

***Resuscitation Outcomes
Consortium:
Overview and Update***



***Resuscitation Science Symposium
Chicago 2006***

Resuscitation Outcomes Consortium: Overview

- **Mandate and Overview**
- **Partners**
- **Project Updates:**
 - ▶ **Epistry**
 - ▶ **HSD Trial**
 - ▶ **CPR Process**
 - ▶ **ROC PRIMED**
 - ▶ **Others**
- **The Future**

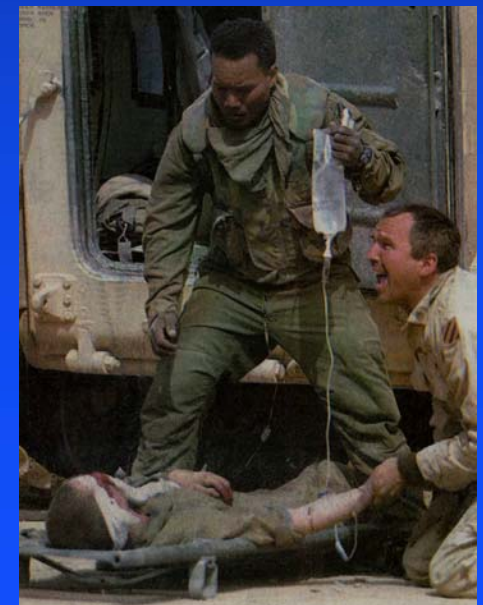


1. Mandate and Overview

- **Cardiac arrest and severe traumatic injury common problems in North America**
- **Mortality high:**
 - ▶ **90-95% for cardiac arrest**
 - ▶ **60% for severe trauma**
- **Much progress in managing acute MI and HF patients due to basic and clinical trial research funded by NHLBI and CIHR**
- **Historically only modest amount of funding for basic research on cardiac arrest and severe traumatic injury**

1. *Mandate and Overview*

- The ROC Consortium the first large-scale effort to conduct clinical trials in cardiac arrest and severe traumatic injury
- Focuses on very early delivery of interventions by Emergency Medical Services (EMS) teams in the field, when optimal potential for benefit



1. Mandate and Overview

In the first two years, ROC investigators have:

- Launched a large out-of-hospital cardiac arrest and trauma registry (**Epistry**)
- Started enrolling trauma patients in clinical trial of hypertonic IV fluid (**HSD Trial**)
- Rolled out a plan to monitor **CPR Process** in all out-of-hospital cardiac arrests
- Prepared to launch a factorial cardiac arrest trial (**ROC PRIMED**) that will evaluate:
 - ▶ ITD valve - small CPR adjunct
 - ▶ Strategy of delayed defibrillation

1. Mandate and Overview

- **Expected enrollment:**
 - ▶ 10,000 major trauma cases/year in Epistry
 - ▶ 17,500 cardiac arrests/year in Epistry
 - ▶ 5,848 patients in HSD Trial
 - ▶ 15,000 patients in ROC PRIMED Trial

Resuscitation Outcomes Consortium: Overview

- **Mandate and Overview**
- **Partners**
 - ▶ **Funding**
 - ▶ **Sites**
 - ▶ **Data Collection**
- **Project Updates:**
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RESUSCITATION OUTCOMES CONSORTIUM



National Heart, Lung and
Blood Institute



Canadian Institutes of
Health Research



U.S. Department of
Defense



National Defence
Canada



ROC – 10 Clinical Sites



2. Partners: Sites and PIs

- **Alabama Resuscitation Center:** Jeff Kerby, MD
- **Dallas, TX:** Ahamed Idris, MD
- **Iowa City, IA:** Richard Kerber, MD
- **Milwaukee, WI:** Tom Aufderheide, MD
- **Pittsburgh, PA:** Clif Calloway, MD
- **Portland, OR:** Jerris Hedges, MD
- **Ottawa, ON / Vancouver, BC:** Ian Stiell, MD
Jim Christenson, MD, Co-PI
- **San Diego, CA:** Dan Davis, MD
- **Seattle / King County, WA:** Peter Kudenchuk, MD
- **Toronto, ON:** Art Slutsky, MD
Laurie Morrison, MD and Paul Dorian, MD, Co-PIs

2. Partners: How Big are We?

- **268 EMS and fire agencies**
- **35,000 square miles**
- **24 million people**
- **3,500 EMS vehicles**
- **30,000 EMS personnel**
- **100 IRB's**
- **289 hospitals**

2. Partners: Data Coordinating Center (DCC)



U of Washington Clinical Trials Center:

