injury was associated with perforated SBI in only 30% of patients. Delays

Chief, Trauma and Surgical Critical Care
Associate Chair for Research and Education
Department of Surgery, Inova Fairfax Hospital
Professor of Surgery
Virginia Commonwealth University - Inova Campus
Falls Church, Virginia

in diagnosis were highly significant as shown in Table 2. No combinations of physical exam, laboratory, radiologic or other data allowed consistent early diagnosis of this injury without subjecting large numbers of patients to non-therapeutic laparotomy. Multiple logistic regression model iterations revealed that the most accurate, clinically relevant diagnostic model was the presence of *abdominal tenderness, peritoneal signs and free fluid without solid organ injury on CT scan.* However this model was only marginally predictive of perforated SBI (sensitivity = 56.1%, specificity = 94.4%, accuracy = 88.4%, R^2 = .44, p<.001). In clinical terms, widespread use of this model would mean that if the surgeon were to operate on 40 patients with the findings mentioned, he or she would correctly diagnose 19 of the 20 patients who actually had perforated SBI but in the process would perform non-therapeutic laparotomy in about 20 (or 50%) of the patients. The clinician would still end up missing/delaying the diagnosis of perforated SBI in 1 of 20 patients. If the surgeon's goal is to obtain timely diagnosis in as many patients with perforated SBI as possible while performing the fewest number of non-therapeutic laparotomies, this model does offer an improvement over current reliance on abdominal CT scan where 1 in 6 patients are likely to have a delay in diagnosis based on a (falsely) negative CT scan.

CHALLENGES

The challenges facing the clinician caring for a patient with perforated blunt SBI are significant. These challenges can be summarized as follows:

1. The injury is relatively rare. Perforated SBI occurs in only 0.3% of blunt trauma patients seen at trauma centers participating in the EAST Multi-Institutional study of HVI, the largest multi-center series on SBI published to date [1]. As a result, most surgeons have limited exposure to this injury and the majority of centers have no standardized approach for its diagnosis.
2. There appears to be no widespread consensus among surgeons as to the optimal approach for the timely diagnosis of blunt perforated SBI. In a survey of members of the American Association for the Surgery of Trauma (AAST), Brownstein et al found that surgeons relied heavily on their previous experience and were guided most often by CT scan results [3].
3. Abdominal CT scan is not sensitive for the diagnosis of hollow viscous injury especially small bowel injury. In the EAST Multi-Institutional HVI Study [1], the following were important findings (Table 1):
   a. Approximately 13% of patients with small bowel perforation proven at surgery had a normal pre-operative CT scan.
   b. The use of oral contrast with abdominal CT scan in the diagnostic work-up of this injury is of no practical value since extravasation of the oral contrast from a bowel perforation is rare: Less than 5% of perforated SBI patients had contrast extravasation on their pre-operative CT scan.
   c. The presence of free air on abdominal CT scan is a highly reliable sign of perforated SBI. However, free air is present in no more than 30% of patients with proven perforated SBI.
   d. Blunt trauma patients with free fluid in the abdomen without solid organ injury have a 30.5% chance of having perforated SBI.
4. Delays in the diagnosis of perforated SBI are associated with significant increase in mortality. In patients with near isolated perforated SBI (no other injuries with an AIS>1), delays of over 24 hours from injury result in a three to four fold increase in mortality (Table 2).
5. Even when employing the best diagnostic models, the surgeon has to accept non-therapeutic laparotomy rates of between 50 and 70% in order to minimize delays in diagnosis.

CONCLUSION

The authors of the EAST Multi-Institutional HVI Study concluded the following in their 2003 paper on HVI:

> "*Perforated SBI is a rare but potentially deadly phenomenon. Alone or in combination, current diagnostic approaches lack sensitivity in the diagnosis of perforated SBI. Approximately 13% of patients with small bowel perforation following blunt trauma will have a normal abdominal CT scan. A negative abdominal CT scan is therefore inadequate to rule out perforated SBI. Delays in the diagnosis of perforated SBI beyond 24 hours carry significantly higher mortality and morbidity rates. Improvements in diagnostic methods and interpretation are needed to ensure the prompt diagnosis of this uncommon but potentially devastating injury. Based on the results of this large, multi-institutional study a diagnostic approach was developed which should decrease the frequency of delays in the diagnosis of SBI. This represents an incremental improvement in our diagnostic ability for patients with perforated SBI. Overall, however, our ability to diagnose blunt SBI is far from perfect and the challenge facing the clinician continues to be a formidable one.*"

In considering all the available evidence and if the intent is to avoid prolonged delays in diagnosis, the only effective approach at the present time appears to be a strategy of liberal operative exploration with the expectation of a high rate of non-therapeutic laparotomy. Attempts to avoid these high rates of non-therapeutic laparotomy until the diagnosis is "established" are likely to result in significant delays in diagnosis and preventable mortality and morbidity.

DIAGNOSTIC FINDINGS ON ABDOMINAL CT SCAN

CT SCAN FINDINGS		Overall	Perforated SBI	Non-Perforated SBI	No SBI	p
N		3258	408	1207	1643	
Free Fluid	(% +)	42.4	71.6	64.7*	18.9*	<.001
Solid Organ Injury	(% +)	29.2	21.1	41.2*	22.5	<.001
Bowel Wall Thickening	(% +)	10.2	21.3	16.4*	2.9*	<.001
Free Air	(% +)	7.2	25.2	9.3*	1.2*	<.001
Mesenteric Stranding	(% +)	8.6	11.0	13.3	4.5*	<.001
Contrast Extravasation	(% +)	3.4	2.9	6.5*	1.2	<.001
Retroperitoneal Blood	(% +)	2.3	3.2	3.2	1.5*	.004
Chance Fracture	(% +)	1.7	2.7	2.1	1.2*	.040
Free Fluid without Solid Organ Injury	(% +)	23.0	55.9*	33.2*	7.2*	<.001
No Abnormalities	(% +)	36.6	13.0	11.8	60.8*	<.001

* significant difference compared to patients with perforated SBI

MORBIDITY AND MORTALITY RATES BY TIME TO OPERATION FOR PERFORATED SBI

	Rates by Time to Operative Repair				
	Overall	≤ 8 hrs.	>8 to <24 hrs.	≥ 24 hrs.	p level
ISOLATED PERFORATED SBI	n = 237	n = 134	n = 69	n = 34	
Any Complication	21	18	19	38*	.030
Intra-abdominal Abscess	4	4	4	6	ns
Acute Renal Failure	2	0	3	6*	.037
ARDS	5	3	6	9	ns
Sepsis	5	4	3	18*	.003
Pneumonia	6	5	7	9	ns
Deep Vein Thrombosis	1	1	0	0	ns
Wound Dehiscence	4	4	1	9	ns
Death	6	4	6	15*	.029

all comparisons are compared to patients repaired within 8 hours

REFERENCES

1. Fakhry SM, Watts DD, Luchette FA and the EAST Multi-Institutional HVI Research Group. Current Diagnostic Approaches Lack Sensitivity in the Diagnosis of Perforated Blunt Small Bowel Injury (SBI): An Analysis from 275,557 Trauma Admissions from the EAST Multi-Institutional HVI Trial. J Trauma. 54:295-306, 2003.
2. Fakhry SM, Brownstein MR, Watts DD, Baker CC, Oller D. Relatively Short Diagnostic Delays (< 8 Hours) Produce Morbidity and Mortality in Blunt Small Bowel Injury (SBI): An Analysis of Time to Operative Intervention in 198 Patients From A Multi-center Experience. Journal of Trauma, 48:408-15, 2000.
3. Brownstein, MR, Bunting, T, Meyer, AA, Fakhry, SM. Diagnosis and Management of Blunt Small Bowel Injury: A Survey of the Membership of the American Association for the Surgery of Trauma. Journal of Trauma, 48:402-07, 2000.
4. Meyer AA, Crass RA, Lim RC, Jeffrey RB, Federle MP, Trunkey DD. Selective Nonoperative Management of Blunt Liver Injury Using Computed Tomography. Arch Sur, 120:550-54, 1985.
5. Rutledge R, Hunt JP, Lentz CW, Fakhry SM, Meyer AA, Baker CC, Sheldon GF. A Statewide, Population Based Analysis of the Increasing Frequency of Nonoperative Management of Abdominal Solid Organ Injury. *Annals of Surgery*, 222:311-326, 1995.
6. Peitzman AB, Heil B, Rivera L, Federle MB, Harbrecht BG, Clancy KD, Croce M, Enderson BL, Morris JA, Shatz D, Meredith JW, Ochoa JB, Fakhry SM, et al. EAST Multi-institutional Trials Committee. Blunt Splenic Injury in Adults: Multi-Institutional Study of the Eastern Association for the Surgery of Trauma. Journal of Trauma 49:177-189, 2000.
7. Watts DD, Fakhry SM and the EAST Multi-Institutional HVI Research Group. Incidence of Hollow Viscous Injury and Small Bowel Injury in Blunt Trauma: An analysis from 275,557 trauma admissions from the EAST Multi-Institutional Trial. Journal of Trauma, 54:289-294, 2003.

Panamerican Journal of Trauma Vol. 14 No. 1 2007 Pages 20 - 23

DAMAGE CONTROL – LIVER

Rao Ivatury, MD, FACS

The patient with exsanguinating, life-threatening liver injury faces many potential land-mines in the operating room. In addition to the massive blood loss, he or she rapidly faces the "triad of death": acidosis, hypothermia and coagulopathy, all intertwined and aggravating one another in a vicious, deadly cycle. The relatively recent concepts of abbreviated laparotomy, physiologic resuscitation and staged reconstructive procedures, appropriately termed "damage-control surgery" has been a major advance in the management of these terminal patients (1-9).

"Damage control" was a term originally coined by the United States Navy, in reference to "the capacity of a ship to absorb damage and maintain mission integrity," . First proposed Stone in 1983 (1) , the technique involved "saving the day for another day in battle" by a staged approach aimed at correcting the physiologic vortex of the triad of death. This approach to the patient with exsanguinating hepatic injury consists of three separate components:

- Rapid control of surgical bleeding ; peri-hepatic gauge packing and temporary abdominal closure (Part I)
- Correction of hypothermia by rewarming; correction of coagulopathy; fluid resuscitation and optimization of tissue perfusion (Part II). Consideration for angiographic embolization of intra-hepatic bleeders is a part of resuscitation (Part IIa).
- Re-exploration for pack removal, abdominal closure, when normal physiology has been or is being restored (Part III).

Abdominal closure of the packed abdomen is best accomplished by temporary measures as described below and also leaving the fascia open to prevent abdominal compartment syndrome (11,12).

Professor of Surgery, Physiology, Emergency Medicine
Virginia Commonwealth University
Chair, Division of Trauma, Critical Care and Emergency General Surgery
VCU Medical Center. Richmond, Virginia

PART I

Triggers for abbreviating the laparotomy are (7,8,9):

- Massive blood loss (10 to 15 units of packed RBC),
- Injury Severity Score >35, hypotension, hypothermia (temperature <34ºC), clinical coagulopathy , and acidosis (pH <7.2)
- Injury pattern recognition (massive intra-abdominal injuries, multi-system injuries, significant brain injury, great vessel injuries etc)
- Inadequate resources in terms of personnel, equipment, and specialty backup

Principles of abbreviated laparotomy are : evaluation of liver injury, control of major, surgical bleeding (by various operative techniques), early decision to pack, peri-hepatic packing to compress the organ (use omentum, hemostatic substances, lap pads, kerlix ; consider using a absorbable mesh between the liver and the packs), rapid control (closure or resection) of bowel perforations and temporary abdominal closure (as described below). ***Caution*** : Do not mobilize the liver extensively!

Table 1 : Part I Damage-control for hepatic injury

Early decision
Do not mobilize liver extensively
Control surgical bleeding
Peri-hepatic packing
Control bowel contamination (rapidly, temporarily)
Application of "poor-man's vac"

PART II

The second phase of damage control consists of resuscitation in the ICU to optimize tissue perfusion, correct hypothermia, and correct coagulopathy. Acidosis associated with hypovolemic shock contributes to coagulopathic bleeding, worsening the shock state. The goal is complete restoration of aerobic metabolism, as indicated by normalization

of serum lactate levels, base deficit, mixed venous oxygen saturation and other tissue markers (gastric mucosal pH, NIRS derived tissue oxygen tension).

Correction of hypothermia is crucial to break the vicious cycle of triad of death (2, 7,8,9). Passive external rewarming techniques include simple covering of the patient to minimize convective heat loss. Active external rewarming techniques include fluid-circulating heating blankets, convective warm air blankets, and radiant warmers. Active core rewarming techniques include warmed airway gases, heated peritoneal or pleural lavage, warmed intravenous fluid infusion, and extracorporeal rewarming. Countercurrent heat exchange mechanisms are excellent for rapid infusion of warmed banked blood products. Continuous arteriovenous rewarming is an excellent technique that is driven by the patient's blood pressure and is currently the procedure of choice in massively injured patients.

Dilution of coagulation factors and platelets by massive blood transfusions and fluid resuscitation, decreased total and ionized calcium concentration, hypothermia, severity of injury, shock, and metabolic acidosis may all contribute to coagulopathy. Replacement of clotting factors (by infusion of several units of Fresh Frozen Plasma simultaneously and cryoprecipitate) and platelets ***based on clinical coagulopathy*** rather than laboratory values is the best approach in these desperate circumstances. One exciting development in the correction of coagulopathy is the introduction of recombinant Factor VIIa . Activated factor VIIa (FVIIa) was developed to treat hemophiliacs with high-titer antibodies to factor VIII. FVIIa initiates thrombin formation by binding with exposed tissue factor. A multi-institutional study of Factor VII a in trauma is in the process of being designed.

PART II A

Increasingly, with complex injuries to the liver, perihepatic packing is followed by prompt angiography to identify and control by embolization bleeding from intraparenchymal vessels that may be difficult to identify by surgical techniques. More and more centers (including us) are routinely taking the patients with severe grade injuries to angiography to identify and embolize bleeders. Johnson et al (10) described their experience with 19 patients who had damage-control for liver injuries. Nine of them had angiography with a 75% rate of therapeutic angiography. In a study of Asensio et al (11), 15 of 22 patients (68%) with "complex hepatic injury" underwent angiographic embolization.

Monitoring for intra-abdominal hypertension (IAH) by regular measurement of intra-abdominal pressure (IAP) is vital in these patients (12). Many advances are made recently in our understanding of the patho-physiology of IAH, including our realization that even small increases in the IAP can cause profound changes in splanchnic blood flow and precipitate multi-organ failure. It is very important to avoid "hyper-resuscitation" in these patients to prevent IAH. The current state of knowledge of IAP and IAH is summarized in a monograph (13).

Table II : Part II Damage-control for hepatic injury

IIA : Consider angiography
Correct acidosis, tissue hypoperfusion, anaerobiosis
Blood transfusions
Adequate oxygenation
Fluid resuscitation
Avoid bicarbonate therapy
Correct Hypothermia
External re-warming
Passive rewarming (warmed gases, fluids, cavitary lavage)
Active rewarming by continuous arterio-venous exchange
Correct coagulopathy
Rewarm
Fresh frozen plasma (2-4 units at once)
Platelet therapy
Consider Factor VII a
Correct acidosis
Monitor IAP
Intervene for IAH , prevent ACS

PART III

This consists of a return to the operating room for definitive organ repair, and fascial closure if possible. ***Timing*** : The operation should be undertaken when the patient is resuscitated and is nearly normalized out of his hypothermia, acidosis, and coagulopathy. A complete correction is not always necessary. However, continuing transfusion needs, uncorrectable acidosis, or increasing bladder pressures suggest ongoing bleeding and the need for early re-exploration. We believe that early removal of packs is important to : 1. reduce the incidence of perihepatic abscesses and 2. improve venous return to the heart and augment cardiac output by removal of the pressure on the IVC by the packs and by reducing intra-abdominal pressure.

At reoperation, hemostasis is further secured and confirmed after literally "washing out" the packs. The peritoneal cavity is thoroughly irrigated. Bowel anastomoses or repairs, if

necessary, are completed. At this stage persistent visceral edema is often the rule and usually limits abdominal closure in many patients. Usually it is necessary to continue with some variant of "vacuum-pack " technique for temporary closure. Drains are usually placed to drain bile leak from high grade hepatic lesions and should be placed with considerable redundancy and be brought out as lateral as possible to avoid damage to the components of the rectus muscle. Feeding in these patients should be accomplished by a naso-duodenal feeding tube placed intra-operatively during the first return to the operating room (***Caution:*** enteral feeding in an incompletely resuscitated patient on pressors may precipitate bowel necrosis!) Surgically placed gastrostomy or jejunostomy should be avoided. Later in the patient's course, sites of tubes and stomas in the abdominal wall make definitive closure, particularly if component separation is necessary, more difficult due to scaring between tissue layers and creating holes in the components. For this reason, when stoma and tubes are deemed necessary, they are brought out lateral to the rectus and well into the oblique muscles. Stomas are brought out on the flank between the costal margin and the iliac crest, at or slightly posterior to the mid-axillary line.

Table III : Part III Damage-control for hepatic injury
Abdominal wash-out
Wash-out of packs
Look for missed injuries
Repair/re-anastomose bowel
Complete vascular repair
Insert naso-enteric tube
Place drains, if necessary, as lateral as possible
Avoid stomas
Irrigate abdomen
Apply "poor-man's vac" or rarely, close fascia.

The patient is returned to the ICU for continued resuscitation, gradual ventilator weaning, aggressive nutritional support and antibiotic therapy as indicated. This "open abdomen" approach has been helpful in reducing the incidence of abdominal compartment syndrome and multi-organ failure (12, 13). The undesirable side-effects of such an approach (loss of fascial closure, ventral hernia and "entero-atmospheric" fistulae) have been remarkably reduced by recent refinements (12-17).

The recent innovations in closure of open abdomen is a result of our understanding that fascial closure of open abdomen is prevented by adherence of bowel to the edges of the fascia, thus preventing easy mobilization of the fascia. The "vacuum-pack" technique (14) consists of a non-adherent polyethylene sheet over the viscera. This is covered by moist surgical towels. Two 10-French silicone drains are placed over the towels and the wound sealed with an airtight idofor-impregnated adhesive dressing. Wall suction is applied at 100-150 mmHg of continuous suction. This helps drainage of intraabdominal fluid Patients are re-explored serially every 3-4 days , the fascia is gradually approximated and, in 2-3 sittings, is finally closed. This method proved to be inexpensive and facilitated a fascial closure rate of 56%. We call this the "Poor-man's vac" and continue with it for the first one or two reexplorations. In many instances, by this time it will be possible to achieve fascial closure. If still not possible, negative pressure therapy is a good option at this time.

Negative pressure therapy (NPT) **:** Vacuum Assisted Closure-VAC therapy (KCI, Inc., San Antonio, TX) applies sub-atmospheric pressure through a reticulated polyurethane foam dressing. The negative pressure is controlled with a computer-controlled vacuum pump that applies a regulated pressure to the wound surface and a sensing device to prevent uncontrolled fluid drainage such as blood. . The technique consists of placing a non-adherent polyurethane layer over the bowel and under the abdominal wall, separating it from the fascial margins. Multiple perforations are cut in this layer to allow egress of fluid. A polyurethane foam sponge is cut to appropriate size and placed over the exposed plastic barrier . The sponge is attached to a 18 Fr suction tubing . The skin is closed as tightly as possible around the catheter. The suction tubing is connected to a suction device and set to a constant pressure of -175 mm Hg. The usual result is an immediate collapseof the entire apparatus and will help to increase blood flow, reduce abdominal wall tension, reduce size of the abdominal wall defect, decrease bowel edema, and potentially remove inflammatory substances that accumulate in the abdomen during inflammatory states. The patients is returned to the operating room every 48 hours , the suction device is removed and the fascial edges are approximated as much as possible with out tension. If complete closure is not possible, the device is re-applied and the process is repeated. Several series (15-17) have reported the use of negative pressure therapy in the early approximation of open abdomen in patients that had a decompressive laparotomy or damage control surgery and showed a success rate of fascial closure ranging from 70% to 90%.

SUMMARY

Damage - control for massive liver injuries is best approached by:

1. Early identification for the need to abbreviate laparotmy
2. Agressive resuscitation of the patient in the ICU, incorporating angiography into the algorithm, prevention of IAH and its sequelae
3. Early return to the O.R. for pack removal and temporary abdominal closure
4. Use of "vacuum-pack" techniques for serial abdominal closure and aggressive pursuit of complications.

REFERENCES

1. Stone HH, Strom PR, Mullins RJ. Management of the major coagulopathy with onset during laparotomy. Ann Surg. 1983; 197: 532–535
2. Rotondo MF, Schwab CW, McGonigal MD, et al : Damage control : an approach for improved survival in exsanguinating penetrating abdominal injury. J Trauma 1993;35:375-83
3. Burch JM, Ortiz VB, Richardson RJ, et al. Abbreviated laparotomy and planned re-operation for critically injured patients. Ann Surg 1992;215:476 B84.
4. Moore EE. Staged laparotomy for the hypothermia, acidosis and coagulopathy syndrome. Am J Surg 1996;172:405-10.
5. Shapiro MB, Jenkins DH, Schwab CW, Rotondo MF. Damage control: collective review. J Trauma. 2000 ;49:969-78
6. Vargo DJ, Battistella FD.Abbreviated thoracotomy and temporary chest closure: an application of damage control after thoracic trauma. ArchSurg.2001;136(1):21-4
7. Johnson JW, Gracias VH, Schwab CW, Reilly PM, Kauder DR, Shapiro MB, Dabrowski GP, Rotondo MF.Evolution in damage control for exsanguinating penetrating abdominal injury. J Trauma. 2001 51:261-9.
8. Asensio JA, McDuffie L, Petrone P, Roldan G, Forno W, Gambaro E, Salim A, Demetriades D, Murray J, Velmahos G, Shoemaker W, Berne TV, Ramicone E, Chan L. Reliable variables in the exsanguinated patient which indicate damage control and predict outcome. Am J Surg. 2001 182:743-51
9. Schwab CW: Damage-control surgery. Injury 35,7 July 2004.
10. Johnson J, Gracias VH, Gupta R et al : Hepatic angiography in patients undergoing damage control laparotomy. J. Trauma 2002; 52:1102-1106.
11. Asensio JA, Demetriades D, Chahwan S et al Approach to the management of complex hepatic injuries. J. Trauma. 2000; 48:66-70.
12. Ivatury RR, Porter JM, Simon RJ, Islam S, John R, Stahl WM. Intra-abdominal hypertension after life-threatening penetrating abdominal trauma: prophylaxis, incidence, and clinical relevance to gastric mucosal pH and abdominal compartment syndrome. J Trauma. 1998;44:1016-21.
13. Ivatury RR, Cheatham M, Malbrain M, Sugrue M (eds) : Abdominal Compartment Syndrome. Landes bio science, 2006. It can also be accessed on line at : http://www.eurekah.com/categories.php?catid=83&category=SURGERY.
14. Barker DE, Kaufman HJ, Smith LA, Ciraulo DL, Richart CL, Burns RP. Vacuum pack technique of temporary abdominal closure: a 7-year experience with 112 patients. .J Trauma 2000 Feb;48(2):201-6.
15. Miller PR, Thompson JT, Faler BJ, Meredith JW, Chang MC :Late fascial closure in lieu of ventral hernia: the next step in open abdomen management. J Trauma 2002 53:843-9
16. Garner GB, Ware DN, Cocanour CS, Duke JH, McKinley BA, Kozar RA, Moore FA Vacuum-assisted wound closure provides early fascial reapproximation in trauma patients with open abdomens. Am J Surg 2001 182 :630-8
17. Markley MA, Mantor PC, Letton RW, Tuggle DW.Pediatric vacuum packing wound closure for damage-control laparotomy. J Pediatr Surg 2002 ;37:512-4.

Panamerican Journal of Trauma Vol. 14 No. 1 2007 Pages 24 - 25

¿WHAT'S NEW IN TRAUMA & CRITICAL CARE? DVT PROPHYLAXIS

George Velmahos, MD, PHD, FACS

The prevention, diagnosis, and therapy of post-traumatic venous thromboembolism (VT) remain a major challenge. Despite the wealth of information existing in the surgical literature, the evidence is confusing or contradicting. For this reason in a recent survey, prevention of VT was ranked as the fifth more important topic requiring clarification.[1]

HIGH-RISK GROUPS

In general, trauma patients are at high risk of VT although the specific risk factors are still under debate. Traditionally, lower extremity fractures, pelvic fractures, spinal injuries, obesity, prolonged immobilization, advanced age, femoral venous catheters, and severe trauma are considered as risk factors of VT. Head injury, pelvic operation, number of transfusions, varicosities, prolonged operation, delayed operation, high levels of positive end-expiratory pressure are additional risk factors found in other studies. This plethora of risk factors includes nearly every trauma patient. Analysis of 318,554 patients from a statewide registry concluded that the incidence of pulmonary embolism (PE) is low in patients without specific risk factors. The authors recommended that prophylactic intervention should not be routinely administered in view of the unclear benefits compared to the risks.[2] It is therefore obvious that we need to define better the risk factors for VT.