- **Scott Emerson, MD, PhD - PI**
- **Graham Nichol, MD - Co-PI**
- **Eileen Bulger, MD - Co-PI**
- **Judy Powell, BSN - Project Director**
- **Art Kerr, MBA - Project Manager**
- **Berit Bardarson, RN - Consultant, Trauma**
- **Lois Von Ottingham, RN – Consultant, Cardiac**
- **Gena Sears, RN – Consultant, Epistery**

2. Partners: Study Chairs and NIH Project Officer



- **Myron L. Weisfeldt, MD - Study Chair**
 - Johns Hopkins Medical Institutions
 - Baltimore, MD

- **Joseph P. Ornato, MD - Co-Chair-Cardiac**
 - Virginia Commonwealth University Health
 - Richmond, VA

- **David Hoyt, MD - Co-Chair-Trauma**
 - University of California
 - San Diego, CA

- **George Sopko, MD – Project Officer**
 - NHLBI

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3. Project Updates: ROC Epistry



A prospective, population-based, epidemiologic **data registry** of patients seen by EMS providers:

- Life-threatening trauma
- Cardiac arrest

Complete this form:
 - any episode where EMS performed CPR (any compressions)
 - for any episode where the ITD was removed from its sealed packaged (even if not used).
 Main data source: PCR
 Other data resource: Dispatch

Patient Enrollment
Page 1 of 1

CARDIAC BLOOD FLOW TRIAL

Episode Information:

Date: / /
(mm/dd/yyyy)

Time call received at dispatch (24hr clock): : : (hh:mm:ss)
 Time is: estimated
 from dispatch

Incident Number(from EMS report):

Episode ID:

Always use this **Episode ID** when referring to this Episode

1) EMS response:

Arriving vehicle	Agency name	Agency #	Time of arrival 24 hours (hh:mm:ss)	ITD Opened		ITD Used		ITD #
				Yes	No	Yes	No*	
1st	<input type="text"/>	<input type="text"/>	<input type="text"/> : <input type="text"/> : <input type="text"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="text"/>
2nd	<input type="text"/>	<input type="text"/>	<input type="text"/> : <input type="text"/> : <input type="text"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="text"/>

3. Project Updates: ROC Epistry



Primary aims:

- **A comprehensive ongoing data infrastructure to facilitate ROC clinical trials**
- **Define the incidence and outcome of major trauma and out-of-hospital cardiac arrest**
- **Describe the relationships between resuscitation performance and EMS structure**
- **Evaluate relationships between outcome and patient, EMS, regional, and temporal factors**

3. Project Updates: **- ROC Epistry**



- Will become world's largest traumatic injury and cardiac resuscitation data sets:
 - ▶ 10,000/year major trauma
 - ▶ 17,500/year cardiac arrest
- Opportunity to develop and assure quality of data collection and communication systems among EMS systems, sites, and DCC
- Will facilitate subsequent clinical trials where timely acquisition of quality data is essential

3. Project Updates: ROC Epistry



- **Launched in December 2005**
- **EMS providers are becoming familiar with rigorous data gathering and quality control**
- **ROC DCC staff conducted field visits to all sites to review sample cases**
- **Employs both web-based or batch upload data entry**
- **Comprehensive operations manual with detailed definitions of all variables**

Epistry Update

October 23 2006



- **15,135 cases enrolled overall**
 - ▶ 58% of estimated annual enrollment
 - ▶ One site has just received IRB approval

- **3,825 trauma cases**
 - ▶ 59% completed
 - ▶ median time to completion 66 days

- **11,310 cardiac arrest cases**
 - ▶ 62% completed
 - ▶ median time to completion 55 days

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3. Project Updates: HSD Trial in Trauma



- **Hypertonic Saline Dextran Trial - hemorrhagic shock and severe traumatic brain injury (TBI)**
- **Data suggest potential benefits from pre-hospital resuscitation with hypertonic fluids**
- **Potential to improve outcome via:**
 - ▶ **Improved tissue perfusion**
 - ▶ **Reduced cerebral swelling in TBI**
 - ▶ **Modulation of inflammatory response**



3. Project Updates: HSD Trial in Trauma



The primary aims are to determine if pre-hospital hypertonic fluid resuscitation:

- Reduces **mortality** after hemorrhagic shock
- Improves **neurologic outcome** after severe TBI
- Reduces the rates of **inflammatory organ injury** (ARDS and MODS) after hemorrhagic shock
- Requires **dextran** as a component to impact outcome

3. Project Updates: HSD Trial in Trauma



- Randomized double-blind trials to evaluate same intervention in **2 patient cohorts**:
 - ▶ Severe TBI
 - ▶ Hemorrhagic shock
- **Compares** field IV administration of 250 ml:
 1. 7.5% saline alone
 2. 7.5% saline / 6% Dextran-70
 3. 0.9% saline
- **Primary outcomes**:
 - ▶ Neurologic outcome at 6 months - TBI cohort
 - ▶ 28-day survival - shock cohort