In the only systematic analysis done exclusively on trauma patients, the groups at high risk for deep venous thrombosis (DVT) or PE were examined.[3] A risk factor was analyzed only if reported in at least three studies. The only risk factors found to place the trauma patient at high risk for development of DVT was spinal injury in the form of either a spinal fracture (OR: 2.260, 95% CI: 1.415, 3.610) or spinal cord injury (OR: 3.107, 95% CI: 1.794, 5.381). It was also found that older patients and patients with high Injury Severity Scores were more likely to develop DVT but a specific cutoff point for age and ISS beyond which the risk increased acutely could not be determined. Patients who developed DVT were older by an average of 8±1.5 years and had an ISS which was higher by an average of 1.4±0.7 points. These differences (particularly the latter one) may not bear particular clinical significance, even if the large sample size examined allowed for statistical significance.

THE BEST METHOD OF PROPHYLAXIS

Unfractionated heparin, low-molecular weight heparin, and mechanical compression have been used extensively to prevent VT. There is ample evidence from the medical and elective surgical (non-trauma) literature that these methods are effective in preventing VT. The question is whether this evidence should be extrapolated to the trauma patients. Critical appraisal of the trauma literature immediately uncovers the controversy. Despite the widespread belief that VT rates are reduced by the commonly used methods of prophylaxis, many studies suggest otherwise.

Among 133 consecutive trauma patients who received vena cava filters the incidence of DVT was 30% despite the fact that 92% of the patients received DVT prophylaxis.[4] In another study of 101 critically injured patients (ISS: 27±10) 28% developed DVT within 12±9 days after admission, even if all the patients received thromboprophylaxis.[5] Among 110 critically ill patients requiring mechanical ventilation over 7 days, 24% developed DVT despite thromboprophylaxis.[6] In a prospective study of 200 trauma patients admitted in the Surgical ICU, the incidence of DVT was 13% although close to 95% of the patients received one method of thromboprophylaxis and nearly 50% of the patients received two methods.[7] It seems that the current methods of thromboprophylaxis, and particular unfractionated heparin, are not efficient, at least at the doses usually given.

The rationale of sequential compression devices makes good sense. According to initial studies, such devices produce a

Professor of Surgery
Harvard Medical School
Chief, Division of Trauma, Emergency Surgery, and Surgical Critical Care
Massachusetts General Hospital. Boston, Massachusetts

mechanical effect by squeezing the muscle (and promoting venous circulation) and a systemic anticoagulant effect by the release of tissue thromboplastin from the wall of the compressed vessels. Even if the theory is good, the reality is different. Two studies have documented very low compliances with the appropriate use of the devices. Among 84 patients only 48% demonstrated properly placed and functioning compression devices.[8] In a total of 1,343 observations of 227 trauma patients with orders for external compression for thromboprophylaxis, the devices were on and functioning in 53%.[9] Only 19% of the patients were fully compliant on all observations.

Low-molecular weight heparin has been suggested to be superior to other methods of prophylaxis. Two randomized controlled trials have shown evidence of this drug's superiority over standard unfractionated heparin.[10,11] However, the disparity in DVT rates between the two studies raises concerns. While in one study the incidence of DVT was over 30%,[10] in the other was only 2%![11] Of note was that the incidence of major bleeding was higher with low-molecular weight heparin, even if the difference did not achieve statistical significance due to the small numbers.

In a systematic analysis of the existing evidence in trauma, no method of prophylaxis was found to be superior to another method.[12] More importantly no prophylaxis was found to be as good (or bad) as any of the tested methods. The authors concluded that there is insufficient evidence to suggest routine administration of routine prophylaxis after injury. In a cost-effectiveness analysis, the existing methods of thromboprophylaxis failed to show a cost benefit, based on their unclear performance.[13]

CONCLUSION

It is evident that the trauma groups at risk and the methods of prophylaxis are still unknown with regard to post-traumatic VT. For many years we have inappropriately extrapolated conclusion from the non-trauma literature to the unique trauma population. It is time that we consider seriously the inadequacies of the existing pharmaceutical and mechanical methods of VT prophylaxis and explore alternative methods to prevent the disease.

REFERENCES

1. Nathens AB, Rivara FP, Jurckovich GJ, et al. Management of the injured patient: Identification of research topics for systematic review using the Delphi technique. J Trauma 2003;54:595-601.
2. Tuttle-Newhall JE, Rutledge R, Hultman CS, Fakhry SM. Statewide, population-based, time-series analysis of the frequency and outcome of pulmonary embolus in 318,554 patients. J Trauma 1997;44:90-9.
3. Velmahos GC, Kern J, Chan LS, Oder D, Murray JA, Shekelle P. Prevention of venous thromboembolism after injury: An evidence-based report. Part II. J Trauma, 2000; 49: 140-4.
4. Duperier T, Mosenthal A, Swan K, Kaul S. Acute complications associated with Greenfield filter insertion in high-risk trauma patients. J Trauma 2003;54:545-9.
5. Mesisner MH, Chandler WL, Elliott JS. Venous thromboembolism in trauma: A local manifestation of systemic hypercoagulability? J Trauma 2003;54:224-31.
6. Ibrahim EH, Iregui M, Prentice D, Sherman G, Kollef MH, Shannon W. Deep vein thrombosis during prolonged mechanical ventilation despite prophylaxis. Crit Care Med 2002;304:771-4.
7. Velmahos GC, Nigro J, Tatevossian R, Murray JA, Cornwell EE III, Belzberg H, Asensio JA, Berne TV, Demetriades D. Inability of an aggressive policy of thromboprophylaxis to prevent deep venous thrombosis in critically injured patients: Are current methods of DVT prophylaxis insufficient? J Am Coll Surg 1998; 187:529-533.
8. Comerota AJ, Katz ML, White JV. Why does prophylaxis with external pneumatic compression for deep vein thrombosis fail? Am J Surg 1994;164:265-8.
9. Cornwell EE,III, Chang D, Velmahos GC, Jindal A, Baker D, Phillips J, Bonar J, Campbell K. Compliance with sequential compression device (SCD) prophylaxis in at-risk trauma patients. A prospective analysis. Am Surg, 2002;68:470-4.
10. Geerts WH, Jay RM, Code KI, et al. A comparison of low-dose heparin with low-molecular-weight heparin as prophylaxis against venous thromboembolism after major trauma. N Engl J Med 1996;335:701-7.
11. Knudson MM, Morabito D, Paiement GD, et al. Use of low molecular weight heparin in preventing thromboembolism in trauma patients. J Trauma 1996;41:446-59.
12. Velmahos GC, Kern J, Chan LS, Oder D, Murray JA, Shekelle P. Prevention of venous thromboembolism after injury: An evidence-based report. Part I. J Trauma, 2000; 49: 132-9.
13. Velmahos GC, Oh Y, McCombs J, Oder D. An evidence-based cost-effectiveness model on methods of prevention of post-traumatic venous thromboembolism. J Trauma, 2000;49:1059-1064.

Panamerican Journal of Trauma Vol. 14 No. 1 2007 Pages 26 - 27

PENETRATING COLON WOUNDS REQUIRING RESECTION – ¿STILL NO COLOSTOMY?

George Velmahos, MD, PHD, FACS

BACKGROUND

In 1943 the U.S. Surgeon General published guidelines for the management of colonic injuries. These guidelines established colostomy as the standard of care and allegedly produced improved survival related to such injuries in combat. These guidelines were also extrapolated in civilian injuries and for decades all colonic injuries, including gunshot wounds, stab wounds, and blunt trauma were managed by mandatory diversion.

PRIMARY REPAIR OR COLOSTOMY FOR UNSELECTED COLON INJURIES: LEVEL 1 EVIDENCE

In 1970, Stone and Fabian[1] challenged the dogma by publishing the results of a prospective randomized study which showed that primary repair was associated with fewer complications than colostomy. Patients with hypotension, long intervals between injury and operation, extensive fecal contamination, and major associated injuries were excluded.

In 1991, Chapuis et al[2] published another prospective randomized study which did not exclude patients due to "high-risk" criteria but included only 56 patients. In this small population the authors detected 7 intra-abdominal abscesses (3 in the primary repair and 4 in the colostomy groups) and 3 wound dehiscences (all in the primary repair group). They concluded that primary repair was appropriate for all patients with penetrating colon injuries, even if only 11 of their patients had injuries that were large enough to require resection.

In 1995, Sasaki et al[3] randomized 71 patients, using no exclusionary criteria based on "high-risk" factors. The complication rate in the primary repair group was 19% and in the colostomy group 36%. The authors recommended that primary repair should be offered to all patients, regardless of severity of injury or physiologic condition. However, only 12 patients with major colonic trauma requiring resection were included.

In 1996, Gonzalez et al[4] randomized 109 unselected patients and again, found no difference in septic complications between the primary repair group (20%) and the colostomy group (25%). Similarly to the previous studies only a minority of patients (17) had major colon injuries requiring resection.

It is evident from the above studies that most colon injuries can be managed safely by primary repair. However, the number of patients with severe colon injuries in these studies is small and therefore, conclusions cannot be made for this subgroup. The risk of anastomotic dehiscence in a full 360° anastomotic line is obviously high. The need for colon resection indicates extensive intra-abdominal trauma. Such patients usually have high rates of significant associated organ injuries inside and outside the abdomen. They also have high rates of shock, blood transfusion, and extensive colonic contamination.

FOCUS ON COLON INJURIES REQUIRING RESECTION

Only three studies exist in the literature examining the appropriate method for colonic repair following resection. None of them has used randomization. Stewart et al[5] in 1994 analyzed 60 patients, 43 managed by primary anastomosis and 17 by diverting colostomy. The incidence of septic complications was 37% in the primary anastomosis group and 29% in the diversion group. Because the anastomotic leak rate among patients with primary repair was 14% and specifically among those with blood transfusion over 6 units 33%, the authors concluded that primary repair is inappropriate for patients who require colonic resection and more than 6 units of blood transfusion.

Professor of Surgery
Harvard Medical School
Chief, Division of Trauma, Emergency Surgery, and Surgical Critical Care
Massachusetts General Hospital. Boston, Massachusetts

Murray et al[6] published a retrospective study of 140 patients requiring resection; 80% of them were managed by primary repair and 20% by colostomy. The trauma group at the Los Angeles County /U.S.C. Medical Center favored primary anastomosis and reserved colostomy only for selected cases, although specific exclusionary criteria for primary repair did not exist. The incidence of abdominal septic complications was 20% for ileocolostomy, 36% for colocolostomy, and 29% for colostomy. The incidence of anastomotic leak was 4% for ileocolostomy and 13% for colocolostomy. Major abdominal injury (as indicated by a Penetrating Abdominal Trauma Index higher than 25) and hypotension were associated with increased likelihood for anastomotic leak, and the authors cautioned about performing primary repair in these patients.

The largest study to date is a prospective non-controlled multi-institutional (and multi-national) study performed by Demetriades et al[7]. Of 297 patients with penetrating colonic injuries requiring resection, 197 (66%) were managed by primary anastomosis and 100 (34%) by colostomy. The overall colon-related mortality was 1.3% (4 deaths in the colostomy group, no deaths in the primary anastomosis group, p=0.012). The rate of colon-related complications was not different between the two groups (22% in primary repair, 27% in colostomy). There were 13 leaks (9 colocolostomies and 4 ileocolostomies) among the primary anastomosis patients. Unfortunately, the two groups were quite different. There was a significantly higher incidence of preoperative shock, delay in operation, left colon injuries, Penetrating Abdominal Trauma Index >25, small bowel and liver injuries, blood transfusions, and severe fecal contamination in the colostomy group. To compensate for this discrepancy the authors performed multivariate analysis controlling for the confounding factors and found that the adjusted relative risk of abdominal complications in primary anastomosis and diversion groups was similar. In another subanalysis, all patients were classified into a high-risk or a low-risk group. High-risk criteria included shock on admission, blood transfusion > 6 units, delay in operation > 6 hours, severe peritoneal contamination, and PATI >25. The colon-related mortality among high-risk patients was 4.5% in the colostomy group (4 of 88) and 0% in the primary anastomosis group (0 of 121).

CONCLUSION

With improved peri-operative care, colostomy is used with decreasing frequency. For the majority of colon injuries, primary repair is a safe option. The question remains partially unsolved for colonic injuries requiring resection. The existing evidence is in favor of primary anastomosis but the studies are uncontrolled and with methodological flaws. Most likely the presence of isolated "risk factors" such as blood transfusion, shock on admission, extensive fecal spillage, extensive colon injuries requiring resection, or the severity of overall injury do not present an absolute criterion to avoid primary anastomosis. Even then, most patients can be safely treated without a colostomy. However, for the few patients who will carry a multitude of risk factors and present a local environment that is unfavorable to a fresh 360º suture line (bowel edema, compromised blood supply), it will be the art rather than the science of surgery that will guide the experienced trauma surgeon to make the correct intra-operative choice.

REFERENCES

1. Stone HH, Fabian TC. Management of perforating colon trauma: randomization between primary closure and exteriorization. Ann Surg 1979;190:430-6.
2. Chappuis CW, Frey DJ, Dietzen CD, et al. Management of penetrating colon injuries: a prospective randomized trial. Ann Surg 1991:213:492-7.
3. Sasaki LS, Allaben RD, Glowala R, Mittal VK. Primary repair of colon injuries: a prospective randomized study. J Trauma 1995;39:895-901.
4. Gonsalez RP, Merlotti GJ, Holevar MR. Colostomy in penetrating colon injury: is it necessary? J Trauma 1996;41:271-5.
5. Stewart RM, Fabian TC, Croce MA, et al. Is resection with primary anastomosis following destructive colon wound always safe? Am J Surg 1994;168:316-9.
6. Murray JA, Demetriades D, Colson M, et al. Colonic resection in trauma: colostomy versus anastomosis. J Trauma 1996;46:250-4.
7. Demetriades D, Murray JA, Chan LS, et al. Penetrating colon injuries requiring resection: Diversion or primary anastomosis? An AAST prospective multicenter study. J Trauma 2001;50:765-7.

Panamerican Journal of Trauma Vol. 14 No. 1 2007 Pages 28 - 36

PENETRATING TRAUMA – SAME PROBLEMS, DIFFERENT SOLUTIONS. THE CNS

Peter Letarte, MD, FACS

PROVIDER ATTITUDE – APPROACHING THE VICTIM OF PENETRATING BRAIN INJURY

The resuscitation and management of the victims of penetrating traumatic brain injury differs very little from the resuscitation of other Traumatic Brain Injury (TBI) with one very large exception. This exception is that many victims of PBI present very close to death. In the first moments of the resuscitation, providers must often decide weather to resuscitate the patient or not. This hesitation on the part of seasoned providers is due to their acute insight into the fact that they have no way of predicting weather their efforts will result in bringing the victim back from deaths door or needlessly delaying their journey through it.

The lethality of firearm related TBI is indisputable. Centers for Disease Control funded surveillance programs have found that in selected states, firearms were responsible for only 9.7% of the overall TBI and yet accounted for 44% of the TBI mortality. That such a small percentage of the total TBI could account for such a large percentage of the deaths is explained by the 90.4% lethality of firearm related TBI(1).

Given this high lethality, it is easy to see how providers could easily develop the prejudice that all penetrating injury is lethal. The fundamental principle in treating PBI is to avoid such dogmatism. While no one can predict the outcome of any given resuscitation, careful application of the known literature can, hopefully, allow the practitioner to proceed with greater confidence and, perhaps, make better decisions from patient to patient and at various stages of the resuscitation.

RESUSCITATION DECISION MAKING

It is not always necessary to make a life or death decision all at once when resuscitating PBI. Many practitioners feel pressure to make such a decision upon presentation. In many cases this is not the best approach. With time, many PBI patients declare themselves for better or for worse. Starting the resuscitation often provides needed care to those who will benefit from it and usually makes little difference to those who are destined to die.

It also gives the provider more time to assess the severity of the injury and make a more thoughtful decision on the patient's salvagability. It is important to understand that the information needed to determine if the patient is salvageable is often obtained from the resuscitation. Glasgow Coma Score can not be determined until the blood pressure is normal, depressed mental status may be due to mass effect from hemorrhage or the intrinsic injury from the projectile, ICP may not rise until blood pressure is restored. The list is long of the parameters needed to determine viability that can not be obtained until resuscitation has been started. Thus the resuscitation and the viability decision are complexly intertwined. To simply call off the resuscitation on the assumption that all PBI is lethal deprives the patient of the careful evaluation they deserve.

It is important to remember too that much of what we believe about the viability of PBI, we have learned from the military. But the civilian environment in which most of us practice is not the battlefield. In the battlefield, resources are scarce and the facilities to save severely injured victims, such as those with PBI are not available. Under these circumstances, many PBI victims die. But in the civilian world the same victim who in the military setting might be under the care of a medic for many hours may well find themselves in a well equipped and staffed emergency department within minutes. To apply the triage rules of an austere environment in this setting is ludicrous. Providers in this setting are required to set their own standards for what might be possible in a resource rich environment and for when it is time to stop even though "all the kings' horses and all the king's men" are available. The blind application of rules from another place and time is not appropriate.

Chief, Section of Neurosurgery
Heinz VA Medical Center. Maywood, Illinois

This paper will follow the course of the resuscitation of a PBI victim and will highlight what is known about each stage of the resuscitation in hopes that this will make decision making a bit easier.

History

Several features of the history may offer clues as to the salvagability of the patient.

Age

Most practitioners suspect that elderly people do not survive head injury as well as younger people. This assumption is born out by the fact that the elderly, while not sustaining TBI in the greatest numbers, have the highest death rate from TBI of any group in the United States(2).

In general, older patients have higher fatality rates in response to head injury than younger patients(3). As an illustration of the effect of age on the susceptibility to TBI, it is interesting to note that falls are the major cause of TBI in both children and the elderly. Children have a death rate from falls of 0.1-0.2/100,000 and are most often discharged from the Emergency Department. The elderly have a death rate from falls of 21.7/100,000 and are most often hospitalized(2).

One might suspect that the elderly also have higher mortality rates when they are the victims of PBI. Only two studies directly address this question. Kaufman and Siccardi have shown higher mortality in patients over 49(4;5). Multiple other studies have shown better outcomes in younger patients, but the results have not been statistically significant.

In fact, there is very little data on PBI which includes older patients. Many studies exclude patients on whom resuscitation is not attempted and it is likely that in many settings, resuscitation is not attempted on older victims of PBI, creating a self fulfilling prophesies. Furthermore, many elderly PBI victims are the victims of self inflicted gun shot wounds. Available data seems to show that suicide is a more lethal mode of PBI, leading to a higher mortality in its victims(6). In addition, physicians are also reluctant to resuscitate suicide victims. It is possible that for these reasons, little data is available on the outcome of attempted resuscitation for PBI in older individuals. Non the less, the Guidelines for the Management of Penetrating Brain Injury state at the Class III level that increasing age correlates with mortality after penetrating brain injury(7).

Cause of Injury

Various types of PBI occur depending on the setting, and caution should be exercised when extrapolating from one setting to another. Civilian gunshot wounds tend to be from lower caliber weapons as opposed to military PBI which tends to be caused by shrapnel, shell fragments and debris, all of which can impact at various energy levels. Lastly, suicide, which is close range PBI, is a somewhat unique mechanism. Studies have shown that victims of suicide have a higher mortality than victims of assault or accidental shooting. This can be understood based on mechanism, but it is also possible, as mentioned above, that provider bias results in a tendency to be less aggressive with the resuscitation of suicide victims(6).

Mode of Injury

It is useful to classify PBI into tangential, perforating or penetrating injuries. Failure to make this distinction can result in over estimation of the severity of a penetrating injury.

Tangential injury occurs when the bullet glances off of the skull, sometimes driving bone into the brain. Tangential injuries have a lower mortality rate(8). Providers should avoid the error of viewing a tangential injury in the same light as a perforating injury.

A penetrating injury occurs when the projectile enters the calvarium, often driving bone before it into the brain. A perforating injury occurs when the projectile also exits the brain, creating a tract completely across the head. Traditional teaching on PBI has held the injuries crossing the midline are the most lethal and some Class III data support the assertion that perforating injuries are more lethal(7;8).

Caliber of Weapon

Large volumes of experimental work in PBI have focused on the role of caliber, projectile characteristics and kinetics in determining lethality in PBI(9). Much of the forensic discussion of PBI surrounds these issues. Interestingly, there is little epidemiologic data to support the assertions of this research(7). While it is most likely correct that caliber, range and kinetics play a key role in the outcome from PBI, this has not been demonstrated with epidemiologic tools. The most likely reason is that in actual shootings, range, angle, wind and other factors so corrupt the fundamental kinetics of the event that the well controlled kinetics of the laboratory are rarely duplicated in the field. For example, while caliber is a determinant of energy delivered to the brain, so is range and any given weapon can be fired at an infinite number of ranges from the impact point. Understanding this leads to the understanding that knowing the caliber of the weapon used does not necessarily add significantly one's knowledge about the energy delivered to the brain.

Physical Examination

A rapid physical assessment soon after presentation of the patient can offer clues to the patient's potential salvagability, help to determine if resuscitation should be aggressively pursued, and begin the formation of a therapeutic plan.

NEUROLOGICAL FINDINGS

GCS as Predictor

An accurate GCS is critical to the early assessment of the victims of PBI. In general, GCS correlates with the outcome from PBI(7). Specifically, the victims of PBI who present with a GCS of 3-5 have only a small chance of an acceptable outcome. Kaufmann published a Class III study comparing treatment at two institutions. Of the 190 patients included in this study, 106 had a GCS of 3 on presentation, 62 a GCS of 4 and 22 a GCS of 5. Of the patients with GCS 3, 101 died and none had a favorable outcome. For the 62 GCS 4 patients, 55 died and 1 had a favorable outcome. One patient with GCS 5 had a favorable outcome and 10 of the patients died(10).

In a prospective study from the Trauma Coma Data Bank, Aldrich found similar results with 116 of 123 patients with GCS 3-5 dieing and 1 of 123 having a good outcome. Two of the 19 patients with GCS 6-8 had a good outcome and 14 died. Two of 8 patients with GCS 9-15 had a favorable outcome and 3 died(11).
At the same time several studies have shown a reasonable prognosis for patients with PBI and GCS 13-15. Aarabi, Brandvold, Grahm and Kaufman have all reported high percentages of favorable outcomes for PBI victims with GCS 13-15(4;8;12;13).

The poor odds of a good outcome must be taken into account when making a resuscitation decision on a patient with GCS 3-5. Complicating the decision process is the fact that often a GCS useful to the salvagability decision can not be obtained until resuscitation has been initiated. Specifically, a useful prognostic GCS can not be obtained until the blood pressure has been restored. This means that patients who present hypotensive must be resuscitated prior to obtaining a meaningful GCS. Complicating the issue further is the fact that hypotension is also a known poor prognostic indicator for PBI(7). In settings with very short prehospital times, victims of PBI who under other circumstances might be considered GSW fatalities may now present to the ER very close to death. The challenge to the provider is to decide if an attempt should be made at resuscitation, if only to obtain an accurate GCS, or if the patient should be allowed to quickly expire.

Similarly, victims of PBI who present with hematomas or other mass lesions in the head present the provider with the dilemma of weather or not to take the patient to the OR in the hope that removal of the mass lesion will improve the GCS. This effort can either result in an improved GCS or an unacceptable survival for the patient.

Kaufman et al examined this problem in their previously mentioned study of 190 patients. Of the 130 patients with GCS 3-5 who were treated without an operative attempt, all but 1 died. That patient, who presented with a GCS of 5, obtained a GOS of 3 for a final outcome.

Of the 60 patients for whom an operative attempt was made, 5 of 21 patients with a GCS of 3 survived, 4 with a GOS of 3 and 1 with a GOS of 2. Seven of 24 patients with a GCS of 4 survived, 1 with a GOS of 4, a relatively good outcome, 4 with a GOS of 3 and 2 with a GOS of 2. The numbers for GCS 5, of which there were 15 patients were 11 survivors, 1 with GOS 4 and the remaining 10 divided 5 each to GOS 2 and 3(10).

Although this is Class III data, it reminds us that good outcomes in patients with GCS 3-5 are possible but rare if operative intervention is attempted but that the cost of being wrong is to save someone for a less than desirable outcome.

Of equal importance is to remember that victims of PBI with GCS 13-15 have highly survivable injuries with good life quality. Being blinded by the fact that the mechanism of injury is PBI and failing to appreciate the fact that GCS 13-15 patients have an excellent prognosis is an unacceptable error.

An accurate GCS must be obtained quickly upon presentation and a decision on how much resuscitation is needed to obtain it is one of the first tasks facing the practitioner.

Pupil Reactivity

Asymmetric, unilateral or bilaterally fixed or dilated pupils have been associated with poor outcomes in TBI. Puppillary dilation is often associated with cerebral swelling and herniation and so with a poor prognosis.

In PBI the same associations are felt to hold. Shaffrey found that patients who presented with bilaterally fixed and dilated pupils had a 79% mortality, those with a unilaterally fixed and dilated pupil, 50% and those with bilaterally reactive pupils,

5%(14). Kaufman found a similar association between pupillary reactivity and mortality(4). Both of these studies were Class III studies. Other studies have observed similar relationships but have failed to demonstrate significance(15;16).

Immediate assessment of GCS and pupillary reactivity are the best first steps in attempting to estimate the survivability of a PBI. Polin, however, has pointed out that GCS and pupillary reactivity may be coupled, that is measuring both may not add any predictive value over measuring one(17). While this statistical observation adds to our understanding of the salvagability assessment, in practice both observations are commonly used in making it.

SYSTEMIC OBSERVATIONS

Several systemic features of the patient's presentation can be used to estimate survivability.

Respiratory Distress

It is commonly known and commonly observed that patients with PBI who present with a depressed respiratory rate are in extremis. Two studies have confirmed this observation with Class III data. Both Kaufman and Jacobs have found respiratory distress to be associated with increased mortality(7;10;18).
As the resuscitation is started, noting the patient's respiratory status can provide further estimates of potential survivability.

Hypotension

Similarly, patients who present with hypotension are at greater risk for a poorer outcome. Kaufman demonstrated this to statistical significance in a Class III study(10). Another study by Kaufman and one by Byrnes also demonstrated this association, though not to statistical significance(4;16). Aldrich failed to show this association(7;11).

Byrnes also showed that patients with hypertension, SBP>150, also had a poorer prognosis in PBI (16).

Coagulation Studies

Abnormalities in coagulation studies may be a marker for poor outcome in PBI. Kaufman noted this in one study and Shaffrey confirmed this observation in a retrospective multivariate analysis(4;14;17). In the Shaffrey study, a single abnormal PT or PTT was associated with 80% mortality, as opposed to a 7.4 % mortality for patients without such an abnormality. Coagulation abnormalities were highly predictive of mortality in a linear regression model in this study(14).

It is postulated that release of tissue thromboplastin by the penetrating injury leads to these coagulation abnormalities and can lead to DIC. Levy observed that PBI victims with DIC suffered 85% mortality(19).

RESUSCITATION

The intertwining of the decision to resuscitate and the actual resuscitation has been discussed above. The actual resuscitation of a victim of PBI is therefore the same as any other trauma resuscitation with the large exception of the issue of whether the resuscitation should be started at all. It is the author's practice, where possible, to start the resuscitation being keenly attuned to the factors discussed above. As the resuscitation progresses, the patient often declares themselves, either by expiring, by manifesting multiple poor prognostic indicators or by demonstrating viability or improving.

If the patient can be stabilized by securing airway and breathing and restoring blood pressure, then a more accurate reassessment of GCS and pupillary function can occur. In addition, the patient will be ready to obtain a head CT, which will lead to the next major decisions in their care.

COMPUTED TOMOGRAPHY

History

Computed tomography plays a crucial role in the management of PBI. CT scanning of PBI was widely used for the first time during the Israeli-Lebanon campaign of 1982-1985. Due to the close proximity of the battlefront to established large medical centers within Israel, CT scanning was routinely available to the victims of PBI from this conflict(12;20). The doctrines developed from this and other experiences have had a large impact on the management of PBI.

CT scanning provides both prognostic and operative planning information. Once again, in order to obtain the information offered by CT the resuscitation must proceed at least to the point where a CT scan can be obtained.

CT Scan as Prognostic Tool

Assessment of Bullet Tract

For most of the 20th century it has been known that penetrating GSW, that is GSW that traverse the entire cranium and exit, have the worst prognosis. With the application of CT scanning to the management of PBI, this observation can be refined. One CT observation, which in multiple Class III studies has portended higher mortality, has been

bihemispheric involvement of the missile tract. With bihemispheric lesions, odds ratios for increased mortality range from 1.18 to 20.05 (4;5;7;10-15;18;20-26).

One exception worth noting is bilateral frontal lobe involvement. Kaufman noted a mortality of 12% in this group and good outcomes of 30%, considerably better than the outcomes for bihemispheric lesions in general (10). This observation is particularly important because it reminds us of the dangers of thoughtless application of rules such as the bihemispheric rule when triaging patients. Projectiles traversing both frontal lobes will do considerably less damage and survival will be better. Giving such a patient the same grim prognosis as one with biventricular involvement would be an error.

Conversely, if the tract is further posterior in the brain, more critical structures will be damaged. Such a posterior tract is likely to traverse the ventricles and ventricular penetration by the tract has been shown to have a strong association with mortality (12;14;22). The odds ratios for death with ventricular penetration range from 3.35 to 27.5(7). . Ventricular penetration is another feature of importance when estimating salvagability from CT.

Another way to assess mortality risk from the tract of the projectile is to look for multilobe involvement. Multilobe involvement of the tract is common in PBI. Patients with unilobe involvement have a better prognosis. The negative predictive value of only unilobular involvement ranges from 77% to 98% (7).

Shaffrey approached the relationship of tract to mortality by dividing the brain with midline axial, saggital and coronal planes. Mortality was then related to the number of planes crossed. As the number of planes crossed increased, so did mortality. Crossing the saggital, and axial planes increased mortality, crossing the mid-coronal plane did not(14).

CT and the Assessment of Cerebral Edema

Evidence of cerebral edema on CT carries the same significance in PBI that it does in non-penetrating injury. Aldrich's analysis of the Trauma Coma Data Bank specifically looked at PBI and found increased mortality with basal cistern effacement but not with midline shift (11). Kaufman also failed to find a relationship with midline shift and mortality (4).

INTRACRANIAL HEMATOMAS

As with all intracranial injury, the mass effect from an intracranial hematoma is a potentially reversible cause of cerebral injury. The quandary in the context of penetrating cerebral injury is whether the patient's depressed mental status is due to the mass effect from the hematoma or from other injury from the projectile. The only way to determine this is to remove the hematoma. If the depressed mental status was largely due to the mass effect, this will improve the patient's outcome. If it was not, this act may save the patient for an unacceptable outcome. As discussed in the section on GCS, in the context of a low GCS, the later is the most common outcome.

Shaffrey found a relationship between the presence of intracranial hematoma and outcome (14). Mancuso failed to find such a relationship in PBI, reinforcing the idea that in PBI many other factors may impact on the patient's survivability (27).

As noted above, injury to the ventricles is a poor prognostic indicator and ventricular hematomas also carry a poor prognosis (4;14;24). The presence of blood in the ventricles can increase the odds of death 2.83 to 96.9 times (7).
Levy found a significant relationship with subarachnoid hemorrhage and mortality (28). Such a relationship has also been observed in non penetrating brain injury. Aldrich and Kaufman also found such a relationship but the statistical correlation with mortality was not as strong(10;11).

OPERATIVE MANAGEMENT

Once the decision has been made for aggressive management of the patient, a decision must be made about operative intervention. It is important when making this decision to remember what surgery can accomplish for the victims of PBI. The goals of surgery for the victim of PBI are to remove mass effect, control bleeding, control infection, to prevent CSF leak and to close the scalp. Any or all of these tasks may need to be performed.

Historically, aggressive debridement of bullet tracts in PBI has been advocated. The rational for this practice was to limit infection and post traumatic seizures. Evaluation of the outcomes from management of PBI in Vietnam and subsequent conflicts has revealed significant morbidity from the practice of extensive searches for bullet and bone fragments in the brain(29-31). In addition, there is evidence that the risk of infection is not higher in patients with retained fragment(32), neither is the increased risk of post traumatic epilepsy felt to warrant the morbidity of such a search (33). For these reasons, aggressive removal of all bone and bullet fragments is not a goal for surgery.

CT as Operative Planning Tool

Once the decision to aggressively manage the patient has been made, the CT scan changes from being a prognostic

tool to a planning tool. The CT can be used to identify bone and missile fragments, assess the bullet trajectory, identify sources of mass effect, such as hematomas or edema, to identify possible cranial sinus injury and to identify potential venous sinus injury. All of this information is critical to surgical planning.

Positioning

Positioning for surgery for PBI often includes preparing the entire head for surgery. Both the entrance and exit wounds need to be explored and access to the entire head is often needed. If the cranial air sinuses are involved, the face may need to be included in the field as well. Access to the neck should be included should vascular access be required. The leg should be prepped to allow harvesting of fascia lata graft.

Removal of Mass Effect

Removal of mass effect in PBI is no different than in TBI. Standard incisions and bone flaps are used where possible but are often modified to accommodate the complex scalp lacerations and skull fractures that accompany PBI.

Control of Bleeding

Standard trauma hemorrhage control can be more difficult in PBI because of venous sinus disruption. Sinus disruption may also be common with the skull fractures which accompany many PBI injuries, and from missile injury to the brain. Since rapid exanguination is possible from these injuries, every effort should be made to identify them preoperatively. If identified, preparations should be made to manage them. Various vessel clips and sutures should be available. Various vascular shunts designed for venous sinus shunting may be available. A Fogerty catheter can be useful in occluding the sinus while it is repaired. Most importantly, a surgeon with good experience in managing venous bleeding should be in the operating suite since the rapidity of venous sinus bleeding leaves little time for exploration of the learning curve.

Control of Infection

The largest advances in the 20th century in the management of PBI have occurred in the reduction in the infection rate. Antibiotics have had a great deal to do with this, but equally important was has been the development of good surgical techniques focused on limiting post operative infection. While retained bullet and bone fragments may not have a large impact on the post operative infection rate, CSF leak does. The practice of tight dural closure, developed during World War II, has likely contributed greatly to modern improvements in the infection rate. Tight dural closure is a mainstay of surgery for PBI.

Another source of CSF leak and infection can be dural disruption from fractures to the cranial air sinus. These fractures need to be identified on CT prior to surgery. At surgery the sinuses should be cranialized and packed. All CSF leaks should be closed.

Wound Debridement

The entrance and exit wounds should be identified. All obvious bone, debris and necrotic brain should be removed and the tract should be generously irrigated. While obvious fragments in the tract may be removed, aggressive dissection of the brain in an attempt to identify fragments is to be avoided. Carey pointed out that in Vietnam, even with aggressive searches for fragments, many were left behind(31). As noted above, the morbidity from this practice is now felt to be excessive and the practice is discouraged.

Closure of the Scalp

Lastly the scalp should be closed. The scalp lacerations which result from PBI are often complex. Scalp incisions for PBI operations should be planned to allow for complex scalp repair at the end of the case. Plastic surgery assistance, either at the time of original surgery or subsequent to that surgery is sometimes needed.

POST OPERATIVE CARE

Intracranial Pressure Monitoring

With the extensive cerebral injury which often attends PBI, elevated ICP is common afterwards. Initially, it has been observed that ICP elevation will not occur in PBI victims until they are resuscitated. The physiology of elevated ICP after PBI is not well understood. Cerebral swelling appears to develop rapidly after injury, perhaps due to loss of autoregulation in the brain. It can not be assumed that the mechanisms of cerebral swelling are the same in TBI and PBI, however, at our current state of knowledge the treatments are the same. There is no evidence that ICP monitoring improves outcome after PBI but given our knowledge of the physiology and anatomy of PBI, it would appear to have the same utility in PBI as it does in TBI.

Post Traumatic Aneurysms

As noted above PBI can lead to serious vascular injury in addition to venous sinus tears. A not uncommon result of

this injury can be delayed post traumatic cerebral aneurysms. Between 3 and 33% of all victims of PBI may have a Post Traumatic Aneurysm(34;35).

Providers of care to the victims of PBI should be aware of this and have a low threshold for obtaining cerebral angiography. Angiography is the best way to detect post traumatic aneurysms. Such aneurysms can develop as late as two weeks after the injury and an early negative cerebral angiogram does not exclude an aneurysm later in the patient's course. Any patient who develops delayed or unexplained subarachnoid hemorrhage or other delayed bleeding should be suspected of harboring a post traumatic aneurysm and should undergo cerebral angiography.

Management of Cerebrospinal Fluid Leaks

Half of all CSF leaks may occur at sites remote from the entry or exit sites in PBI. These CSF leaks will not be apparent at surgery and will manifest after surgery. 72% of these leaks will appear within 2 weeks of surgery and 44% will seal spontaneously(36).

Antibiotic Prophylaxis for Penetrating Brain Injury

Infection is a major risk after PBI. As noted above, the first efforts in infection control occur at surgery. The vast majority of the data on infections in PBI is in patient populations in the post antibiotic era. The data that is available from the preantibiotic era tells us that in World War I the infections rate after PBI was 58.1%. With the use of Sulpha in World War II the rate dropped to 21-31% and once penicillin was available it dropped to 5.7 -13%. All of this is military data. Current military rates are reported at 4-11%. Current civilian rates are at 1-5%(37).

The rate of brain abscess formation in the military was 8.5% during World War II, it is currently 1.6-3.1% in the military and less than 1% in the civilian world.
Half (55%) of all intracranial infections occur within 3 weeks of the injury and 90% occur within 6 weeks(37).

Factors affecting infection risk are CSF leaks, air sinus wounds and wound dehiscence. In the presence of cranial air sinus wounds the infection rate is 29%. With CSF leak, it has been reported at 49%.

Because of the high infections rates with this injury, long term antibiotics are commonly used. It is presumed that without this practice that the infection rates would approximate the World War I rates, although the role of improved surgical techniques, including tight dural closure, may play a larger role in this improvement than is appreciated(37). No data exists to support this assumption since all modern data on patient outcomes is obtained on patient on antibiotics. A study which withheld antibiotics from some patients would raise ethical concerns and is unlikely to be done.

Antiseizure Prophylaxis for Penetrating Brain Injury

A major rational for extensive debridment of penetrating head injuries was the prevention of post traumatic seizures. In fact, the victims of PBI appear to have an increased risk for posttraumatic epilepsy which appears to be even greater than for close TBI.

In PBI, 30-50% of victims develop PTE(38;39). This is slightly higher than the estimates of 4-42% for non penetrating TBI(40-42). In addition, early seizures in the TBI literature are defined as seizures in the first 7 days after injury, when the vast majority of early seizures occur(42). There is data in the PBI literature implying a slightly higher incidence of seizures in the second week after injury, but the numbers in these studies are low(40).

Current guidelines for antiepileptic therapy after TBI distinguish between two uses for antiepileptic drugs post injury, treatment and prophylaxis. Antiepileptic drugs do appear to be effective in treating an established post traumatic seizure disorder and in preventing immediate post injury seizures in the first week after injury. They do not appear to be effective in reducing the incidence of posttraumatic epilepsy, that is, maintenance of TBI victims on prophylactic doses of anticonvulsant medications beyond the first week of therapy does not appear to reduce the incidence of post traumatic seizures. The recommendation in TBI is to treat the patient with anticonvulsants for seven days and then discontinue the medication, only restarting it if seizures develop(43).

Ultimately, follow the same logic as for non penetrating TBI and in the absence of contradictory data, the Guidelines for the Management of Penetrating Brain Injury does not recommend prophylactic anticonvulsants(40).

The data on retained metal fragments and epilepsy is contradictory. Salazar in his analysis of the Vietnam Head Injury Study Data, found a significant relationship between retained metal and PTE(33). Aarbi, however, in a retrospective univariate analysis of predictors of PTE in 489 victims in the Iran-Iraq war failed to identify retained metal fragments as a predictor of PTE(40).

Lastly, the risk of PTE after PBI appears to decline with time. While 18% of victims may not have their first seizure until 5 or more years after the injury, 80% will have their first seizure within 2 years of the injury and 95% of patients will remain seizure free if they remain seizure free for 3 years following injury(38;39). Followed out to 15 years, 50% of patients who do develop PTE will stop having seizures(38).

SUMMARY

In World War II the principles of management for penetrating gunshot wounds were 1) Immediate saving of life 2) prevention of infection 3) preservation of nervous tissue and 4) restoration of anatomic structures(44). While our understanding of what these goals mean and how to accomplish them has changed, this list remains a good check list of how to approach penetrating injury, once the decision to resuscitate has been made. This list, coupled with a modern understanding of how to determine who should be saved should equip the clinician with a good set of tools with which to approach these most difficult of trauma victims.

REFERENCES

1. Thurman DJ, Alverson C, Browne D, Dunn KA, Guerrero J, Johnson R et al. Traumatic Brain Injury in the United States: A Report to Congress. 1999. Atlanta, Centers for Disease Control and Prevention, National Center for Injury Prevention and Control. Ref Type: Report
2. Langlois JA, Rutland-Brown W, Thomas KE. Traumatic Brain Injury in the United States: Emergency Department Visits, Hospitalizations, and Deaths. 2004. Centers for Disease Control and Prevention, National Center for Injury Prevention and Control. Ref Type: Report
3. Adekoya N, Thurman DJ, White DD, Webb KW. Surveillance for traumatic brain injury deaths--United States, 1989-1998. Morb Mortal Wkly Rep Surveill Summ 2002; Surveillance Summaries. 51(10):1-14.
4. Kaufman HH, Makela ME, Lee KF, Haid RW, Jr., Gildenberg PL. Gunshot wounds to the head: a perspective. Neurosurg 1986; 18(6):689-695.
5. Siccardi D, Cavaliere R, Pau A, Lubinu F, Turtas S, Viale GL. Penetrating craniocerebral missile injuries in civilians: a retrospective analysis of 314 cases. Surg Neurol 1991; 35(6):455-460.
6. Kaufman HH, Schwab K, Salazar AM. A national survey of neurosurgical care for penetrating head injury. Surg Neurol 1991; 36(5):370-377.
7. Part 2: Prognosis in penetrating brain injury. [Review] [52 refs]. J Trauma 2001; 51(2 Suppl):S44-S86.
8. Arabi B. Surgical outcome in 435 patients who sustained missile head wounds during the Iran-Iraq War. Neurosurg 1990; 27(5):692-695.
9. Carey ME. Experimental missile wounding of the brain. Neurosurg Clin N Am 1995; 6(4):629-642.
10. Kaufman HH, Levy ML, Stone JL, Masri LS, Lichtor T, Lavine SD et al. Patients with Glasgow Coma Scale scores 3, 4, 5 after gunshot wounds to the brain. [Review] [63 refs]. Neurosurg Clin N Am 1995; 6(4):701-714.
11. Aldrich EF, Eisenberg HM, Saydjari C, Foulkes MA, Jane JA, Marshall LF et al. Predictors of mortality in severely head-injured patients with civilian gunshot wounds: a report from the NIH Traumatic Coma Data Bank. Surgical Neurology 1992; 38(6):418-423.
12. Brandvold B, Levi L, Feinsod M, George ED. Penetrating craniocerebral injuries in the Israeli involvement in the Lebanese conflict, 1982-1985. Analysis of a less aggressive surgical approach. [Review] [23 refs]. Journal of Neurosurgery 1990; 72(1):15-21.
13. Grahm TW, Williams FC, Jr., Harrington T, Spetzler RF. Civilian gunshot wounds to the head: a prospective study.[see comment]. Neurosurgery 1990; 27(5):696-700.
14. Shaffrey ME, Polin RS, Phillips CD, Germanson T, Shaffrey CI, Jane JA. Classification of civilian craniocerebral gunshot wounds: a multivariate analysis predictive of mortality. J Neurotrauma 1992; 9 Suppl 1:S279-S285.
15. Suddaby L, Weir B, Forsyth C. The management of .22 caliber gunshot wounds of the brain: a review of 49 cases. [Review] [16 refs]. Can J Neurol Sci 1987; 14(3):268-272.
16. Byrnes DP, Crockard HA, Gordon DS, Gleadhill CA. Penetrating craniocerebral missile injuries in the civil disturbances in Northern Ireland. Br J Surg 1974; 61(3):169-176.
17. Polin RS, Shaffrey ME, Phillips CD, Germanson T, Jane JA. Multivariate analysis and prediction of outcome following penetrating head injury. [Review] [25 refs]. Neurosurg Clin N Am 1995; 6(4):689-699.
18. Jacobs DG, Brandt CP, Piotrowski JJ, McHenry CR. Transcranial gunshot wounds: cost and consequences. Am Surg 1995; 61(8):647-653.
19. Levy ML, Masri LS, Lavine S, Apuzzo ML. Outcome prediction after penetrating craniocerebral injury in a civilian population: aggressive surgical management in patients with admission Glasgow Coma Scale scores of 3, 4, or 5. Neurosurg 1994; 35(1):77-84.
20. Levi L, Borovich B, Guilburd JN, Grushkiewicz I, Lemberger A, Linn S et al. Wartime neurosurgical experience in Lebanon, 1982-85. I: Penetrating craniocerebral injuries. Isr J Med Sci 1990; 26(10):548-554.
21. Cavaliere R, Cavenago L, Siccardi D, Viale GL. Gunshot wounds of the brain in civilians. Acta Neurochir (Wien) 1988; 94(3-4):133-136.

22. Clark WC, Muhlbauer MS, Watridge CB, Ray MW. Analysis of 76 civilian craniocerebral gunshot wounds. J Neurosurg 1986; 65(1):9-14.

23. Lillard PL. Five years experience with penetrating craniocerebral gunshot wounds. Surg Neurol 1978; 9(2):79-83.

24. Nagib MG, Rockswold GL, Sherman RS, Lagaard MW. Civilian gunshot wounds to the brain: prognosis and management. Neurosurg 1986; 18(5):533-537.

25. Kennedy F, Gonzalez P, Dang C, Fleming A, Sterling-Scott R. The Glasgow Coma Scale and prognosis in gunshot wounds to the brain. J Trauma 1993; 35(1):75-77.

26. Shoung HM, Sichez JP, Pertuiset B. The early prognosis of craniocerebral gunshot wounds in civilian practice as an aid to the choice of treatment. A series of 56 cases studied by the computerized tomography. Acta Neurochir (Wien) 1985; 74(1-2):27-30.

27. Mancuso P, Chiaramonte I, Passanisi M, Guarnera F, Augello G, Tropea R. Craniocerebral gunshot wounds in civilians. Report on 40 cases. J Neurosurg Sci 1988; 32(4):189-194.

28. Levy ML, Masri LS, Levy KM, Johnson FL, Martin-Thomson E, Couldwell WT et al. Penetrating craniocerebral injury resultant from gunshot wounds: gang-related injury in children and adolescents. [Review] [2 refs]. Neurosurg 1993; 33(6):1018-1024.

29. Hammon WM. Analysis of 2187 consecutive penetrating wounds of the brain from Vietnam. J Neurosurg 1971; 34(2 Pt 1):127-131.

30. Chaudhri KA, Choudhury AR, al Moutaery KR, Cybulski GR. Penetrating craniocerebral shrapnel injuries during "Operation Desert Storm": early results of a conservative surgical treatment. Acta Neurochir (Wien) 1994; 126(2-4):120-123.

31. Carey ME, Young HF, Rish BL, Mathis JL. Follow-up study of 103 American soldiers who sustained a brain wound in Vietnam. J Neurosurg 1974; 41(5):542-549.

32. Gonul E, Baysefer A, Kahraman S, Ciklatekerlioglu O, Gezen F, Yayla O et al. Causes of infections and management results in penetrating craniocerebral injuries. Neurosurg Rev 1997; 20(3):177-181.

33. Salazar AM, Schwab K, Grafman JH. Penetrating injuries in the Vietnam war. Traumatic unconsciousness, epilepsy, and psychosocial outcome. [Review] [34 refs]. Neurosurg Clin N Am 1995; 6(4):715-726.

34. Aarabi B. Traumatic aneurysms of brain due to high velocity missile head wounds. Neurosurgery 1988; 22(6 Pt 1):1056-1063.

35. Aarabi B. Management of traumatic aneurysms caused by high-velocity missile head wounds. [Review] [263 refs]. Neurosurgery Clinics of North America 1995; 6(4):775-797.

36. Meirowsky AM, Caveness WF, Dillon JD, Rish BL, Mohr JP, Kistler JP et al. Cerebrospinal fluid fistulas complicating missile wounds of the brain. J Neurosurg 1981; 54(1):44-48.

37. Antibiotic prophylaxis for penetrating brain injury. [Review] [40 refs]. J Trauma 2001; 51(2 Suppl):S34-S40.

38. Salazar AM, Jabbari B, Vance SC, Grafman J, Amin D, Dillon JD. Epilepsy after penetrating head injury. I. Clinical correlates: a report of the Vietnam Head Injury Study. Neurology 1985; 35(10):1406-1414.

39. Caveness WF, Meirowsky AM, Rish BL, Mohr JP, Kistler JP, Dillon JD et al. The nature of posttraumatic epilepsy. J Neurosurg 1979; 50(5):545-553.

40. Antiseizure prophylaxis for penetrating brain injury. [Review] [18 refs]. J Trauma 2001; 51(2 Suppl):S41-S43.

41. Annegers JF, Hauser WA, Coan SP, Rocca WA. A population-based study of seizures after traumatic brain injuries. New England Journal of Medicine 1998; 338(1):20-24.

42. Temkin NR, Dikmen SS, Wilensky AJ, Keihm J, Chabal S, Winn HR. A randomized, double-blind study of phenytoin for the prevention of post-traumatic seizures.[see comment]. New England Journal of Medicine 1990; 323(8):497-502.

43. Bullock R, Chesnut RM, Clifton G, Ghajar J, Marion DW, Narayan RK et al. Guidelines for the management of severe head injury. Brain Trauma Foundation. [Review] [46 refs]. European Journal of Emergency Medicine 1996; 3(2):109-127.

44. Surgical management of penetrating brain injury. [Review] [39 refs]. J Trauma 2001; 51(2 Suppl):S16-S25.

Panamerican Journal of Trauma Vol. 14 No. 1 2007 Pages 37 - 41

ECONOMICS OF TRAUMA CARE RE-VISITED

Samir Fakhry, MD, FACS

INTRODUCTION

Trauma care is expensive with approximately 150,000 deaths annually in the United States and total costs from motor vehicle crashes alone estimated at as much as $383.6 billion [1]. A careful review of the economics of trauma care should reveal an interesting observation: if one's ultimate goal was to become exceptionally rich, it would have been better to have obtained a business degree than a medical degree [2]. On the other hand it is not necessarily true that being engaged in the practice of trauma care will result in a uniformly poor balance sheet for both physicians and hospitals. It appears possible for trauma surgeons and trauma centers to be profitable, or at least to break even. There are a number of conditions that increase a center's likelihood of positive financial outcomes:

1. Large volumes of severely injured trauma patients [3,4]. An adequately large volume of patients allows a center to spread overhead costs over more patients and justify the substantial standby costs of trauma readiness.
2. High quality care and the practice of evidence based medicine.
3. Efficient, comprehensive documentation, coding and billing systems for physicians and hospitals.
4. A favorable (or at least tolerable) patient payer mix to allow adequate reimbursement.
5. Optimally negotiated managed care contracts
6. Availability of specialty coverage for call.

The increasing financial pressures in areas such as those noted above have forced many trauma centers to close or reduce their levels of care [5]. The outlook for the future is not rosy.

Chief, Trauma & Surgical Critical Care Services
Associate Chair for Research and Education
Department of Surgery. Inova Fairfax Hospital
Professor of Surgery
Virginia Commonwealth University – Inova Campus
Falls Church, Virginia

TRAUMA SYSTEM CHALLENGES: NATIONAL

Trauma care in the United States has received minimal support from the federal government. The federal legislation for the support of trauma systems has never provided more than about $3.5 million dollars annually. This translates into approximately $40,000 per state. This funding has been available inconsistently in the past decade and this year does not appear promising given the budget constraints that Congress is encountering. Funding for research in trauma has always been extremely limited in relationship to the productive years of life lost or to the overall cost of trauma to society [6]. Following the tragic events of September 11, 2001 significant federal funding became available for the war on terror and for homeland security. Unfortunately only a minimal amount of money found its way to trauma centers in the United States.

Current statistics suggest that 678,000 injured people are treated in a regional trauma center annually in the United States. The severity adjusted national norm for per patient costs in a trauma center is $14,896.00. Total trauma center costs for hospitals in the United States are estimated at 10.1 billion with trauma center losses estimated at 1 billion [5].

Historically these difficult economic outcomes were the result of:

1. Poor patient payer mix in many centers, especially those in urban regions (managing penetrating trauma)
2. Low rates of reimbursement for the complex care delivered in trauma centers
3. Little if any support for the cost of readiness incurred by trauma centers.

These challenges have forced the closure of many trauma centers over the years. In addition to the more familiar problems of previous years, several new threats to trauma center viability have appeared. Foremost among these is the significant problem of adequate specialty coverage for trauma and emergency department care. In a recent report

from the American College of Emergency Physicians [7] funded by the Robert Wood Johnson Foundation, "On-call Specialist Coverage in United States Emergency Departments", 65.9 % of a large sample of emergency departments (n=1427) reported that they had significant difficulties finding adequate on-call specialty coverage for their emergency departments. It should be noted that 63% of these hospitals were not trauma centers while 21% were Level I or Level II trauma centers. 75% of these hospitals were not for profit hospitals. The ED directors responding to this survey were asked "What is the most significant consequence of this shortage?" The leading response (27%) was "risked or harmed patients who need specialists care" followed by "delay in patient care" (21%) and "more transfers of patients between emergency departments" (18%). The survey also revealed that emergency department transfers were increasing in 33% of these departments and in approximately one half of those cases the transfers were made only because their emergency department did not have access to a specialist physician. Although there are many possible reasons for the difficulties that these hospitals are encountering in securing adequate on call specialty coverage, three deserve special mention.

These are:
1. Lifestyle choices
2. Organized efforts by specialty organizations at securing compensation for on-call coverage for trauma and emergency department cases
3. Perceived impact of malpractice coverage

The increasing shortages of physicians interested in surgery and in particular, trauma care, have only increased the severity of these challenges[8,9]. Faced with the need to provide trauma services for their community, hospitals have struggled to meet these challenges. The percentage of hospitals around the country providing on call stipends to their specialty physicians is at an all time high. Hospitals that choose not to abandon their trauma designation have been forced to invest increasing amounts of scarce resources into trauma care. This has added to the financial losses incurred by many trauma centers. In addition to poor reimbursement and uninsured patients, this new category of on-call compensation to specialty physicians must be considered in any assessment of the economics of trauma centers, especially those in the private sector.

TRAUMA SYSTEM CHALLENGES: STATE

In 2004, the Virginia House Joint Resolution 183 directed the Joint Legislative Audit and Review Commission (JLARC) to study the use and financing of trauma centers in Virginia. This resulted in part from the coordinated efforts of a group of trauma center physicians in Virginia, the Physician's Injury Reduction Coalition (PIRC). The exceptionally fine report produced by the JLARC in response to this legislative mandate provides an excellent case study of the current status of the economics of trauma centers in the United States [10].

Among the highlights of the JLARC report:
1. Nearly 14,000 patients were treated at designated trauma centers in Virginia in 2003 (Fig1). The most common mechanisms of injury were motor vehicle crashes (35%) and falls (32%). Penetrating injuries were the third most common injuries but accounted for only 8% of the total.
2. The financial analysis of trauma programs in Virginia revealed that uncompensated care, low reimbursement rates from public insurers, and readiness costs created a $44 million loss across Virginia trauma centers in 2003. The cost of readiness was a loss leader among trauma centers (Fig 2).
3. Hospital administrators consistently cited physician availability as the primary issue that could jeopardize access to trauma centers. The shortage of orthopedic surgeons was especially pronounced. Not surprisingly, the majority of trauma coverage was through physicians in private practice (Fig 4). Significant numbers of the on-call private physicians were being paid to be on-call (Fig 5). This was especially true for general/ trauma surgeons.
4. Trauma care has become less attractive to physicians. Factors related to this problem included:
   - Inadequate reimbursement. This affected private physicians more than those in university practice. Trauma patients were more likely to be uninsured than other patients (fig 6) and their care disrupts the care of other, more lucrative patients with higher reimbursement rates.
   - Malpractice concerns.
   - Quality of life issues.
   - The dwindling supply of trauma surgeons.
5. Public insurers (including Medicare and Medicaid) reimburse trauma care at levels below the actual cost of care (Fig 7).
6. Analysis of triage effectiveness in the State found that a large number of critically injured trauma patients are not treated in designated trauma centers, while many moderately injured patients receive the highest level of trauma care.

The JLARC report also offered a variety of potential methods for the legislature to support Trauma Centers in

Virginia. Partially as a result of this report, the legislature created a "Trauma Fund" to be supported by monies collected as fines from repeat offenders of DUI laws and from individuals seeking to reinstate a suspended driver's license. It is expected that this fund will raise funds to cover approximately 10% of Trauma Center losses in Virginia.

CONCLUSION

Trauma Centers in America are facing increasing challenges to their operational integrity. Some of these challenges are similar to those faced in past years but there are new challenges that arise predominantly from the difficulties in securing specialty on-call coverage and from the dwindling numbers of physicians interested in caring for trauma patients. These manpower issues are unlikely to disappear in the foreseeable future since they are rooted in basic trends affecting Medicine and Surgery. Most current solutions for the manpower shortages (especially the sub-specialty crisis) involve reimbursement for on-call coverage. In the long run, such solutions run the risk of overextending trauma center finances (a "slippery slope") and do not address the fundamental issues driving these manpower trends. Other temporary solutions (such as Virginia' Trauma Fund) offer short term relief but can also be exhausted by increasing volumes of patients and spiraling costs. Fundamental solutions that address the root causes of this crisis in trauma care must be considered by policy makers and healthcare professionals to ensure the viability of our Trauma Centers.

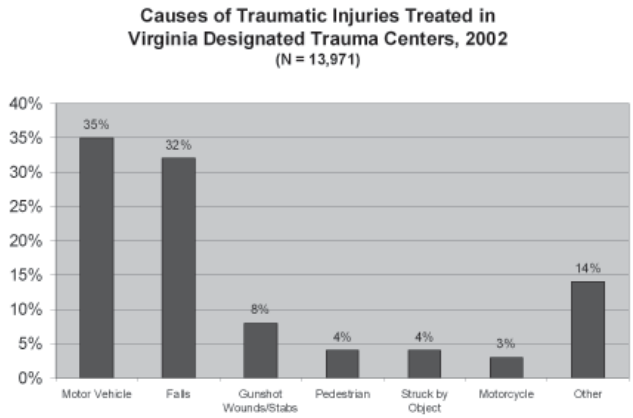


Figure 1. Source: JLARC staff analysis of trauma registry data

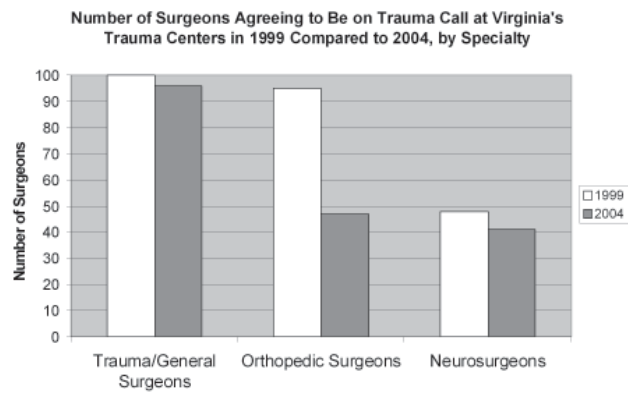


Figure 3. Note: Includes only those trauma centers reporting staffing levels for both 2004 and 1999. Does not include Lynchburg General Hospital, Carilion New River Valley Medical Center and Orthopedic and Neurosurgeon levels at UVA Medical Center. Source: JLARC staff analysis of survey data.

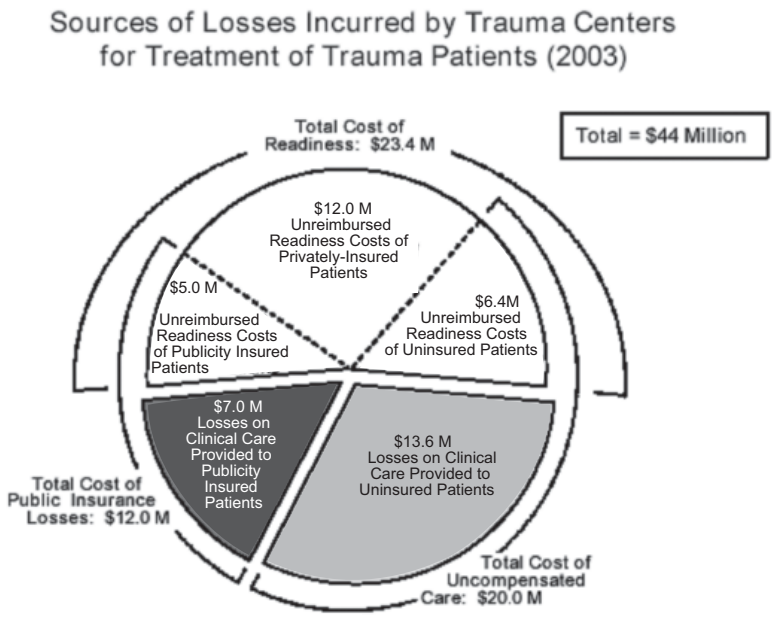
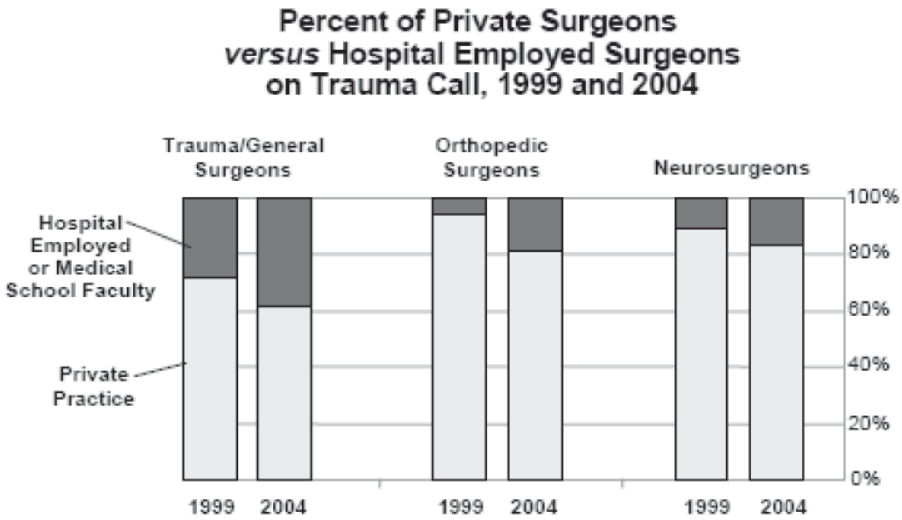


Figure 2

Note: Data exclude Southside Regional Medical Center.



Note: Includes only those trauma centers reporting staffing levels for both 2004 and 1999. Does not include Lynchburg General Hospital, Carilion New River Valley Medical Center and Orthopedic and Neurosurgeon levels at UVA Medical Center.

Source: JLARC staff analysis of survey data.

Figure 4

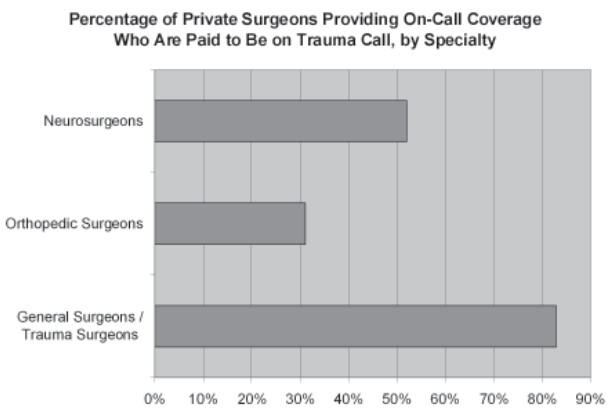


Figure 5

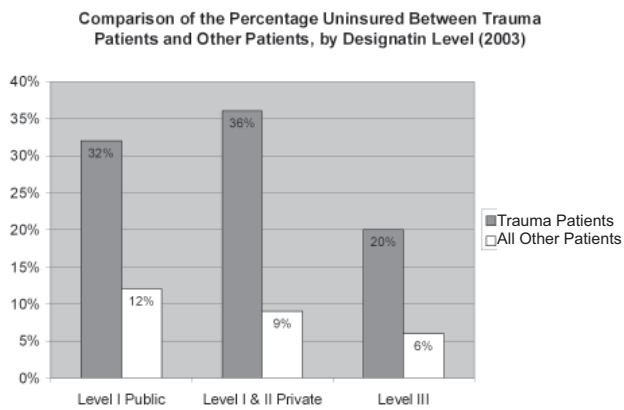
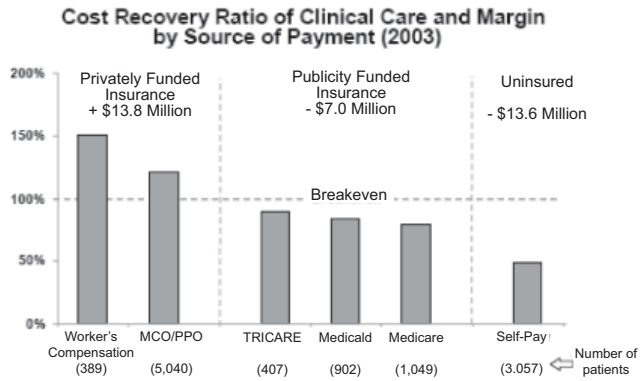


Figure 6. Source: JLARC staff analysis of 2003 trauma center financial data, excluding Southside Regional Medical Center.



Note: Data exclude Southside Regional Medical Center, and "Other" payer groups (191 patients)

Source: JLARC staff analysis of financial data provided by Virginia trauma centers.

Figure 7

REFERENCES

1. Segui-Gomez, M, MaKenzie, E. Measuring the Public Health Impact of Injuries. Epidemiologic Reviews, 25:3-19, 2003.
2. Fakhry, SM, Watts, DD. What's a Trauma Surgeon Worth? A Salary Survey of the Membership of the Eastern Association for the Surgery of Trauma. Journal of Trauma, 49:833-38, 2000.
3. Taheri, P, Butz, D, Griffes, LC, Morlock DR, Greenfield, LJ. Physician Impact on the Total Cost of Care. Annals of Surgery, 231:432-435, 2000.
4. Taheri, P, Butz, D, Greenfield, LJ. Paying a Premium: How Patient Complexity Affects Costs and Profit Margins. Annals of Surgery, 229:807-8145, 1999.

5. National Foundation for Trauma Care. U.S. Trauma Center Crisis: Lost in the Scramble for Terror Resources. May 2004. At www.traumafoundation.org/public/files-misc/NFTC_CrisisReport_May04.pdf. Accessed 5/5/06.

6. Committee on Trauma Research, Commission on Life Sciences, National Research Council and Institute of Medicine. Injury in America: A continuing Health Problem. Washington, DC: National Academy Press, 1985.

7. American College of Emergency Physicians. On-call Specialist Coverage in United States Emergency Departments, ACEP Survey of Emergency Departments, 2004.

8. Fakhry SM, Watts DD, Michetti C, Hunt JP and the EAST Multi-Institutional HVI Research Group. The Resident Experience On Trauma: Declining Surgical Opportunities And Career Incentives? Analysis of data from a large multi-institutional study. Journal of Trauma, 54:1-8, 2003.

9. Richardson JD, Miller FB. Will future surgeons be interested in trauma care? Results of a resident survey. J Trauma, 32:229-235, 1992.

10. The use and Financing of Trauma Centers in Virginia. Joint Legistlative Audit and Review Commission, Document number 62 (2004). At http:\\JLARC.state.va.us/reports/rpt313.pdf. Accessed 5/5/2006.

Panamerican Journal of Trauma Vol. 14 No. 1 2007 Pages 42 - 51

¿WHAT'S NEW IN TRAUMA & CRITICAL CARE? HEAD TRAUMA MANAGEMENT

Peter Letarte, MD, FACS

INTRODUCTION

The Guidelines for the Management of Traumatic Brain Injury introduced in 1995, was an evidence based document. This evidence based focus has continued in the field of TBI management and has lead to a dynamic evaluation of the history and assumptions about how we treat the victims of TBI. This discussion has reached beyond TBI to areas of broader concern to health care such as the merits of an evidence based approach and the implementation of guidelines. This article will review some of the most recent developments in our understanding of the management of TBI.

SURGICAL GUIDELINES

A significant recent development in the management of TBI has be the publication of the Guidelines for the Surgical Management of Traumatic Brain Injury(1). This document has been an evidence based examination of the most fundamental of all the treatments for the management of traumatic brain injury. The most interesting observation made by this effort has been fact that these time honored and tested interventions are supported by no more than Class III data and can be recommended at no more than the option level.

Some practitioners find this alarming. In fact these guidelines provide an opportunity to put some issues about an evidence based approach to health care into perspective.

The first of these issues is the "parachute issue." Many practitioners who object to evidence based medicine are fond of bringing up the parachute argument. The parachute argument points out that we do not need to do a randomized prospective clinical trial to prove that parachutes work. We are certain that the control group would have very close to 100% mortality. We are so certain of this that to do the experiment would be unethical(2).

Chief, Section of Neurosurgery
Heinz VA Medical Center. Maywood, Illinois

The parachute argument is often inappropriately applied. What is not commonly understood about the parachute argument is that in the case of jumping from airplanes, we have a very good sense of the natural history of the event and of the outcome should we fail to intervene. We can be very certain that any intervention will improve on what are sure is a 100% mortality.

Unfortunately, for many injuries that we treat, the expected outcome is not as clear as the expected outcome of jumping from an airplane. As our certainty about the outcome with out intervention declines, our need for an evidence based approach rises.

Secondly, it often goes unnoticed that we are not always clear on what outcome we are trying to change. In the case of jumping out of airplanes, we are trying to reduce our speed of impact to a survivable range. In the case of removing epidural hematomas, we are trying to save our patients for lives of high quality. What is interesting is that we have very little data which demonstrates that we do that. What perpetuates the practice of removing intracranial hematomas in patients with a unilateral fixed and dilated pupil is the common observation that when we do this the pupil often comes down, which we assume means that the threat has been removed and that the patient will therefore do better. We have data to support this assumption but in fact, this assumption is probably correct.

We need to be critical of how we apply the parachute argument but there are times when it is appropriate. If we open the abdomen and encounter audible hemorrhage, the outcome without intervention is clear; we do not need a randomized prospective clinical trial to validate what we must do. The parachute argument applies. So it is with the removal of mass effect. While our certainty about the outcome should we fail to remove mass effect in the head may not be as high as that for jumping out of airplanes or managing audible hemorrhage, it is high enough that we could not ethically propose an experiment to demonstrate improved outcomes with

removal. What the Guidelines for the Surgical Management of Traumatic Brain Injury have taught us is that in the case of removal of hematomas, the parachute argument applies.

But not for all hematomas and not in all circumstances. The guidelines review what is known about when to remove hematomas.

Acute Epidural Hematoma

The Guidelines recommend that all epidural hematomas with a volume > 30cm^2 be evacuated, regardless of the patient's Glasgow Coma Score. The criteria for non operative management are a volume on CT > 30cm^2, a thickness of < 15 mm and midline shift < .5 mm in a patient with a GCS > 8 and no focal deficit. All of these criteria should be met for the patient to be managed non-operatively(3).

Patients with an acute epidural hematoma, anisocoria and a GCS <9 should undergo craniotomy "as soon as possible", regardless of the size of the hematoma(3).

No recommendation on the method of evacuation is made but the authors mention that craniotomy allows a more complete removal(3).

Acute Subdural Hematomas

For subdural hematomas, those with a thickness greater than 10mm or a midline shift greater than 5 mm should be evacuated regardless of the patient's GCS. A patient with an acute subdural hematoma that is less than 10 mm thick and midline shift less than 5mm but who has fixed and dilated or asymmetric pupils, an ICP > 20 mmHg or a decline in GCS of 2 or more points from the time of injury to hospital admission should also have their hematoma removed(4). Patients with acute subdural hematomas also need to have their clots removed as soon as possible(4). Subdural hematomas should be removed using craniotomy with our without bone removal(4). All patients with a GCS< 9 and an acute subdural hematoma should be monitored with an ICP monitor(4).

Parenchymal Lesions

Parancymal lesions consist of interparenchymal clots and contusions. Their management has always been less clearly defined than the management of epidural and subdural hematomas

Focal parenchymal lesions should be removed in three circumstances. Any patient with a parenchymal mass lesion and signs of progressive neurological deterioration due to the lesion, medically refractory intracranial hypertension, or signs of mass effect on computed tomographic (CT) scan should be treated operatively(5). Any patient with any lesion greater than 50 cm^3 in volume should be treated operatively(5). Patients with Glasgow Coma Scale (GCS) scores of 6 to 8 with frontal or temporal contusions greater than 20 cm^3 in volume with midline shift of at least 5 mm and/or cisternal compression on CT scan should be treated operatively(5).

Craniotomy with evacuation of mass lesion is recommended for these patients(5).

Patients with parenchymal mass lesions who do not show evidence for neurological compromise, have controlled intracranial pressure (ICP), and no significant signs of mass effect on CT scan may be managed nonoperatively with intensive monitoring and serial imaging(5).

For patients with diffuse cerebral swelling, bifrontal decompressive craniectomy within 48 hours of injury is a treatment option. These patients should have diffuse, medically refractory posttraumatic cerebral edema and resultant intracranial hypertension(5).

In addition to bifrontal decompressive craniectomy other decompressive procedures, including subtemporal decompression, temporal lobectomy, and hemispheric decompressive craniectomy, are treatment options for patients with refractory intracranial hypertension and diffuse parenchymal injury with clinical and radiographic evidence for impending transtentorial herniation(5).

Posterior Fossa Lesions

Posterior Fossa lesion as particularly dangerous. These lesions often do not manifest their mass effect may mental status change but rather by vital sign changes. These changes are often subtle and missed with the ensuing herniation then presenting as cardiopulmonary collapse.

Patients with mass effect on computed tomographic (CT) scan or with neurological dysfunction or deterioration referable to the lesion should undergo operative intervention. Mass effect on CT scan is defined as distortion, dislocation, or obliteration of the fourth ventricle; compression or loss of visualization of the basal cisterns, or the presence of obstructive hydrocephalus. The operation should take place as soon as possible. A suboccipital craniectomy is the procedure most commonly performed(6).

Patients with lesions and no significant mass effect on CT scan and without signs of neurological dysfunction may be managed by close observation and serial imaging(6).

Depressed Skull Fractures

The management of patients with depressed skull fractures has remained fairly standard for many years, although there has been a recent trend towards more non-operative management. Patients with open (compound) cranial fractures depressed greater than the thickness of the cranium should undergo operative intervention to prevent infection although nonoperative management is appropriate for patients with no clinical or radiographic evidence of dural penetration, significant intracranial hematoma, depression greater than 1 cm, frontal sinus involvement, gross cosmetic deformity, wound infection, pneumocephalus, or gross wound contamination. Closed (simple) depressed cranial fractures may be treated non operatively(7).

Early operation is recommended to reduce the incidence of infection. And elevation and debridement is recommended as the surgical method of choice. Replacement of the bone at the time of surgery is appropriate if no infection is present and antibiotics should be started on all patients with open (compound) depressed fractures(7).

HYPERVENTILATION

The realization that lowering the pCO2 could reduce brain swelling is at least 40 years old. In his description of the first management of cerebral swelling using continuous ICP monitoring in 1959, Lundberg described the use of hyperventilation in the management of elevated ICP.(8) Subsequently, most large centers incorporated hyperventilation into their ICP protocols.

Surprisingly, little work was ever done to confirm that it actually improved patient outcomes. Most practitioners apparently continued to use hyperventilation in their management of elevated ICP motivated not so much by the available literature as by the fact that it appeared to work, at least measured by its ability to reduce a dilating pupil, if not improve outcome.

In the early 1970s, work by Raichle pointed out that hyperventilation in addition to reducing cerebral swelling also reduced cerebral blood flow. Raichle also pointed out that prolonged hyperventilation had not been shown to be beneficial to patients(9).

Obrist published work on cerebral blood flow after trauma which demonstrated that hyperventilation reduced cerebral blood flow far more consistently than it reduced ICP(10).

Furthermore, Raichle's assertion that prolonged hyperventilation might not be beneficial was carried further by work by Muizelaar which demonstrated that patients who were hyperventilated for prolonged periods of time actually did worse at 3 and 6 months from the time of injury(11). The first edition of the Guidelines for the management of Severe Brain Injury therefore included cautions about the use of hyperventilation and suggested limiting its use to emergencies and ICP management scenarios where most other first tier therapies had failed(12).

Because of the evidence that hyperventilation can cause cerebral ischemia and because of the increasing awareness that its efficacy on outcome has never been demonstrated, hyperventilation is being used more judiciously. What keeps it appropriately in the armamentarium of most providers for emergency response to elevated ICP or a dilating pupil is the fact that in most provider's experience, it will bring down the pupil or the ICP a significant percentage of the time.

HYPEROSMOLAR THERAPY

Hyperosmotic therapy was first proposed in 1919 by Weed and McKibben who noted that infusion of intravenous distilled water increased brain tissue mass and infusion of 30% saline dehydrated the brain(13). Fremont-Smith and Forbes began the clinical use of hyperosmolar urea the late 1920s(14). Javid became aware of urea's dehydrating properties in 1956 and published an extensive clinical experience with it in controlling cerebral edema, popularizing its use(15-17). In 1962, Mannitol was proposed as a hyperosmotic agent(18). Although urea could be given in much smaller volumes than mannitol, mannitol replaced urea as the hyperosmolar agent of choice because of concerns about rebound intracranial hypertension associated with urea's use(19;20). Recently, hypertonic saline has been proposed as an alternative hyperosmotic agent, with volume expansion qualities as well as brain dehydrating qualities(20-27).

Hyperosmolar therapies reduce ICP by two distinct mechanisms. The commonly- appreciated mechanism is via the establishment of an osmolar gradient across the blood brain barrier, with the gradient favoring the flow of water out of the brain and into the circulation. This mechanism is estimated to require 15- 30 minutes to act and can last 90 minutes to six hours.

Osmolar agents, however, can act in a much shorter time frame via a second mechanism. These agents also improve the rheology of the blood via plasma expansion, reduced hematocrit and reduced blood viscosity resulting in more efficient cerebral blood flow. This increased efficiency means that at any given CPP, the cerebrovascular resistance will be higher, the cerebral blood volume will be lower, ICP

will therefore be lower while cerebral blood flow remains unaltered(28). Mannitol and hypertonic saline are believed to utilize both of these mechanisms(29).

MANNITOL

Mechanism of Action

Mannitol has long been accepted as an effective tool for reducing intracranial pressure(30-34). Numerous mechanistic laboratory studies support this conclusion. Its impact on outcome has never, however, been directly demonstrated via a Class I trial testing mannitol against placebo. Schwartz conducted a Class I study comparing mannitol to pentobarbital which failed to demonstrate the superiority of pentobarbital and which did demonstrate better outcomes and maintenance of CPP in the mannitol group(33).

Recently, however, Cruz has published 3 Class II studies demonstrating benefit of high dose mannitol vs. conventional dose mannitol in the very early stages of a patient's treatment. Patient populations with acute subdural hematomas, temporal lobe hemorrhages and diffuse brain swelling have been studied. Patients who received early high dose mannitol had better preoperative improvement of pupillary widening and better Glasgow Outcome Scores at 6 months(35-37).

Rate of Infusion

There is a commonly held belief that mannitol administration can cause or exacerbate hypotension in the early resuscitation of trauma victims. There is Class III data that infusion of mannitol at rates of 0.2-0.8 g/kg/min can lead to transient drops in blood pressure(38-40). From these observations, a recommended rate of no higher than 0.1 g/kg/min or 1 g/kg delivered over 10 minutes or more is recommended(28). Careful monitoring of urine output with aggressive replacement of this fluid loss is also recommended to prevent hypotension associated with the use of mannitol.

Sayre et al. tested the hypothesis that mannitol would exacerbate hypotension in a prehospital environment in a Class II study. Patients were randomized to a mannitol or normal saline group. Mannitol was allowed to be given rapidly over as little as 5 minutes. No difference in heart rate or blood pressure was observed over the two hour subsequent observation period between the two groups(41).

Dose

Mannitol can be given in response to an elevated ICP or as a continuous drip in a more prophylactic fashion. Class II data have found bolus administration to be effective and some Class III data have found no difference between the two routes(30;32;42-45)5.

Mannitol and other hyperosmotics are known to be able to briefly open the blood brain barrier. Furthermore, at rates of administration which exceed the rate of excretion of mannitol, mannitol can accumulate in the extracellular space. These factors lead to the accumulation of mannitol in the extracellular space and a reverse osmotic gradient which can lead to a "rebound effect" or movement of water into the brain. Class III data suggests that this effect is more likely with continuous infusion of mannitol as opposed to bolus administration(46;47)7.

Class II and Class III data have shown that doses of 0.25 – 1.0 g/kg of mannitol may be needed to achieve a reduction in ICP. This required dose varies from patient to patient and even may vary from time to time in the same patient(32;47;48)3.

The more recent Cruz data show that doses from 1.4 – 2.1 g/kg can be effective in early in a patient's care in response to pupillary widening, declining mental status or asymmetric motor examination, with beneficial effects on papillary response and outcome(49-52).

HYPERTONIC SALINE

Hypertonic saline offers an attractive alternative to mannitol as a therapy for elevated intracranial pressure. Its ability to reduce elevated ICP has been demonstrated with Class II and III data in the ICU and in the operating room(25-27;53).

Hypertonic saline has been used in two very different ways in the resuscitation of trauma victims. In addition to being proposed as a hyperosmolar agent for the management of elevated ICP, it is also advocated as a low volume resuscitation fluid. While the qualities that make it useful both as a low volume resuscitation fluid and as a brain- targeted therapy are related, its efficacy in one role does not guarantee its efficacy in the other. Each therapeutic endpoint must be analyzed independently.

There is no consensus on what is meant by "hypertonic saline". Concentrations of 3%, 7.2%, 7.5%, 10% and 23.4% have all been used and described in the literature. There is no consensus on a standard concentration for reduction of ICP(21;25-27).

In addition, hypertonic saline is described in the literature as being administered in a variety of different ways. The goals and endpoints in each of these studies is different.

In some studies, hypertonic saline is given as an infusion, the goal of which is to elevate serum sodium to 155- 160 mEq/L, although some investigators have gone as high as 180 mEq/L. This elevated serum sodium is thought to help stabilize ICP and reduce the therapeutic intensity required to manage elevated ICP(54;55).

Another way to use hypertonic saline is as a bolus in an attempt to achieve an immediate reduction in ICP. This method takes advantage of the rapid rheologic improvement and improved cerebral blood flow which, like mannitol, hypertonic saline can create.

Multiple animal studies and several human studies have demonstrated that hypertonic saline, as a bolus, can reduce ICP in a monitored environment such as the operating room or ICU where ICP monitoring is present(56-58). Comparison of these studies is difficult since they do not use the same concentrations or protocols. No study has demonstrated an effect on clinical indicators of herniation such as pupillary widening or posturing such as Cruz demonstrated for mannitol.

One Class I study looked at the impact of prehospital hypertonic saline on neurological outcome. In this study, hypertonic saline did not demonstrate any advantage over normal saline on neurological outcome when given as a prehospital resuscitation fluid(59). Based on this data, hypertonic saline is not yet a mainstream treatment for elevated ICP.

ADVANCED CEREBRAL MONITORING

Hypoxia has long been known to be a significant source of secondary brain injury. Significant Class II and III data have validated the concept that patients with an oxygen saturation <90% have significantly worse outcome than patients whose oxygen saturations are >90%(60;61). Knowing that blood oxygen saturation is >90%, however, is a long way from knowing anything about oxygen delivery to the brain.

Several methods for measuring oxygen delivery to the brain are available. One method to estimate how much oxygen the brain uses is to measure how much oxygen it removes from the blood, the arterial-venous oxygen difference. This value is measured by measuring the oxygen content of the blood entering the cranial vault and the content of the blood leaving the cranial vault, which is done by placing a sensor or sampling catheter high in the jugular vein. By subtracting the oxygen content of the blood leaving the head from the content of the blood entering the head, a rough estimate of the brain oxygen utilization can be obtained. The resulting number is known as the AVO_2 difference.

This number reflects the balance between the oxygen delivered to the brain and the metabolic activity, and therefore the oxygen demand, of the brain. A metabolically active brain will require more oxygen and more delivery of oxygen than a quiet brain. The brain will be injured when this demand is not met. The AVO_2 difference really assesses if brain demand is being met.

The AVO_2 difference is useful, but some estimates of the adequacy of oxygen delivery to the brain can be made by simply measuring the saturation of blood leaving the brain in the jugular bulb, the $SjvO_2$. Most patients have saturations of 55-69% in blood leaving the brain.

$SjvO_2$ appears to adequately reflect the status of oxygen delivery to the brain. While it has never been shown that maintaining $SjvO_2$ in the normal range improves outcome, multiple studies have shown that patients with increased numbers of episodes of $SjvO_2$ desaturation <50% have worse outcomes (10;62-65).

A more direct approach, however, is to measure cerebral tissue oxygen tension. This can be measured via cerebral tissue oxygen monitoring. Normal cerebral tissue oxygen pressures, $PbrO_2$, are approximately 32mmHg. Studies have shown that patients whose $PbrO_2$ is allowed to dip to 15 or lower do significantly worse(66). Elegant work has stratified patients into groups with episodes of progressively lower brain tissue oxygen pressures, with increasingly poorer outcomes as the brain tissue oxygen pressure is allowed to go lower and the time the brain stays at these suppressed levels increases(65). Some brain tissue data has suggested that hypoxic brain injury is cumulative, that periods of recovery between episodes of hypoxia do not erase the negative effect of the hypoxia and that, in fact, multiple brief episodes of hypoxia can be as damaging as a single prolonged hypoxic event. One study compared TBI populations who were managed in equivalent fashions for ICP and CPP control. The experimental group also had $PbrO_2$ actively managed to stay above 25 mmHg. The mortality rate in the historical control group was 44%, in the $PbrO_2$ managed group, 25%(67).

It appears that active management of cerebral oxygen delivery has the potential to improve outcomes from TBI. Applying technologies that allow the $SjvO_2$ to be kept above 50% and the $PbrO_2$ above 15 mmHg is now a reasonable option to pursue in the management of TBI.

CPP MANAGEMENT

Cerebral Perfusion Pressure is the difference between the mean arterial pressure and the Intracranial Pressure

(CPP=MAP=ICP). Maintaining the correct CPP has always been important in the treatment of TBI. The role of CPP in TBI is complex and our understanding of it is incomplete and controversial. Establishing what the correct CPP should be is therefore difficult.

There are many reasons cited to maintain an adequate CPP. The most common is to reduce the incidence of secondary insults to the injuries brain. With this approach, the focus on CPP prevents inadvertent hypotension to the brain and reduced the incidence of secondary insults. The endpoint for this approach is a reduced number of hypotensive episodes.

A second reason to maintain adequate CPP is assure that the brain is functioning within the autoregulatory limits. Autoregulation uses cerebral vasodilation to maintain constant Cerebral Blood Flow in the face of varying CPP. For autoregulation to function, the CPP must be above a certain threshold. In injured brains, this threshold may rise. Maintaining the CPP above the autoregulatory threshold allows substrate delivery to be maintained via efficient flow rather than large volume. As cerebral vasoconstriction is allowed to work, Cerebral Blood Volume (CBV) falls. The endpoint for this approach is to assure that the autoregulatory threshold is met.

In general, a CPP designed to reduce the number of hypotensive episodes will be above the autoregulatory threshold but it should not be forgotten that these are two separate goals.

Yet another way to evaluate the effectiveness of CPP is to look at is effect on oxygen delivery to the brain, the $PbrO_2$. In these studies, above a certain CPP threshold, $PbrO_2$ is no longer dependant on CPP. In most studies this threshold is 60 mmHg, in one it is 70 mmHg. One caveat to this approach to CPP management is the issue of regional ischemia. It is well documented that in many TBI victims, there can be areas of injury that can be saved if adequately perfusion. These areas may have lost autoregulation and will require higher CPP than the non injured areas of the brian(68;69). While a CPP of 60 mmHg may be adequate for most of the brain, it will be inadequate for the injured areas of greatest interest. Guiding therapy based on average CPP for the whole brain will result in suboptimal perfusion and treatment for these areas of injury. Patients with areas of regional ischemia may require higher CPP(70).

A fourth school of thought, the advocates of "Lund Therapy," believe that elevated CPP increases transcapillary hydrostatic pressure, increasing cerebral edema and mass effect. While not advocating the old practice of keeping TBI patients dry, this group believes that once the goals of adequate cerebral perfusion, meeting the autoregulatory threshold and preventing hypotensive episodes are met, further increases in CPP are detrimental.

Robertson et al. examined some of these issues in a study published in 1999. In this Class I study, patients were randomized to either a CBF targeted therapy or an ICP targeted therapy. In the ICP treatment group, standard ICP control strategies were used, MAP > 70, CPP > 50. Hyperventilation, with its subsequent ischemic effects, was included in the techniques being used to control ICP. In the CBF group, much more aggressive CBF management was utilized with MAP>90, CPP> 70 and, while elevated ICP was controlled, hyperventilation was not used as a modality(71).

The study showed that CBF focused therapy was more successful in meeting some of the surrogate markers of adequate CBF. The incidence of $SjvO_2$ desaturation was 50.6% in the ICP focused group and 30% in the CBF focused group. The median length of time the CPP was < 60 mmHg in the ICP targeted group was 13 hours, it was 4 hours in the CBF targeted group. The total length of time the $SjvO_2$ was low for the ICP targeted group was 58.9 hours for the ICP targeted group and 7.8 hours for the CBF targeted group.

While CBF targeted therapy in this study demonstrated considerable improvement in many surrogate markers for CPP success, the study failed to show any improvement in outcome for CBF directed therapy over ICP focused therapy. Further the study showed that patients with CPP of 70 mmHg had a higher incidence of ARDS.

Multiple studies have looked on outcomes when CPP is maintained at 70 mmHg, none has convincing demonstrated improved outcomes(70). Oxygen delivery studies have demonstrated that over a CPP of 60 mmHg, little improvement in cerebral oxygen delivery is achieved by higher levels, with the important exception of patients with regional ischemia. Patients whose CPP is kept at 70 mmHg appear to have a higher incidence of ARDS. While the advocates of Lund therapy would recommend a CPP of 50 mmHg, there is not enough data make this a widely accepted approach. The current synthesis of this data appears to be that of Robertson which is that, except in cases of regional ischemia, a CPP of 60 mmHg is adequate and no benefit and some harm may come from elevating CPP to 70 mmHg(70).

BARBITURATE THERAPY

Barbiturate therapy or barbiturate "coma" can be used as a third tier therapy for elevated ICP when other more standard therapies have failed. It has been demonstrated be

effective in reducing ICP(72). As is true with many therapies for elevated ICP, studies have not been done which demonstrate that it improves outcome(73).

Barbiturate therapy also carries with it a high morbidity(73). Barbiturates affect the function of not only the brain but also the heart and kidneys, among other organs. Significant declines in the functioning of both of these organ systems can occur during therapy. For this reason, barbiturate coma should not initiated if the victim of malignant ICP is also hemodynamically unstable. Patient's should be hemodynanmically stable prior to entering barbiturate therapy and should be carefully monitored to assure maintenance of hemodymanic stability during therapy.

Propofol is commonly used as a sedative in TBI. While it is convenient and can be reversed quickly during the first few days of use, there is little data that it useful for ICP control. Propofol has been associated with myocardial death in children and this complication is also possible in adults. Propofol infusion syndrome can present with hyperkalemia, hepatomegaly, lipemia, metabolic acidosis, myocardial failure, and rhabdomyolysis.. The possibility of this complication must be considered in propofol is used in doses greater than 5 mg/kg/hr or for more than 48 hrs(74).

HYPOTHERMIA

It has long been suspected that cooling the brain would have a protective effect and limit injury. Anecdotal observations of phenomenon such as brain survival after prolonged immersion and near drowning in very cold have lead providers to assume that the cold provides some beneficial effect.

Hypothermia has been shown to reduce elevated intracranial pressure(75-78). There is good also some clinical data which demonstrates that hypothermia has a beneficial effect on the outcome from TBI(75;79;80).

The National Acute Brain Injury Study: Hypothermia (NABISH) study was a large randomized prospective clinical trial designed to demonstrate this beneficial effect for hypothermia on the outcome from TBI. It failed to do so(81).

The study showed that there were groups, specifically younger patients, who did benefit from hypothermia. There were several factors that may have hidden the beneficial effects of hypothermia in this study. One of them was the high impact of the medical complications of the hypothermia on older victims of trauma. This impact was so high, that the morbidity of the procedure out weighed the benefit of the hypothermia for TBI(81).

Therapeutic hypothermia for TBI is considered to be the rapid reduction and maintenance of a core body temperature to 32-35º C for 48 hours or less is a complex therapy to perform. Most practitioner are not aware that to be effective, the decision to induce the hypothermia must be made almost immediately upon presentation and the patient must have the hypothermia induced and reach target temperature within 60 or perhaps even 30 minutes of presentation(82). Once the hypothermia is induced, careful management of electrolytes, in particular potassium, is essential. Rewarming requires careful cardiac monitoring and detailed monitoring of the electrolyte and fluid shifts that occur during this period.

The therapy has no demonstrated efficacy as a third tier therapy that could be considered for use several days into treatment as other therapies fail(82).

Because of this complexity, hypothermia requires a sophisticated and nimble hospital infrastructure. The rapid cooling and unique monitoring tasks require advanced nursing expertise. This capability must be available 24/7since the capability must be available within 30 minutes of the patient's presentation. This requirement mandates a commitment to extensive nursing training for large numbers of nurses.

Even the highly expert and well organized study group which lead NABISH had a difficult time assuring that these standard were uniformly and consistently met at the study hospitals(83).

Although the NABISH study failed to demonstrate the efficacy of hypothermia, many still believe that it has potential value as a therapy. Both the analysis of the factors which confounded the NABISH study and other research leave room for this opinion. What is clear, however, is that hypothermia should only be performed at centers that are willing to make the substantial commitment to doing it correctly. It appears that marginal or inept application of this therapy at best will do no good and at worst will harm the patients. Centers wishing to use this therapy need to have physicians and nurses well trained in these techniques immediately available to presenting trauma victims, as well as the appropriate cooling technologies and ancillary services. For these reasons, it is anticipated that hypothermia will only be available to patients at large specialty centers.

REFERENCES

1. Bullock MR, Chesnut R, Ghajar J, Gordon D, Hartl R, Newell DW et al. Guidelines for the surgical management of traumatic brain injury author group: acknowledgments. Neurosurgery 2006; 58(3 Suppl):S2-vi.

2. Smith GC, Pell JP. Parachute use to prevent death and major trauma related to gravitational challenge: systematic review of randomised controlled trials. [Review] [11 refs]. BMJ 2003; 327(7429):1459-1461.
3. Bullock MR, Chesnut R, Ghajar J, Gordon D, Hartl R, Newell DW et al. Surgical Management of Acute Epidural Hematomas. Neurosurgery 2006; 58(3 Suppl):S2-7-S2-15.
4. Bullock MR, Chesnut R, Ghajar J, Gordon D, Hartl R, Newell DW et al. Surgical Management of Acute Subdural Hematomas. Neurosurgery 2006; 58(3 Suppl):S2-16-S2-24.
5. Bullock MR, Chesnut R, Ghajar J, Gordon D, Hartl R, Newell DW et al. Surgical management of traumatic parenchymal lesions. Neurosurgery 2006; 58(3 Suppl):S25-S46.
6. Bullock MR, Chesnut R, Ghajar J, Gordon D, Hartl R, Newell DW et al. Surgical management of posterior fossa mass lesions. Neurosurgery 2006; 58(3 Suppl):S47-S55.
7. Bullock MR, Chesnut R, Ghajar J, Gordon D, Hartl R, Newell DW et al. Surgical management of depressed cranial fractures. Neurosurgery 2006; 58(3 Suppl):S56-S60.
8. Lundberg N, Kjallquist A, Bien C. Reduction of increased intracranial pressure by hyperventilation. A therapeutic aid in neurological surgery. Acta Psychiatrica Scandinavica 1959; 34(Suppl 139):1-64.
9. Raichle ME, Plum F. Hyperventilation and cerebral blood flow. [Review] [78 refs]. Stroke 1972; 3(5):566-575.
10. Obrist WD, Langfitt TW, Jaggi JL, Cruz J, Gennarelli TA. Cerebral blood flow and metabolism in comatose patients with acute head injury. Relationship to intracranial hypertension. Journal of Neurosurgery 1984; 61(2):241-253.
11. Muizelaar JP, Marmarou A, Ward JD, Kontos HA, Choi SC, Becker DP et al. Adverse effects of prolonged hyperventilation in patients with severe head injury: a randomized clinical trial. Journal of Neurosurgery 1991; 75(5):731-739.
12. Bullock R, Chesnut RM, Clifton G, Ghajar J, Marion DW, Narayan RK et al. Guidelines for the management of severe head injury. Brain Trauma Foundation. [Review] [46 refs]. European Journal of Emergency Medicine 1996; 3(2):109-127.
13. Weed LH, McKibben P.S. Experimental alteration of brain bulk. American Journal of Physiology 1919; 48:531-558.
14. Fremont-Smith F., Forbes H.S. Intraocular and intracranial pressure:An experimental study. Archives of Neurology and Psychiatry 1927; 18:550-564.
15. Javid M., Settlage P., Monfore T. Urea in the management of increased intracranial pressure. Surgical Forum 1957; 7:528-532.
16. Javid M., Settlage P. Effect of Urea on cerebrospinal fluid pressure in human subjects. Preliminary Report. JAMA 1956; 160:943-949.
17. Javid M.J. Urea- new use of an old agent:Reduction of intracranial and intraocular pressure. Surgery Clinics of North America 1958; 8:1-22.
18. Wise B.M., Chaitile W. The value of hypertonic mannitol solution in decreasing brain mass and lowering cerebrospinal fluid pressure. Journal of Neurosurgery 1962; 18:51-57.
19. Paczynski R.P. Osmotherapy. Critical Care Medicine 1997; 13:105-129.
20. Prough D.S., Zornow M.H. Mannitol:An old friend on the skids. Critical Care Medicine 1998; 26(6):997-998.
21. Suarez J.I., Qureshi A.I., Bhardwaj A. Treatment of refractory intracranial hypertension with 23.4% saline. Critical Care Medicine 1998; 26:1118-1122.
22. Freshman SP, Battistella FD, Matteucci M, Wisner DH. Hypertonic saline (7.5%) versus mannitol: a comparison for treatment of acute head injuries. J Trauma 1993; 35(3):344-348.
23. Berger S, Schurer L, Hartl R, Messmer K, Baethmann A. Reduction of post-traumatic intracranial hypertension by hypertonic/hyperoncotic saline/dextran and hypertonic mannitol. Neurosurgery 1995; 37(1):98-107.
24. Berger S, Schurer L, Hartl R, Deisbock T, Dautermann C, Murr R et al. 7.2% NaCl/10% dextran 60 versus 20% mannitol for treatment of intracranial hypertension. Acta Neurochirurgica - Supplementum 1994; 60:494-498.
25. DeVivo P., Del Gaudio A., Ciritella P. Hypertonic saline solution: a safe alternative to mannitol 18% in neurosurgery. Minerva Anestesiol 2001; 67:603-611.
26. Gemma M., Cozzi S., Tommasino C. 7.5% hypertonic saline versus 20% mannitol during elective neurosurgical supratentorial proceedures. J Neurosurg Anesthesiol 1997; 9:329-334.
27. Munar F., Ferrer A.M., de Nadal M. Cerebral hemodynamic effects of 7.2% hypertonic saline in patients with head injury and raised intracranial pressure. J Neurotrauma 2000; 17:41-51.
28. Schrot R.J., Muizelaar J.P. Is there a "best" way to give Mannitol? In: Valadka A.B., Andrews B.T., editors. Neurotrauma. New York: Thieme, 2005: 142-147.
29. Management and Prognosis of Severe Traumatic Brain Injury. 2 ed. Brain Trauma Foundation, 2000.
30. Becker D.P., Vries J.K. The alleviation of increased intracranial pressure by the chronic administration of osmotic agents. Springer, 1972.
31. Eisenberg HM, Frankowski RF, Contant CF. High-dose barbiturate control of elevated intracranial pressure in patients with severe head injury. J Neurosurg 1988; 69:15-23.
32. James H.E. Methodology for the control of intracranial pressure with hypertonic mannitol. Acta Neurochir (Wein) 1980; 51:161-172.
33. Schwartz M.L., Tator C.H., Rowed D.W. The University of Toronto Head Injury Treatment Study: A prospective, randomized comparison of pentobarbitol and mannitol. J Neurol Sci 1984; 11:434-440.

34. Smith HP, Kelly DL, Jr., McWhorter JM, Armstrong D, Johnson R, Transou C et al. Comparison of mannitol regimens in patients with severe head injury undergoing intracranial monitoring. J Neurosurg 1986; 65(6):820-824.

35. Cruz J, Minoja G, Okuchi K. Improving clinical outcomes from acute subdural hematomas with the emergency preoperative administration of high doses of mannitol: a randomized trial. Neurosurgery 2001; 49(4):864-871.

36. Cruz J, Minoja G, Okuchi K. Major clinical and physiological benefits of early high doses of mannitol for intraparenchymal temporal lobe hemorrhages with abnormal pupillary widening: a randomized trial. Neurosurgery 2002; 51(3):628-637.

37. Cruz J, Minoja G, Okuchi K, Facco E. Successful use of the new high-dose mannitol treatment in patients with Glasgow Coma Scale scores of 3 and bilateral abnormal pupillary widening: a randomized trial.[see comment]. J Neurosurg 2004; 100(3):376-383.

38. Cote C.J., Greenhow D.E., Marshall B.E. The hypotensive response to rapid intravenous administration of hypertonic solutions in man and in the rabbit. Anesthesiology 1979; 50:30-35.

39. Domaingue C.M., Nye D.H. Hypotensive effect of mannitol administered rapidly. Anaesth Intensive Care 1985; 13:134-136.

40. Ravussin P., Archer D.P., Tyler J.L. Effects of rapid mannitol infusion on cerebral blood volume: a positron emission tomographic study in dogs and man. J Neurosurg 1986; 64:104-113.

41. Sayre MR, Daily SW, Stern SA, Storer DL, van Loveren HR, Hurst JM. Out-of-hospital administration of mannitol to head-injured patients does not change systolic blood pressure. Acad Emerg Med 1996; 3(9):840-848.

42. Smith H.P., Kelly D.L., McWorter J.M., et al. Comparison of mannitol regimens in patients with severe head injury undergoing intracranial monitoring. J Neurosurg 1986; 65:820-824.

43. Marshall L.F., Smith R.W., Rausher L.A. Mannitol dose requirements in brain-injured patients. J Neurosurge 1978; 48:169-172.

44. Muizelaar JP, Lutz HA, III, Becker DP. Effect of mannitol on ICP and CBF and correlation with pressure autoregulation in severely head-injured patients. J Neurosurg 1984; 61(4):700-706.

45. Unterberg AW, Kiening KL, Hartl R, Bardt T, Sarrafzadeh AS, Lanksch WR. Multimodal monitoring in patients with head injury: evaluation of the effects of treatment on cerebral oxygenation. Journal of Trauma-Injury Infection & Critical Care 1997; 42(5 Suppl):S32-S37.

46. Kaufmann A.M., Cardoso E.R. Aggravation of vasogenic cerebral edema by multiple-dose mannitol. J Neurosurg 1992; 77:584-589.

47. McGraw C.P., Alexander E., Howard G. Effect of dose and dose schedule on the response of intracranial pressure to mannitol. Surg Neurol 1978; 10:127-130.

48. Marshall LF, SMith RW, Rauscher LA, Shapiro HM. Mannitol dose requirements in brain-injured patients. J Neurosurg 1978; 48(2):169-172.

49. Cruz J, Minoja G, Okuchi K, Facco E. Successful use of the new high-dose mannitol treatment in patients with Glasgow Coma Scale scores of 3 and bilateral abnormal pupillary widening: a randomized trial.[see comment]. J Neurosurg 2004; 100(3):376-383.

50. Cruz J, Minoja G, Okuchi K. Improving clinical outcomes from acute subdural hematomas with the emergency preoperative administration of high doses of mannitol: a randomized trial. Neurosurgery 2001; 49(4):864-871.

51. Cruz J, Minoja G, Okuchi K. Major clinical and physiological benefits of early high doses of mannitol for intraparenchymal temporal lobe hemorrhages with abnormal pupillary widening: a randomized trial. Neurosurgery 2002; 51(3):628-637.

52. Cruz J, Minoja G, Okuchi K, Facco E. Successful use of the new high-dose mannitol treatment in patients with Glasgow Coma Scale scores of 3 and bilateral abnormal pupillary widening: a randomized trial.[see comment]. J Neurosurg 2004; 100(3):376-383.

53. Peterson B, Khanna S, Fisher B, Marshall L. Prolonged hypernatremia controls elevated intracranial pressure in head-injured pediatric patients.[see comment]. Crit Care Med 2000; 28(4):1136-1143.

54. Peterson B, Khanna S, Fisher B, Marshall L. Prolonged hypernatremia controls elevated intracranial pressure in head-injured pediatric patients.[see comment]. Crit Care Med 2000; 28(4):1136-1143.

55. Qureshi AI, Wilson DA, Traystman RJ. Treatment of elevated intracranial pressure in experimental intracerebral hemorrhage: comparison between mannitol and hypertonic saline. Neurosurgery 1999; 44(5):1055-1063.

56. Doyle JA, Davis DP, Hoyt DB. The use of hypertonic saline in the treatment of traumatic brain injury. [Review] [232 refs]. J Trauma 2001; 50(2):367-383.

57. Schatzmann C, Heissler HE, Konig K, Klinge-Xhemajli P, Rickels E, Muhling M et al. Treatment of elevated intracranial pressure by infusions of 10% saline in severely head injured patients. Acta Neurochir Suppl 1998; 71:31-33.

58. Shackford SR. Effect of small-volume resuscitation on intracranial pressure and related cerebral variables. J Trauma 1997; 42(5 Suppl):S48-S53.

59. Cooper D.J., Myles P.S., McDermott F.T. Prehospital hypertonic saline resuscitation of patients with hypotension and severe traumatic brain injury: A randomized controlled trial. JAMA 2004; 291(11):1350.

60. Chesnut RM, Marshall LF, Klauber MR, Blunt BA, Baldwin N, Eisenberg HM et al. The role of secondary brain injury in determining outcome from severe head injury. Journal of Trauma-Injury Infection & Critical Care 1993; 34(2):216-222.

61. Stocchetti N, Furlan A, Volta F. Hypoxemia and arterial hypotension at the accident scene in head injury. Journal of Trauma-Injury Infection & Critical Care 1996; 40(5):764-767.

62. Robertson CS, Narayan RK, Gokaslan ZL, Pahwa R, Grossman RG, Caram P, Jr. et al. Cerebral arteriovenous oxygen difference as an estimate of cerebral blood flow in comatose patients.[see comment]. Journal of Neurosurgery 1989; 70(2):222-230.

63. Robertson C. Desaturation episodes after severe head injury: influence on outcome. Acta Neurochir Suppl (Wien) 1993; 59:98-101.

64. Gopinath SP, Robertson CS, Contant CF, Hayes C, Feldman Z, Narayan RK et al. Jugular venous desaturation and outcome after head injury. Journal of Neurology, Neurosurgery & Psychiatry 1994; 57(6):717-723.

65. Gopinath SP, Valadka AB, Uzura M, Robertson CS. Comparison of jugular venous oxygen saturation and brain tissue Po2 as monitors of cerebral ischemia after head injury.[see comment]. Critical Care Medicine 1999; 27(11):2337-2345.

66. Kiening KL, Hartl R, Unterberg AW, Schneider GH, Bardt T, Lanksch WR. Brain tissue pO2-monitoring in comatose patients: implications for therapy. Neurological Research 1997; 19(3):233-240.

67. Stiefel MF, Spiotta A, Gracias VH, Garuffe AM, Guillamondegui O, Maloney-Wilensky E et al. Reduced mortality rate in patients with severe traumatic brain injury treated with brain tissue oxygen monitoring. Journal of Neurosurgery 2005; 103(5):805-811.

68. Marion DW, Darby J, Yonas H. Acute regional cerebral blood flow changes caused by severe head injuries. Journal of Neurosurgery 1991; 74(3):407-414.

69. McLaughlin MR, Marion DW. Cerebral blood flow and vasoresponsivity within and around cerebral contusions.[see comment]. Journal of Neurosurgery 1996; 85(5):871-876.

70. Hlatky R, Robertson C. Does Raising Cerebral Perfusion Pressure Help Head Injured Patients? In: Valadka AB, Andrews BT, editors. Neurotrauma. New York: Thieme, 2005: 75-82.

71. Robertson CS, Valadka AB, Hannay HJ, Contant CF, Gopinath SP, Cormio M et al. Prevention of secondary ischemic insults after severe head injury. Critical Care Medicine 1999; 27(10):2086-2095.

72. Eisenberg HM, Frankowski RF, Contant CF, Marshall LF, Walker MD. High-dose barbiturate control of elevated intracranial pressure in patients with severe head injury. Journal of Neurosurgery 1988; 69(1):15-23.

73. Ward JD, Becker DP, Miller JD, Choi SC, Marmarou A, Wood C et al. Failure of prophylactic barbiturate coma in the treatment of severe head injury. Journal of Neurosurgery 1985; 62(3):383-388.

74. Kang TM. Propofol infusion syndrome in critically ill patients.[see comment]. [Review] [13 refs]. Annals of Pharmacotherapy 2002; 36(9):1453-1456.

75. Marion DW, Penrod LE, Kelsey SF, Obrist WD, Kochanek PM, Palmer AM et al. Treatment of traumatic brain injury with moderate hypothermia. New England Journal of Medicine 1997; 336(8):540-546.

76. Shiozaki T, Sugimoto H, Taneda M, Yoshida H, Iwai A, Yoshioka T et al. Effect of mild hypothermia on uncontrollable intracranial hypertension after severe head injury.[see comment]. Journal of Neurosurgery 1993; 79(3):363-368.

77. Shiozaki T, Sugimoto H, Taneda M, Oda J, Tanaka H, Hiraide A et al. Selection of severely head injured patients for mild hypothermia therapy.[see comment]. Journal of Neurosurgery 1998; 89(2):206-211.

78. Shiozaki T, Hayakata T, Taneda M, Nakajima Y, Hashiguchi N, Fujimi S et al. A multicenter prospective randomized controlled trial of the efficacy of mild hypothermia for severely head injured patients with low intracranial pressure. Mild Hypothermia Study Group in Japan. Journal of Neurosurgery 2001; 94(1):50-54.

79. Marion DW, Obrist WD, Carlier PM, Penrod LE, Darby JM. The use of moderate therapeutic hypothermia for patients with severe head injuries: a preliminary report.[see comment]. Journal of Neurosurgery 1993; 79(3):354-362.

80. Zhi D, Zhang S, Lin X. Study on therapeutic mechanism and clinical effect of mild hypothermia in patients with severe head injury. Surgical Neurology 2003; 59(5):381-385.

81. Clifton GL, Miller ER, Choi SC, Levin HS, McCauley S, Smith KR, Jr. et al. Lack of effect of induction of hypothermia after acute brain injury.[see comment]. New England Journal of Medicine 2001; 344(8):556-563.

82. Markgraf CG, Clifton GL, Moody MR. Treatment window for hypothermia in brain injury. Journal of Neurosurgery 2001; 95(6):979-983.

83. Clifton GL, Choi SC, Miller ER, Levin HS, Smith KR, Jr., Muizelaar JP et al. Intercenter variance in clinical trials of head trauma--experience of the National Acute Brain Injury Study: Hypothermia.[see comment]. Journal of Neurosurgery 2001; 95(5):751-755.

Panamerican Journal of Trauma Vol. 14 No. 1 2007 Pages 52 - 59

¿WHAT'S NEW IN TRAUMA & CRITICAL CARE? HEMOSTATICS

John Hunt, MD, MPH, FACS

INTRODUCTION

Hemorrhage accounts for over 30 % of the mortality seen in the civilian population[1] and over 50% of the mortality seen in military action.[2] As such, this makes uncontrolled bleeding the leading cause of death in the military setting[3] and second in the civilian trauma population.[4] Although the rudiments of hemorrhage control, namely proficient surgical technique, coagulation component replacement, and prevention of hypothermia, will never be replaced, adjuncts in the form of local and systemic therapy hold promise in further reducing blood loss and decreasing morbidity and mortality associated with trauma. These adjuncts hold the most promise in areas of so-called "non-surgical bleeding". Primary interests and uses for the trauma surgeon have been in the areas of solid organ injury, retroperitoneal/pelvic injury, and in the pre-hospital abatement of hemorrhage until definitive operative management can be obtained.

Adjunts to hemostasis can be broken down into two broad categories; local and systemic. These local accessories can further be broken down into topical hemostats and tissue sealants/adhesives, with a great deal of overlap and mixing between the two. The early, rudimentary, but still used, hemostat groups include the gelatin matrices, the oxidized regenerated celluloses, and the collagens.

HEMOSTATS

These three categories of hemostats provide a scaffold upon which the host coagulation system can start to build clot in the injured area, but rely on the patient's clotting factors to be functioning

Gelatin-based Topical Hemostats

The first hemostats devised were the gelatins with Gelfoam, coming into clinical use in the 1945.[5] Gelfoam has been a long-standing player in the hemostat world and is derived from a porcine source. It is a water-insoluble, off-white, nonelastic, porous, pliable product prepared from a purified pork skin gelatin. Itis able to absorb and hold within its interstices, many times its weight of blood and other fluids. It can be cut without fraying and does come in a powdered form. It is absorbed with in 4-6 weeks. Gelfoam can be applied dry or after being soaked in saline. It is important to eliminate air from the interstices and apply with moderate pressure until hemostasis is achieved. Generally the price per application is between $10-20.

Oxidized Regenerated Cellulose

Shortly after the introduction of the Gelfoam, the oxidized cellulose product Oxycel was introduced to the market and found to be efficacious in arresting bleeding in the clinical setting in the field of neurosurgery.[6] This has in large part been replaced by Surgicel, which arrived on market in 1960. These are derived from cellulose, a plant source, and as such has a low risk for transmitting any viral or prion related illness. The traditional Surgicel is light weight and compressible coming in sheets of varying size. It is resorbable, has reasonable clotting character, but poor adhering capability. The typical application is $10-20 and it can be applied to flat surfaces, crevasses, or deep wounds. A new variant on surgical is the relatively newer oxidized regenerated cellulose, Nu-Knit. It is surgical with a thicker and sturdier construction. Advantages include being able to pack more efficiently and the product will hold sutures easily. A 2" X 3" piece of nu-knit is $40-50.

Collagens

There was dearth in the development of new hemostats until the 1970's when the utility of collagen products in abating hemorrhage was demonstrated.[7] From these early beginnings a multitude of products have emerged including Avitene, Actcel, Ultrafoam, and Instat among many others. Their common m*echanism involves increasing the sur-*

Associate Professor of Surgery
Section Chief, LSU Trauma & Critical Care
New Orleans, Louisiana

face area upon which hosts normal coagulation proteins can aggregate and potentially by activation of platelets.[8,9] *Early clinical work showed that these collagen matrices achieved hemostasis earlier and decreased blood loss in the clinical arenas of* neurosurgery,[10] vascular surgery,[11] and gynecological surgery.[12] Differences in these three topical hemostat types are difficult to demonstrate[13] and their use frequently is dictated by the hospital or surgeon preference. The source of these products is bovine collagen which has caused some concern in terms of transmission of animal illnesses. It is biocompatible and absorbs in less than 30 days, but has poor adhering properties. The cost is typically $10-20 per application. Topical thrombin is frequently added to any of the above to enhance performance.

HEMOSTAT/SEALANTS

Fibrin Glues

Fibrin glues, in general, are hemostatic agents that coagulate and seal upon application. They are made up from a fibrinogen concentrate and a thrombin/calcium solution that are kept separate and dispensed simultaneously resulting in the formation of a coagulum. The original glues were made from fibrinogen concentrate from the blood bank from single donor plasma and mixed with thrombin when needed. Several animal experiments have demonstrated efficacy in adverse situations. In a swine hepatic injury model with hypothermia and coagulopathy, the use of fibrin glue had a significant decrease in blood loss (Control: 875 +/- 265 mL; Fibrin glue: 300 +/- 59 mL) and total fluid resuscitation (Control: 2.9 +/- 0.4 L; Fibrin glue: 1.9 +/- 0.3 L) Six of seven control pigs required packing, but none with fibrin glue did suggesting this could be a replacement or adjunct to packing severe liver injuryies.[14]

This efficacy has also been demonstrated in the clinical arena of solid organ injury management. In one study, Twenty-six patients sustaining hepatic or splenic trauma had fibrin glue either applied topically or injected into the parenchyma of solid organs. The glue was effective after one application in 21 patients and after a second in five. Hemostasis was achieved despite coagulopathy and thrombocytopenia in eight patients and there were no re-explorations for bleeding.[15] In another study, fibrin glue (FG) was used to achieve hemostasis of 16 splenic injuries of varying etiology. The intraoperative blood loss averaged 1.8 +/- 2.4 (SD) liters and patients were transfused 3 +/- 2 units of blood perioperatively with the amount of fibrin glue required to achieve splenic hemostasis averaged 11 +/- 8 ml and varying directly with the grade of injury. Only one patient with a splenic hilar vascular injury (Grade V) underwent splenectomy.[16] With the use of special applicators the technique has been used in the laparoscopic management of trauma also.[17,18]

Tisseel

This was the first commercially available fibrin glue/sealant available, entering the market in 1998. The product has 4 components some of which must be kept refrigerated until use. The freeze-dried protein sealer is reconstituted in a fibrinolysis inhibitor solution and the thrombin is reconstituted in a calcium chloride solution. The protein sealer mixture must be heated in a special bath. The two are then mixed as they are applied by a syringe mechanism that has a single applicator connected to the two syringes. The efficacy and safety of this fibrin sealant as a topical hemostatic agent in was demonstrated in reoperative cardiac in a multicenter study (n=333 in 11 centers). In 92.6% of cases, bleeding was controlled within 5 minutes using fibrin sealant, compared with a 12.4% success rate using conventional topical agents ($p<0.001$). Fibrin sealant also controlled 82.0% of the bleeding episodes not initially controlled by conventional agents. Only 1.8% of patients receiving fibrin sealant lost more than 1499 mL blood within 12 hours, compared with 14.3% in conventionally treated controls ($p<0.05$).[19] Although the storage and processing can be laborious, the price has come down to approximately $250 per application.

FloSeal

This Baxter product has been on the market for approximately 5 years and has met with great success. It consists of a bovine gelatin matrix, human thrombin (pooled human plasma), and calcium chloride. The calcium is added to the thrombin and then the mixture is added to the gelatin matrix via a two syringe mixing system. The slurry is then applied with one of the syringes. If application is delayed the mixture will harden and not be usable.

Floseal performed well in the lab. In a model of renal injury in rats comparing Floseal to gelatin sponge mean blood loss was less in the Floseal group than gelatin sponge bolster compression alone (202.4 mL vs. 540.4 mL, respectively, $p = 0.016$) and hemois was complete in 60% (three out of five) of experimental animals after 2 minutes, but was incomplete in all control animals.[20] In a liver injury rat model FloSeal was associated with a reduction in the amounts of fluid lost into the abdominal cavity ($p < 0.01$) (19.2 +/- 1.5 versus 25.1 +/- 1.5 g) and enhanced mean arterial pressure at 5, 20, and 30 minutes after injury ($p = 0.02$).[21]

Early clinical studies are also promising showing 97% vs. 77% control of bleeding at ten minutes in cardiothoracic

patients when compared to gelatin matrix and thrombin.[22] In another study of a surgical sub-population, 18 patients with FloSeal placed after sinus surgery. Had comparable time to cessation of bleeding and no impairment of healing.[23] Floseal is easier to store and mix, but also costs more at approximately $250 per application

Costasis

This hemostat uses both bovine collagen as well as thrombin. The fibrinogen source is harvested in the operating room using the patient's blood and some special equipment. This product has been on market for approximately 5 years and has performed well in a number of surgical settings. In an industry sponsored study of surgical patients, hemostatis was achieved in more than 90% (153/167) of CoStasis subjects compared with 58% (88/151) of control subjects (P =.01). The duration of bleeding was also significantly shorter with CoStasis. The median time to controlled bleeding (42 seconds vs 150 seconds, P =.0001) and time to complete hemostasis (75 seconds vs 252 seconds, P =.0001) were both markedly longer with the control intervention. This effect was realized in general surgery (77/79 vs 49/75, P =.01), hepato-biliary (38/39 vs 20/29, P =.01), cardiac (28/37 vs 17/37, P =.02), and orthopedic surgery (10/12 vs 2/10, P =.01).[24] This technique has also been applied in the field of trauma in the specific case of retroperitoneal bleeding. In a study by Bochicchio, a total of 78 patients received a fibrin glue or Gelfoam and Thrombin. The latter group had a significantly greater number of early postoperative transfusions ($p < 0.001$) and a longer hospital ($p < 0.001$) and intensive care unit length of stay ($p < 0.007$).[25]

Coseal

This innovation is the most recent addition to the hemostat/sealant group. It gained approval and access to the market in 2003. The application is very similar to the double barreled injector used in the Tisseel product. Its distinct advantage over other glues is that it contains no human or animal components, giving it an advantage over other products in terms of potential infectious disease of allergic complications. The active ingredients are two polyethyleneglycols which form a coagulum upon contacting one another.

The potential of this new hemostat/sealant has been demonstrated in some limited settings. In the elective vascular surgery setting, anastomotic suture hole bleeding was treated intraoperatively with Gelfoam/thrombin or CoSeal. Grafts treated with CoSeal achieved immediate anastomotic sealing at more than twice the rate of subjects treated with Gelfoam/thrombin (47% vs 20%; P<.001). Consequently, the median time needed to inhibit bleeding in control subjects was more than 10 times longer than for experimental subjects (16.5 seconds vs 189.0 seconds; P =.01).[26] This success was duplicated in another elective vascular setting. In a randomized controlled trial, CoSeal was compared to Gelfoam/thrombin for managing anastomotic bleeding after implantation of Dacron grafts during aortic reconstruction for nonruptured aneurysms. CoSeal treated suture lines achieved immediate sealing following reestablishment of blood flow more frequently when compared with Thrombin/Gelfoam treated anastomoses (48 of 59 (81%) vs 10 of 27 (37%); P = 0.002)].[27] The only reported trauma application has been in the treatment of persistent traumatic pneumothoraces, a testament to its properties as a sealant.[28] The price of an application of Coseal is approximately $1,400.

A summary of the available Hemostats and Sealants is in Table1.

NEW INNOVATIONS

One of the downsides of many of the Hemostats/Sealants is that they can be ineffective in the setting of profuse bleeding and in uncontrolled circumstances. The hemostats tend to have poor adhering properties and the sealants are applied as liquids prior to hardening and can be washed away prior to setting. They are also more difficult to apply successfully when large surface areas are bleeding. The military has been seeking field dressings which are easy to apply in adverse circumstances, store well, and achieve adequate hemostasis in a wet field. The products of interest include the dry fibrin sealant dressings, several polysaccharride products, and granular zoolite.

Dry Fibrin Sealant

The most prominent of the dry fibrin sealant products is Tachocomb. It is not currently available in United States, but has been used extensively in Europe. It is comprised of dressing with impregnated lyophilized human thrombin and fibrinogen and can be applied to wounds as a dry dressing. Extensive animal research have demonstrated efficacy in vascular,[29] soft tissue,[30] and visceral injury.

*Several studies have shown promise in the area of severe liver trauma. In hypothermic and coagulopathic swine Holcomb et al. showed decreased blood loss (*669 mL, (range, 353-1,268 mL), versus 3,321 mL (range, 1,891-5,831 mL) and 4,399 mL (range, 2,321-8,332 mL) observed in the packing and IgG groups, respectively ($p<0.01$). There was also a significant decrease in resuscitation volume and the one-hour survival in the dry fibrin sealant group was

83%, whereas survival in the packing and IgG groups were 0% ($p < 0.05$).[31] In a separate study by the same group no evidence of intrahepatic abscess, unusual adhesions, or hepatic vein, vena caval, or pulmonary thromboses were noted in the long-term survival animals.[32] In another model of solid organ injury, rats undergoing partial nephrectomy showed a decrease in blood loss when treated with a dry fibrin sealant dressing when compared to control dressings (3.39 +/- 0.63 mL) versus (8.64 +/- 2.26 mL) ($p < 0.001$) and less of a decrease in the mean arterial pressure (34.09 +/- 15.58%) versus (59.66 +/- 16.19%) ($p = 0.015$).[33]

Glycosaminoglycans

These new polysaccharide-based hemostats/sealants fall into two categories based upon the level of polysaccharide acetylation. Hemcon (Sigma Chemicals Inc.) uses chitosan, a natural polymer of N-acetyl glucosamine, refined from crustacean shells, which has varying molecular weights, compositions, levels of acetylation, and configurations. The Rapid Deployment Hemostat (RDH) Trauma Dressing (Marine Polymer Technologies Inc.) uses Poly-N-Acetyl glucosamine manufactured from large-scale microalga cultures, which yield polymers of fully acetylated polysaccharide molecules capable of stimulating platelets ligands and causing activation.[34] Poly-N-Acetyl glucosamine initiates platelet activation as demonstrated by platelet surface elaboration of phosphatidylserine, P-selectin, and $\alpha_{IIb\beta3}$ Integrin. Platelet IIbβ3 inhibitors prevented fibrin polymerization.[35] Poly-N-Acetyl glucosamine also induced Factor X binding with platelets.[36] Others mechanisms which may promot hemostatsis include red cell interactions with poly-N-acetyl glucosamine is mediated via ionic interactions with cell surface proteins. This does not appear to occurs with the chitosans.[37]

These materials have been tested extensively in several animal models. In two models of arterial injury the RDH product showed efficacy. In a femoral arterial injury model, the Rapid Deployment Hemostat bandage outperformed guaze and Tachocomb (Fibrin bandage). The average blood loss in the gauze group was 35cc's±14% vs, 14cc's±9% in the RDH group. In an aortic injury model RDH achieved hemostasis in 100% of injuries as opposed to 40% and 20% for Tacho comb and gauze respectively.[38]

Although originally designed as field dressings the glucosamines have shown promise in visceral injuries as well. In a swine coagulopathic liver injury model, animals were randomized to standard abdominal packing or packing plus RDH bandage. The RDH bandage reduced mortality, total blood loss, and total intravenous fluid requirements and increased survival time when used as an adjunct to standard abdominal packing after severe liver injury.[39] In another liver injury experiment Hemcon was shown to reduce blood loss (264 mL; CI, 82-852 mL) compared with the gauze group (2,879 CI 788-10,513 mL) ($p < 0.01$), decrease fluid use in the chitosan group (1,793 CI 749-4,291) compared with the gauze group (6,614 CI 2,519-17,363) ($p = 0.03$). Survival was seven of eight and two of eleven in the chitosan and gauze groups ($p = 0.04$), respectively. Hemostasis was improved in the chitosan group ($p = 0.03$).[40]

The recent conflicts in Iraq and Afganistan have given opportunity to evaluate clinical efficacy in the battlefield setting. In a review of 64 uses of the HemCon dressing in combat, dressings were utilized externally on the chest, groin, buttock, and abdomen in 25 cases; on extremities in 35 cases; and on neck or facial wounds in 4 cases. In 66% of cases, dressings were utilized following gauze failure and were 100% successful. In 62 (97%) of the cases, the use of the HemCon dressing resulted in cessation of bleeding or improvement in hemostasis with only two reported dressing failures occurring in application to large cavitational injuries. Dressings were reported to be most useful on areas where tourniquets could not be applied to control bleeding and most difficult to use in extremity injuries. No complications or adverse events were reported.[41] King and colleagues reported early use in the civilian population and in visceral injuries. Ten patients were enrolled: nine severe hepatic injuries, and one major abdominal vascular injury. All patients were hypothermic, acidotic, and clinically coagulopathic with intraoperative hemostasis being immediately obtained after RDH placement in 9 of 10 cases.[42]

Granular Zoolite (QuikClot)

This product works by creating marked water absorption, RBC and platelet aggregation, and an exothermic reaction. There are few clinical reports of the efficacy of QuikClot, but there have been several animal studies which have suggested that if may be efficacious. When compared with gauze gressing in a severe liver injury model post-treatment blood loss was reduced with QuikClot (1,397 mL), as compared with gauze (5,338 mL) ($p < 0.01$). The survival rate was seven of eight in the QuikClot group and one of eight in the gauze group ($p < 0.01$). Peak temperature at the tissue interface was increased ($p < 0.01$) with QuikClot (93.3 +/- 10.5[degrees]C), as compared with gauze (37.5 +/- 6.5[degrees]C).[43] In a swine model of complex groin injury with complete division of the femoral artery and vein and the use of 1% ZH decreased blood loss and reduced mortality to 0% ($p < 0.05$).[44] Other studies have caused concern when

application of the agent resulted in elevated tissue surface temperatures in excess of 95[degrees]C and internal tissue temperatures exceeding 50[degrees]C, 3 mm deep to the bleeding surface. Necrosis of fat and muscle were noted as well as full and partial thickness cutaneous burns.[45] The clinical data on this product are confined to case reports.[46]

COMPARISON STUDIES

Comparing the newer products to one and another is difficult ay best. There does seem to be some experimental evidence that suggests the dry fibrin sealant may be more efficacious in unbridled arterial hemorrhage. In a swine model of lethal extremity arterial injury when compared to QuikClot and a chitosan dressing, the fibrin sealant dressing reduced bleeding ($p < 0.05$) and prevented exsanguination in 10/15 (2/3) animals, and resulted in a significantly longer average survival time ($p < 0.0001$).[47] in a model of aortic hemorrhage in swine both chitosan dressing and fibrin sealant dressing stopped initial arterial bleeding that could not be controlled by a standard dressing, but fibrin sealant dressing secured hemostasis for up to 4 days, whereas the Chitosan dressing consistently failed within 2 hours after application.[48] Other studies of arterial hemorrhage have supported this observation[49] and it may hold true for large venous and liver injuries.[50] A summary of the newer hemostatic agents is in Table2

SYSTEMIC HEMOSTATIC AGENTS

The trauma surgeon must always be cognizant of the role of host systemic factors in hemostasis. Prevention of hypothermia and replacement of clotting factors lost to hemorrhage are rudimentary and should not be forgotten. An additional promising implement on the systemic side of hemostasis is the use of recombinant Factor VIIa.

Factor VIIa

This agent was originally designed and used for hemophiliacs resistant to Factor VIII administration. Its application to the trauma patient was supported by early laboratory work which demonstrated an effect in arresting non-surgical hemorrhage. Pilot studies in adult swine with induced liver injury showed enhanced in vitro coagulation (prothrombin time, activated partial thromboplastin time, thromboelastographic split-point and R times) with rFVIIa administration[51] and a 43% vs 0% mortality in controls vs factor VIIa treated animals and higher blood pressure in the treatment group.[52] Other liver injury models have supported the above observations and demonstrated an significant decrease in blood loss[53] and ability for Factor VIIa to improve the coagulation profile despite profound hypothermia.[54]

Several case-series demonstrated the promise of Factor VIIa in the trauma setting. Martinowitz and colleagues reported cessation of bleeding, shortening of prothrombin time from 24 seconds (range, 20-31.8 seconds) to 10.1 seconds (range, 8-12 seconds) ($p < 0.005$) and activated partial thromboplastin time 79 seconds (range, 46-110 seconds) to 41 seconds (range, 28-46 seconds) ($p < 0.05$) in 7 massively transfused trauma patients (median 40 units of PRBCs) that failed conventional methods to obtain hemostasis.[55] Two case-control studies confirmed improved coagulation profiles with The average pro-thrombin time being 19.6 vs 10.8 in the Factor VIIa group ($p<0.00001$)[56] and a decrease in transfusion requirements with the rFVIIa group required significantly fewer PRBC transfusions than the control group (18.3 +/- 7.5 vs. 22.0 +/- 9.7; $p = 0.036$), fewer platelet transfusions (1.4 +/- 1.2 vs. 2.3 +/- 2.1; $p = 0.01$), and less cryoprecipitate (0.59 +/- 0.54 vs. 1.5 +/- 1.8; $p = 0.006$).[57]

In a compilation of studies, a total of 117 patients were found in 8 case series and 24 case reports and rFVII was effective in restoring hemostasis in 99/117 (85%) patients with 76/99 (77%) surviving to hospital discharge. In trauma patients, hemostasis was achieved in 20/26 (77%) patients and 17/20 (85%) survived. There were 5 (4%) thromboembolic events observed in the 117 cases and much disparity was noted with the initial dose.[58] Finally, in a randomized prospective study of 301 (143 blunt trauma patients and 134 penetrating) patients, Boffard et al. demonstrated a significant reduction in transfusion (2.6 RBC units, ($p = 0.02$)) was noted in blunt trauma patients receiving rFVII and the need for massive transfusion (>20 units of RBCs) was reduced (14% vs. 33% of patients; $p = 0.03$). In penetrating trauma, similar analyses showed trends toward rFVIIa reducing RBC transfusion (estimated reduction of 1.0 RBC units, $p = 0.10$) and massive transfusion (7% vs. 19%; $p = 0.08$). Trends toward a reduction in mortality and critical complications were observed.[59]

The cost of NovoSeven is $1128.75 for a 1.2 mg vial, $2257.50 for a 2.4 mg vial and $4515 for a 4.8 mg vial. The doses used in trauma patients are generally 90–200 μg/kg, which amounts to about $10 000 for a 70 kg man.[60] As such, guidelines for its use should try to avoid futile administration. Early work in this area has demonstrated that Revised Trauma Score (RTS), lactate, and pre-administration prothrombin time (PT) each predicted lack of response ($p < 0.05$ for each). An RTS of less than 4.09 and a PT of greater than or equal to 17.6 seconds were associated with futile administration of FVIIa.[61]

Table 1. Available Hemostatics/Sealants.

Class	Name/Company	Mechanism	Source	Application
Gelatin Sponge	Gelfoam/Pharmacia Surgifoam/Ferrosan	Provides matrix for normal coagulation	Porcine	Applied as powder or in sheets
Oxidized regenerated Cellulose	Surgicel/Nu-knit/Ethicon BloodStop/Life Science Oxycel/Becton	Provides matrix for normal coagulation	Manufactured	Applied in sheets. Nu-knit more durable able to be sutured
Collagen	Avitene/Bard Actcel/Actsys Ultrafoam/Davol Instat/Ethicon	Provides matrix and activates platelets	Bovine	Apply in sheets. Also with applicator for solution
Thrombin	Thrombogen/ Gen Trac	Facilitates fibrinogen to fibrin	Bovine	Reconstitute/Spray or soak gauze
Gelatin/Thrombin	Floseal/Baxter	Gelatin matrix with thrombin converting fibrinogen to Fibrin	Bovine	Reconstitute thrombin/Mix with matrix in double syringe/Apply with one of the syringes
Fibrin Glue	Tisseel/Baxter	Includes Thrombin, Calcium, and fibrinogen which yields fibrin matrix	Human/Bovine	Reconstitute (Fibrinogen+Aprotinin) Reconstitute (Thrombin+Calcium) Duploject (3-5 minutes to harden)
Collagen/ Thrombin	Costasis/Cohesion	Collagen matrix with thrombin	Bovine	Harvest fibrinogen in OR from patient's blood/Mix collagen and thrombin/Mix and apply
Synthetics	Coseal/Baxter	2 Polyethylene glycols mixed	Manufactured	Mix two syringes/Spray or syringe

Table 2. Newer/Experimental Hemostatic's Characteristics

Name	Active Ingredients	Mechanism	FDA	Product	Cost	Company
Dry Fibrin Sealant Dressing	Fibrinogen, Thrombin, Factor XIII, Ca^{++}	Concentrated coagulation factors; Fibrin crosslinking	IND	4 X 4 Dressing	$500-1000/ Dressing	Tachocomb/Red Cross, Holland Labs, Rockville, MD
Rapid deployment Hemostat	Fully acetylated Poly-N-acetyl-glucosamine	Concentrates RBCs, Platelets, factors; Vasospasm	Yes	4 X 4 Dressing	$300/ Dressing	Marine Polymer Technologies, Danver MA
Chitosan Dressing	Deacetylated Poly-N-acetyl-glucosamine	Adherence/sealing, RBC and Platelet concentration	Yes	4 X 4 Dressing	$100/ Dressing	HemCon, Tigard OR
QuickClot	Granular Zeolite	Absorbs water, concentrates RBCs, Platelets; Exothermic	Yes	3.5 oz/100 gm Granules	$10/Packet	Z-Medica, Wallingford CT

REFERENCES

1. Simon D, Taylor MJ, Elrifai AM. Hypothermic blood substitution enables resuscitation after hemorrhagic shock and two hours of cardiac arrest. ASAIO J. 1995;41:297-298.
2. Gourley SR. Battlefield Medicine. Defence Security Rev. 1998
3. Sandia A, Moore FA, Moore FA. Epidemiology of trauma deaths: a reassessment. J Trauma 1995;38:185-193.
4. Champion HR, Bellamy RF, Roberts CP, Leppaniemi A. A profile of combat injury. J Trauma 2003;54:S13-19.
5. Light RE, Prentice HZ. Surgical investigation of a new absorbable sponge derived from gelatin for use in hemostasis. J Neurosurgery 1945;2(5):435-55.
6. Scarff JE, Stookey B, Garcia F. The use of dry oxidised cellulose as a primary hemostatic agent in neurosurgery. J Neurosurg. 1949;6:304-306.
7. Morgenstern L. Microcrystalline collagen used in experimental splenic injury. A new surface hemostatic agent. Arch Surg 1974;109(1):44-7.
8. Murphy DJ, Clough CA. A New Microcrystallline Collagen Hemostatic Agent. Surgical Neurology 1974;2:77-79.
9. Arand, AG, Sawaya, R; Intraoperative Use of Topical Hemostatic Agents in Neurosurgery. Neurosurgery Second Edition, Volume I, Chapter 62 , Wilkins, Robert H., Rengachary, Setti S., Editors. McGraw-Hill Health Professions Division, New York (1996).

10. Abbott WM, Austen WG; Microcrystalline Collagen as a Topical Hemostatic Agent for Vascular Surgery. Surgery 1974;75:925-933.

11. Rybock JD, Long DM; Use of Microfibrillar Collagen as a Topical Hemostatic Agent in Brain Tissue. J Neurosurgery 1977;46:501-508.

12. Cameron WJ; A New Topical Hemostatic Agent in Gynecologic Surgery. Obstetrics & Gynecology 1978;51:118-122.

13. Coln D, Horton J, Ogden ME, Buja LM. Evaluation of hemostatic agents in experimental splenic lacerations. Am J Surg 1983;145(2):256-9

14. Cohn SM, Cross JH, Ivy ME, Feinstein AJ, Samotowka MA. Fibrin Glue Terminates Massive Bleeding after Complex Hepatic Injury. J Trauma 1998;45(4):666-672.

15. Ochsner MG; Maniscalco-Theberge ME; Champion HR. Fibrin glue as a hemostatic agent in hepatic and splenic trauma. J Trauma 1990;30(7):884-7.

16. Kram HB, del Junco T, Clark SR, Ocampo HP, Shoemaker WC. Techniques of splenic preservation using fibrin glue. J Trauma 1990 30(1):97-101.

17. Chen RJ, Fang JF, Lin BC, Hsu YuB, Kao JL, Kao YC, Chen MF. Selective Application of Laparoscopy and Fibrin Glue in the Failure of Nonoperative Management of Blunt Hepatic Trauma. J Trauma 1998;44(4):691-695.

18. Schmal H, Geiger G. Laparoscopic Splenic Salvage in Delayed Rupture by Application of Fibrin Glue in a 10-Year-Old Boy. J Trauma 2005;58(3):628-630.

19. Rousou J., Levitsky S., Gonzales-Lavin L. Cosgrove D, Magilligan D, Weldon C.: Randomized Clinical Trial of Fibrin Sealant in Patients Undergoing Resternotomy or Reoperation after Cardiac Operations. A Multicenter Study. J. Thorac. Cardiovasc Surg., 1989; 97: 194-203.

20. Pursifull NF, Morris MS, Harris RA, Morey AF. Damage Control Management of Experimental Grade 5 Renal Injuries: Further Evaluation of FloSeal Gelatin Matrix. J Trauma 2006; 60(2):346-350.

21. Klemcke HG. Evaluation of FloSeal as a potential intracavitary hemostatic agent. J Trauma 2006;60(2):385-9.

22. Oz MC, Rondinone JF, Shargill NS. Floseal Matrix:. New Generation Topical Hemostatic Sealant. J Card Surg 2003;18(6):486-90.

23. Gall RM, Witterick IJ, Shargill NS, Hawke M. Control of bleeding in endoscopic sinus surgery: use of a novel gelatin-based hemostatic agent. J Otolaryngol. 2002;31(5):271-4.

24. A novel collagen - based composite offers effective hemostasis for multiple surgical indications: Results of a randomized controlled trial. CoStasis Multi-center Collaborative Writing Committee. Surgery. 2001 Apr;129(4):445-50.

25. Bochicchio G, Dunne J Bochicchio K, Scalea T. The Combination of Platelet-Enriched Autologous Plasma with Bovine Collagen and Thrombin Decreases the Need for Multiple Blood Transfusions in Trauma Patients with Retroperitoneal Bleeding. J Trauma 2004;56(1):76-79.

26. Glickman M, Gheissari A, Money S, Martin J, Ballard JL. A polymeric sealant inhibits anastomotic suture hole bleeding more rapidly than gelfoam/thrombin: results of a randomized controlled trial. Arch Surg 2002;137(3):326-31.

27. Hagberg RC, Safi HJ, Sabik J, Conte J, Block JE. Improved intraoperative management of anastomotic bleeding during aortic reconstruction: results of a randomized controlled trial. Am Surg. 2004 Apr;70(4):307-11.

28. Carrillo EH, Kozloff M, Saridakis A, Bragg S, Levy J. Thoracoscopic Application of a Topical Sealant for the Management of Persistent Posttraumatic Pneumothorax. J Trauma 2006;60(1)111-114.

29. Jackson MR, Friedman SA, Carter. Hemostatic efficacy of a fibrin sealant-based topical agent in a femoral artery injury model: a randomized, blinded, placebo-controlled study. J Vasc Surg 1997;26:274-280.

30. Holcomb JB, MacPhee M, Hetz S. Efficacy of a dry fibrin sealant dressing for hemorrhage control after ballistic injury. Arch Surg 1998;133:32-35.

31. Holcomb JB, Pusateri AE, Harris RA, Reid TJ, Beall LD, Hess JR, MacPhee MJ. Dry Fibrin Sealant Dressings Reduce Blood Loss, Resuscitation Volume, and Improve Survival in Hypothermic Coagulopathic Swine with Grade V Liver Injuries. J Trauma 1999;47(2):233-242.

32. Holcomb JB, Pusateri AE, Harris RA, Charles NC, Gomez RR, Cole JP, Beall LD, Bayer V, MacPhee MJ, Hess JR. Effect of Dry Fibrin Sealant Dressings versus Gauze Packing on Blood Loss in Grade V Liver Injuries in Resuscitated Swine. J Trauma 1999;46(1):49-57.

33. Jackson, MR, Taher MM, Burge JR, Krishnamurti C, Reid TJ, Alving BM. Hemostatic Efficacy of a Fibrin Sealant Dressing in an Animal Model of Kidney Injury. J Trauma 1998;45(4):662-665.

34. Vournakis J, Demcheva M., Whitson A., Guirca R., Pariser E. Isolation, Purification, and Characterization of Poly-N-Acetyl Glucosamine Use as a Hemostatic Agent. J Trauma 2004;57(1):S2-S6.

35. Thatte HS, Zagarins SK, Shukri F, Fischer TH. Mechanisms of Poly-N-Acetyl Glucosamine Polymer-Mediated Hemostasis: Platelet Interactions. J Trauma 2004;57(1):S13-S21.

36. Valeri CR, Srey R, Tilahun D, Ragno G. In Vitro Effects of Poly-N-Acetyl Glucosamine on the Activation of Platelets in Platelet-Rich Plasma with and without Red Blood Cells. J Trauma 2004;57(1):S22-S25.

37. Thatte HS, Zagarins SE, Amiji M, Khuri SF. Poly-N-Acetyl Glucosamine-Mediated Red Blood Cell Interactions. J Trauma 2004;57(1):S7-S12.

38. Connolly RJ. Application of the Poly-N-Acetyl Glucosamine-Derived Rapid Deployment Hemostat Trauma Dressing in Severe/Lethal Swine Hemorrhage Trauma Models. J Trauma 2004;57(1):S26-S28.

39. Jewelewicz DD, Cohn SM, Crookes BA, Proctor KG. Modified Rapid Deployment Hemostat Bandage Reduces Blood Loss and Mortality in Coagulopathic Pigs with Severe Liver Injury. J Trauma 2003;55(2):275-281.

40. Pusateri AE, McCarthy SJ, Gregory KW, Harris RA, Cardenas L, McManus AT, Goodwin CW. Effect of a Chitosan-Based Hemostatic Dressing on Blood Loss and Survival in a Model of Severe Venous Hemorrhage and Hepatic Injury in Swine. J Trauma 2003;54(1):177-182.

41. Wedmore I, McManus JG, Pusateri AE, Holcomb JB. A Special Report on the Chitosan-based Hemostatic Dressing: Experience in Current Combat Operations. J Trauma 2006;60(3):655-658.

42. King DR, Cohn SM, Proctor KG. Modified Rapid Deployment Hemostat Bandage Terminates Bleeding in Coagulopathic Patients with Severe Visceral Injuries. J Trauma 2004;57(4):756-759.

43. Pusateri AE, Delgado AV, Dick EJ, Martinez RS, Holcomb JB, Ryan KL. Application of a Granular Mineral-Based Hemostatic Agent (QuikClot) to Reduce Blood Loss After Grade V Liver Injury in Swine. J Trauma 2004;57(3):555-568.

44. Alam HB, Chen Z, Jaskille A, Querol RI, Luis C, Koustova E, Inocencio R, Conran R, Seufert, A Ariaban N, Toruno K, Rhee P. Application of a Zeolite Hemostatic Agent Achieves 100% Survival in a Lethal Model of Complex Groin Injury in Swine. J Trauma 2004;56(5):974-983.

45. Wright JK, Kalns J, Wolf EA, Traweek F, Schwarz S, Loeffler CA, Snyder W, Yantis LD, Eggers J. Thermal Injury Resulting from Application of a Granular Mineral Hemostatic Agent. J Trauma 2004;57(2):224-230.

46. Wright FL, Hong TH, Velmahos G, Thoman D, Demitriades D, Rhee PM. Intracorporeal Use of the Hemostatic Agent QuickClot in a Coagulopathic Patient with Combined Thoracoabdominal Penetrating Trauma. J Trauma 2004;56(1):205-208.

47. Acheson EM, Kheirabadi BS, Deguzman R, Dick EJ, Holcomb JB. Comparison of Hemorrhage Control Agents Applied to Lethal Extremity Arterial Hemorrhages in Swine. J Trauma 2005;59(4):865-875.

48. Kheirabadi BS, Acheson EM, Deguzman R, Sondeen JL, Ryan KL, Delgado A, Dick EJ, Holcomb JB. Hemostatic Efficacy of Two Advanced Dressings in an Aortic Hemorrhage Model in Swine. J Trauma 2005;59(1):25-35.

49. Sondeen JL, Pusateri AE, Coppes VG, Gaddy CE, Holcomb JB. Comparison of 10 Different Hemostatic Dressings in an Aortic Injury. J Trauma 2003;54(2):280-285.

50. Pusateri AE, Modrow HE, Harris RA, Holcomb JB, Hess JR, Mosebar RH, Reid TJ, Nelson JH, Goodwin CW, Fitzpatrick GM, McManus AT, Zolock DT, Sondeen JL, Cornum RL, Martinez RS. Advanced Hemostatic Dressing Development Program: Animal Model Selection Criteria and Results of a Study of Nine Hemostatic Dressings in a Model of Severe Large Venous Hemorrhage and Hepatic Injury in Swine. J Trauma 2003;55(3):518-526.

51. Klemcke HG, Delgado A, Holcomb JB, Ryan KL, Burke A, DeGuzman R, Scherer M, Cortez D, Uscilowicz J, Macaitis JM, Bliss J, Wojtaszczyk J, Christensen S, Currier H, Pusateri AE. Effect of Recombinant FVIIa in Hypothermic, Coagulopathic Pigs with Liver Injuries. J Trauma 2005;59(1):155-161.

52. Lynn M, Jerokhimov I, Jewelewicz D, Popkin C, Johnson E, Rashid Q, Brown M, Martinowitz U, Cohn SM. Early Use of Recombinant Factor VIIa Improves Mean Arterial Pressure and May Potentially Decrease Mortality in Experimental Hemorrhagic Shock: A Pilot Study. J Trauma 2002;52(4):703-707.

53. Schreiber MA, Holcomb JB, Hedner U, Brundage SI, Macaitis JM, Hoots K. The Effect of Recombinant Factor VIIa on Coagulopathic Pigs with Grade V Liver Injuries. J Trauma 2002;53(2):252-259.

54. Martinowitz U, Holcomb JB, Pusateri AE, Stein M, Onaca N, Freidman M, Macaitis JM, Castel D, Hedner U, Hess JR. Intravenous rFVIIa Administered for Hemorrhage Control in Hypothermic Coagulopathic Swine with Grade V Liver Injuries. J Trauma 2001;50(4):721-729.

55. Martinowitz U, Kenet G, Segal E, Luboshitz J, Lubetsky A, Ingerslev J, Lynn M. Recombinant Activated Factor VII for Adjunctive Hemorrhage Control in Trauma. J Trauma 2001;51(3):431-439.

56. Dutton RP, McCunn M, Hyder M, D'Angelo M, O'Connor J, Hess J, Scalea TM. Factor VIIa for Correction of Traumatic Coagulopathy. J Trauma 2004;57(4):709-719. October 2004.

57. Harrison TD, Laskosky J, Jazaeri O, Pasquale MD, Cipolle M. "Low-Dose" Recombinant Activated Factor VII Results in Less Blood and Blood Product Use in Traumatic Hemorrhage. J Trauma 2005;59(1):150-154.

58. Barletta JF, Ahrens CL, Tyburski JG, Wilson RF. A Review of Recombinant Factor VII for Refractory Bleeding in Nonhemophilic Trauma Patients. J Trauma 2005;58(3):646-651.

59. Boffard KD, Riou B, Warren B, Choong PT, Rizoli S, Rossaint R, Axelsen M, Kluger Y. Recombinant Factor VIIa as Adjunctive Therapy for Bleeding Control in Severely Injured Trauma Patients: Two Parallel Randomized, Placebo-Controlled, Double-Blind Clinical Trials. J Trauma 2005;59(1):8-18.

60. Rosenfeld JV, Kossmann T. New haemostatic agents, blood substitutes and the implications for military medicine ADF Health 2004; 5 (2): 59-63.

61. Stein DM, Dutton RP, O'Connor J, Alexander M, Scalea T. Determinants of Futility of Administration of Recombinant Factor VIIa in Trauma. J Trauma 2005;59(3):609-615.

Panamerican Journal of Trauma Vol. 14 No. 1 2007 Pages 00-00

REDEFINING THE ROLE OF HYPERTONIC SALINE IN RESUSCITATION

Steven B. Johnson, MD, FACS,[1] Matthew Lissauer, MD,[1]

The use of hypertonic saline has been advocated in the resuscitation of trauma patients. Over 300 papers have been published in the past 25 years evaluating the safety and efficacy of hypertonic saline in animal models and human studies. Despite the multitude of these investigations, controversy and questions remain about the role and value of hypertonic saline in trauma resuscitation. This review is intended to provide an overview of the literature and update of recent contributions that are redefining the role of hypertonic saline in trauma management.

TYPES OF HYPERTONIC SALINE

Hypertonic saline (HTS) refers to any saline solution that has an osmolality significantly greater than plasma. (table 1) The most commonly referred to hypertonic saline solutions are 3% and 7.5% normal saline although studies have utilized 7.2% concentrations. The important point to consider is not the concentration but the amount and rate of solute infused that determines the effect. Hypertonic saline solutions result in a transient increase in plasma osmolality. The magnitude of hyperosmolality is dependent on amount of solute infused, blood volume, and rate of infusion. A standard 4 ml/kg bolus of 7.5% HTS would be expected to increase serum osmolality transiently by 30-50 mOsm resulting in an increased interstitial to intravascular transcapillary force of 50-100 mmHg[1]. An increased intravascular to interstitial transcapillary force results in a net intravascular volume increase[2]. Frequently colloid containing solutions are added to increase the oncotic pressure and prolong the duration of hyperosmolar condition. Of the various colloid solutions combined with HTS, 6% Dextran 70 is most frequently used and has been found to be more effective than hetastarch[3]. The addition of Dextran 70 has been found to result in a 2 fold greater net blood volume expansion at 120 minutes compared to HTS alone[4].

[1] Division of Critical Care
R Adams Cowley Shock Trauma Center
University of Maryland School of Medicine
Baltimore, Maryland

PHYSIOLOGIC EFFECTS OF HYPERTONIC SALINE

Although commonly considered a physiologic fluid, hypertonic saline has additional pharmacologic considerations. In addition to increasing serum osmolality and net intravascular volume expansion, HTS has been shown to effect cardiac performance, pulmonary and systemic vascular resistance, microcirculatory flow, and immunologic function.

Blood Volume Expansion

As mentioned earlier, a significant increased transcapillary gradient is generated by HTS promoting net fluid movement from intracellular and interstitial spaces into the intravascular space. This appears independent of prior dehydration status as animals without hydration for up to 4 days demonstrate an effect[5]. Volume expansion is rapid, occurring shortly after initiation of HTS administration and reaching maximal shortly after completion of infusion. The maximal volume expansion is dependent on HTS volume (ml/kg) and rate administration. A maximal increase of approximately 3-4 ml per ml HTS infused has been reported which decreases, in the absence of Dextran, to less than 1ml per ml HTS infused by 120 minutes.

Cardiac Performance

Hypertonic saline has paradoxical effects on cardiac performance. Hyperosmolality is a positive inotrope and chronotrope while hypernatremia has been associated with negative inotropy. Overall contractility and cardiac performance are improved by HTS, mostly likely related to increased intracellular calcium concentrations[6].

Pulmonary and Systemic Vascular Resistance

Hypertonic saline results in both pulmonary and systemic vasodilatation that is independent of increased blood volume. This is a result of HTS direct effect on vascular smooth muscle relaxation and can be associated with higher

rates of infusion. Excessively rapid infusion rates can result in transient hypotension that can be avoided when 250 ml HTS boluses are infused over 15 – 20 minutes. An additional impact on vascular resistance may exist in shock states where endothelial swelling can reduce luminal diameter and microcirculatory flow. Hypertonic saline has been shown to decrease endothelial swelling in hemorrhagic shock, thereby improving microcirculatory flow and perfusion[7].

By increasing cardiac preload, and contractility, and decreasing vascular resistance (afterload), HTS improves cardiac output. These changes improve tissue perfusion and blood pressure in normovolemic and hypovolemic conditions.

Immunologic Function

Recently studies have demonstrated significant changes in immunologic function related to HTS[8, 9, 10]. These changes involve T cells, neutrophils, and macrophages and appear to be related to hyperosmolar induced cell membrane deformities. These deformities are related to duration and magnitude of the hyperosmolar condition. Intracellular signaling, especially via the inflammatory modulating p38 MAPK pathway, is altered by HTS. Neutrophils appear particularly responsive to HTS infusions. This appears to be both concentration and timing dependent. If HTS is administered prior to PMN stimulation, HTS attenuates PMN activation. If administered after PMN stimulation, HTS will enhance oxidative burst and degranulation. In addition, HTS results in decreased PMN chemotaxis, rolling, and adherence. Therefore HTS appears to have major effects on key aspects of PMN activation and tissue injury. HTS inhibits macrophage but not PMN phagocytosis. Interestingly the effect of HTS on T cells may be to reverse post-traumatic immunosuppression and restore normal T cell function[11].

CLINICAL UTILIZATIONS OF HYPERTONIC SALINE

Post-Traumatic Hemorrhagic Shock

It has long been noted that HTS will increase blood pressure following hemorrhage and that significantly smaller volumes than isotonic saline are effective. Animal studies have suggested that HTS 4 ml/kg is effective in restoring blood volume and reducing mortality from near uniformally fatal hemorrhage. This has been translated into human studies using fixed 250 ml HTS infusions. In a multicenter prospective randomized blinded study evaluating 7.5% HTS with 6% Dextran 70 250 ml versus isotonic saline 250 ml for post-traumatic hypotension, HTS significantly improved blood pressure but failed to improve outcome[12]. On post hoc analysis, HTS did reduce mortality in patients with penetrating injuries requiring surgery and was associated with reduced incidence of organ dysfunction. In a subsequent meta-analysis of 14 HTS studies in trauma, HTS without dextran failed to have any mortality advantage while HTS with dextran was associated with trend towards improved outcomes (OR 1.20, 95% C.I. 0.94 to 1.57, p=0.14)[13]. On post hoc analysis, hypotensive penetrating injuries requiring surgery appear to be the subset that is most likely to benefit from HTS with dextran therapy although there are no prospective, randomized, blinded studies supporting this conclusion.

A concern with any intervention following trauma that increases blood pressure without hemorrhage control is that increased bleeding and mortality will occur. Increased mortality has been demonstrated in hypotensive penetrating truncal injuries receiving aggressive isotonic fluid resuscitation prior to hemorrhage control[14]. In an animal model of uncontrolled hemorrhage, HTS 4 ml/kg was shown to promote bleeding and increase mortality. This adverse impact on survival can be reduced by lower volume (1 ml/kg)[15], slower rate (20 ml/kg/h vs. 240 ml/kg/hr)[16], or administration of HTS after hemorrhage control.

Traumatic Brain Injury

The role of HTS in the management of traumatic brain injury has been extensively evaluated and has a more established role compared to other post-traumatic HTS indications[17]. Hypertonic saline is an effective osmotherapeutic intervention for lowering ICP[18]. As opposed to mannitol, HTS can improve blood pressure and intravascular volume while reducing intracranial pressure and cerebral edema. This is especially important in patients with hypovolemic hypotension and intracranial hypertension. The primary indication for HTS in traumatic brain injury is for the management of increased ICP with or without evidence of herniation. Administration of prehospital HTS for severe traumatic brain injury (GCS < 9) in the presence of hypotension did not affect mortality or neurologic outcome[19]. This study was limited by the lack of early ICP monitoring or management. At the present time the R Adams Cowley Shock Trauma Center traumatic brain injury guideline recommendation for HTS is for the management of increased ICP in euvolemic or hypovolemic patients with serum sodium less than 155 mEq/l.

Post-Traumatic Immunomodulation

Hypertonic saline is receiving considerable interest as an immunomodulating agent following trauma. It acts to reduce the hyperinflammatory response and restore

immunologic function. By reducing neutrophil activation and tissue injury, HTS has been shown to reduce lung inflammation following hemorrhagic shock[20]. In a prospective randomized blinded study of blunt trauma patients with hypovolemic shock comparing 250 ml of 7.5% HTS with 6% Dextran 70 to 0.9% saline, significant reduction in TNF and CD14 levels with increased IL-10 and IL-1ra levels was noted in the HTS group[21]. These findings are consistent with HTS inhibiting pro-inflammatory cytokines but stimulating anti-inflammatory cytokines. These finding persisted up to 24 hours following HTS administration and were present for significantly longer than HTS induced hemodynamic changes.

Miscellaneous Post-traumatic Considerations

Sepsis is a frequent complication of seriously injured patients. Hypertonic saline has been shown to improve the hemodynamic status of patients with severe sepsis[22].

The abdominal compartment syndrome can occur even in the absence of intra-abdominal pathology or injury. In burn patients, hypertonic lactated saline resusciatation is associated with decreased incidence in abdominal compartment syndrome following major burn resuscitation[23].

POTENTIAL COMPLICATIONS OF HYPERTONIC SALINE

Hyperchloremic Metabolic Acidosis

Due to the large concentration of chloride ion present in HTS, patients receiving HTS can develop profound metabolic acidosis. This non-anion gap metabolic acidosis can cause a significant increase in the base deficit that can lead to confusion about perfusion status.

Hypernatremia

Due to the large concentration of sodium, marked hypernatremia can occur. Extreme caution should be exercised when serum sodium exceeds 160 mEq/l or rapid changes (>20 mEq/l/day) occur because of the risk of central and extrapontine myelinolysis[24].

SUMMARY

Hypertonic saline has multiple potential benefits compared to isotonic fluids in the resuscitation and management of trauma patients. The use of HTS for acute hypovolemia resuscitation has advantages related to small volume requirements, and immunomodulatory effects. The immunomodulatory effects are just recently being appreciated and may contribute significantly to the restitution of a normal immunologic status. Potential issues related to uncontrolled hemorrhage and timing of administration must be considered when assessing clinical efficacy. The use of HTS in traumatic brain injury is more established and accepted for ICP management. Hypertonic saline is becoming the osmotherapeutic agent of choice in specific situations associated with intracranial hypertension. It is generally considered safe when administered within the context of acceptable volumes[25].

REFERENCES

1. Kramer GS: Hypertonic Resuscitation: Physiologic Mechanisms and Recommendations for Trauma Care. J Trauma 54:S89-S99, 2003.
2. Tollofsrud S, Tonnessen T, Skraastad O, et al: Hypertonic saline and dextran in normovolemic and hypovolemic healthy volunteers increases interstitial and intravascular fluid volumes. Acta Anaesthesiolo Scand. 42:145-153, 1998.
3. Kramer GC, Walsh JC, Perron PR, et al: Comparison of hypertonic saline dextran versus hypertonic saline hetastarch for resuscitation of hypovolemia. Braz J Med Biol Res. 22:269-272, 1989.
4. Velasco IT, Rocha e Silva M, Oliveira MA, et al: Hypertonic and hyperoncotic resusciatiaon from severe hemorrhagic shock in dogs. Crit Care Med. 17:261-264, 1989.
5. Matthew CB, Durkot MJ, Patterson DR. Fluid shifts induced by the administration of 7.5% sodium chloride in 6% Dextran 70 in dehydrated swine. Circ Shock. 41:150-155, 1993.
6. Mouren S, Delayance S, Mion G, et al: Mechanisms of increased myocardial contractility with hypertonic saline solutions in isolated blood-perfused rabbit hearts. Anesth Analg. 81:771-7782, 1995.
7. Mazzoni MC, Borgstrom P, Intaglietta M, et al: Capillary narrowing in hemorrhagic shock is rectified by hyperosmotic saline-dextran reinfusion. Circ Shock. 31:407-418, 1990.
8. Kilson-Petersen, JA: Immune effect of hypertonic saline: fact or fiction? Acta Anesthesiol Scand. 48:667-678, 2004.
9. Rotstein OD: Novel strategies for immunomodulation after trauma: revisiting hypertonic saline as a resuscitation strategy for hemorrhagic shock. J Trauma. 49:580-583, 2000
10. Shukla A, Hashiguchi N, Chen Y, et al: Osmotic regulation of cell function and possible clinical applications. Shock 21:391-400, 2004.
11. Loomis WH, Namiki S, Hoyt DB, et al: Hypertonicity rescues T cells from suppression by trauma-induced anti-inflammatory mediators. Am J Physiol Cell Physiol. 281:C840-C848, 2001.

12. Mattox KL, Maningas PA, Moore EE, et al: Prehospital hypertonic saline/dextran infusion for post-traumatic hypotension. Ann Surg. 213:482-491, 1991.

13. Wade CE, Kramer GC, Grady JJ, et al: Efficacy of hypertonic 7.5% saline and 6%dextran 70 in treating trauma: A meta-analysis of controlled clinical studies. Surgery 122:609-616, 1997.

14. Bickell WH, Wall MJ, Pepe PE, et al: Immediate versus delayed fluid resuscitation for hypotensive penetrating torso injuries. N Engl J Med. 331:1105-1109, 1994.

15. Riddez L, Drobin D, Sjostrand F, et al: Lower dose of hypertonic saline dextran reduces the risk of lethal rebleeding in uncontrolled hemorrhage. Shock 17:377-382, 2002.

16. Bruttig SP, O'Benar JD, Wade CE, et al: Benefit of slow infusion of hypertonic saline/dextran in swine with uncontrolled aortotomy hemorrhage. Shock 24:92-96, 2005.

17. Doyle JA, Davis DP, Hoyt DB: The use of hypertonic saline in the treatment of traumatic brain injury. J Trauma 50:367-383, 2001.

18. Zornow MH: Hypertonic saline as a safe and efficacious treatment of intracranial hypertension. J Neurosurg Anaesthiol. 8:175-177, 1996.

19. Cooper DJ, Myles PS, McDermott FT, et al: Prehospital hypertonic saline resuscitation of patients with hypotension and severe traumatic brain injury. JAMA 291:1350-1357, 2004.

20. Rizoli SB, Kapus A, Fan J, et al: Immunomodulatory effects of hypertonic resuscitation on the development of lung inflammation following hemorrhagic shock. J Immunol. 161:6288-6296, 1998.

21. Rizoli SB, Rhind SG, Shek PN, et al: The immunomodulatory effects of hypertonic saline resuscitation in patients sustaining traumatic hemorrhagic shock. Ann Surg 243:47-57, 2006.

22. Oliveira RP, Weingartner R, Ribas EO, et al: Acute hemodynamic effects of a hypertonic saline/dextran solution in stable patients with severe sepsis. Int Care Med. 28:1574-1581, 2002.

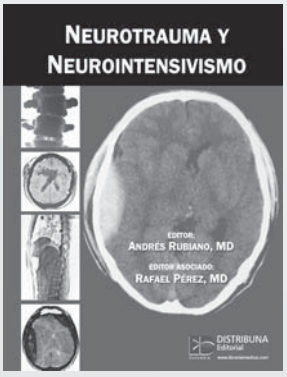
23. Oda J, Ueyama M, Yamashita K, et al: Hypertonic lactated saline resuscitation reduces the risk of abdominal compartment syndrome in severely burned patients. J Trauma. 60:64-71, 2006.

24. Kleinschmidt-Demasters BK, Rojiani AM, Filley CM: Central and Extrapontine Myelinolysis. J Neuropathol Exp Neurol. 65:1-11, 2006.

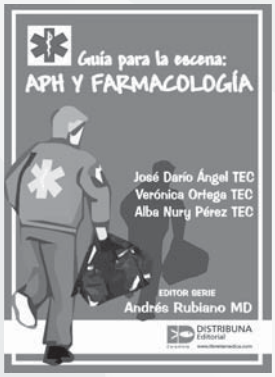
25. Dubick MA, Bruttig SP, Wade CE: Issues of concern regarding the use of hypertonic/hyperoncotic fluid resuscitation of hemorrhagic hypotension. Shock 25:321-328, 2006.

Títulos publicados en trauma

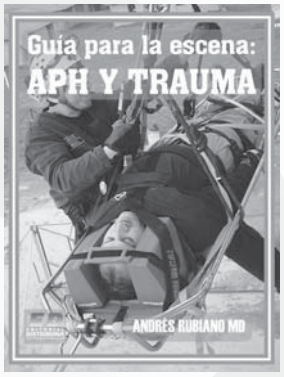
DISTRIBUNA Editorial
Colombia
www.libreriamedica.com



Neurotrauma y neurointensivismo
Autores:
Andrés Rubiano
Rafael Pérez
Edición: 2008

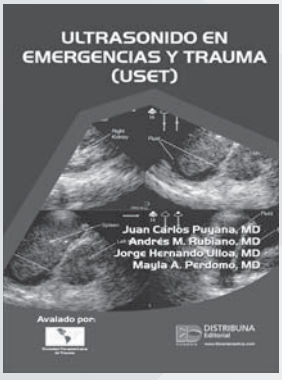


Guía para la escena. APH y farmacología
Autores:
Andrés Rubiano
José Darío Angel
Verónica Ortega
Alba Nury Pérez
Edición: 2008

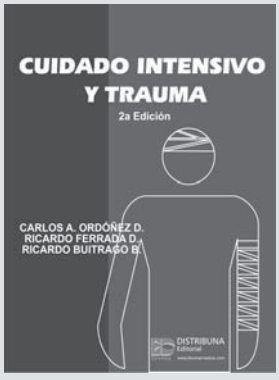


Guía para la escena. APH y trauma
Autor:
Andrés Rubiano
Edición: 2006

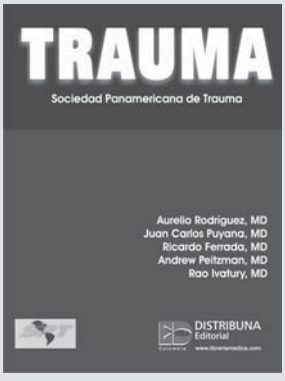
En preparación



Ultrasonido en emergencias y trauma (USET)
Autores:
Juan Carlos Puyana
Andrés Rubiano
Jorge Hernando Ulloa
Mayla Perdomo
Edición: 2008



Cuidado intensivo y trauma 2ª Edición
Autores:
Carlos Ordoñez
Ricardo Ferrada
Ricardo Buitrago



Trauma
Autores:
Soc. Panam. de Trauma
Aurelio Rodríguez
Juan Carlos Puyana
Ricardo Ferrada
Andrew Peitzman
Rao Ivatury

Adquieralos en:

Editorial Médica Distribuna · Bogotá: Autopista Norte Nº 123-93 ·
Tel: (1) 6202294 - 2158335 · Fax: (1) 2132379 · Apartado Aéreo: 265006
gerencia@libreriamedica.com · servicioalcliente@libreriamedica.com

www.libreriamedica.com

PANAMERICAN JOURNAL OF TRAUMA

CONTENT

CONTENIDO