3. Project Updates: HSD Trial in Trauma



- **Sample size 5,848:**
 - ▶ 2,122 in TBI cohort
 - ▶ 3,726 in shock cohort
- **Timeline:**
 - ▶ 24 months for TBI
 - ▶ 42 months for shock
- **Importance:**
 - ▶ Definitively define the role of these therapies in the early resuscitation of trauma
 - ▶ Potential to change the standard for resuscitation that has not changed in 30 years

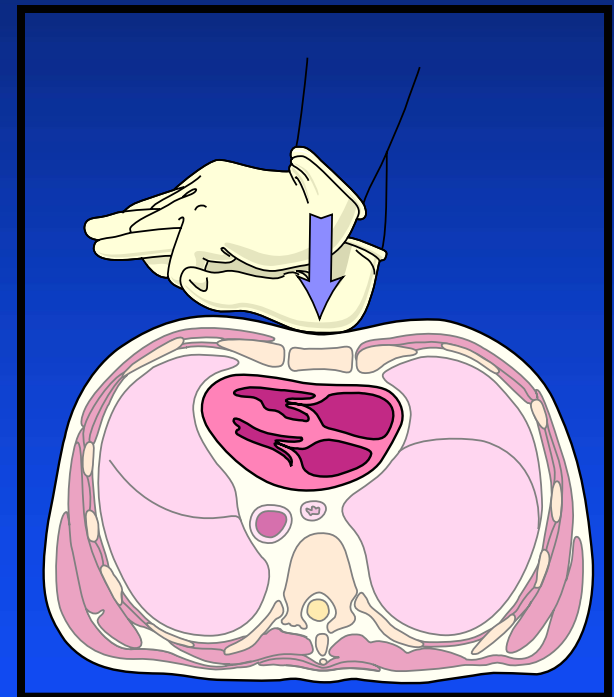
HSD Trial in Trauma Status – October 26th



- **1st site commenced enrollment June 2006**
- **5 of the 10 ROC sites had started**
- **All sites expected to have IRB approval by Jan 2007**
- **140 cases enrolled**

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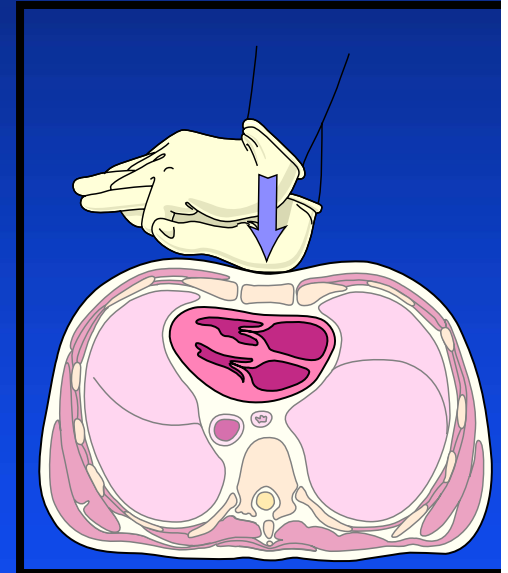


3. Project Updates: CPR Process Monitoring



Rationale:

- Recent studies have demonstrated that CPR is often not performed according to guidelines
- Greater rate of chest compressions associated with higher rate of ROSC
- Observation of deleterious hyperventilation in recent study confirms importance of monitoring CPR process



3. Project Updates: CPR Process Monitoring



Evolving Technologies offer the ability to monitor CPR process through AEDs:

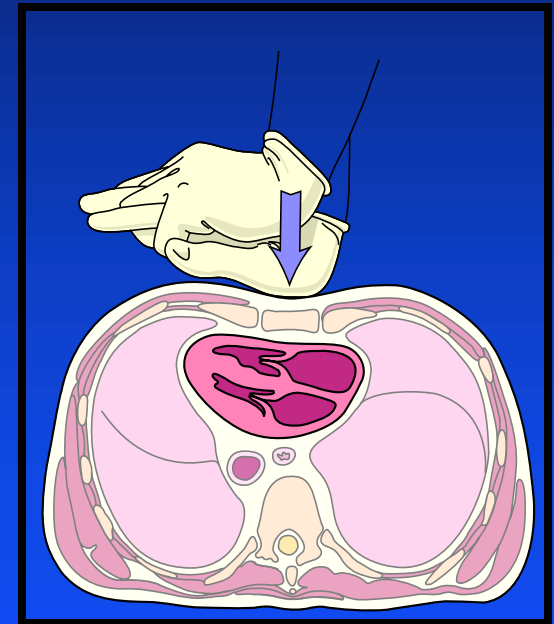
- **Chest impedance** to monitor chest compression rate and ventilation rate
- **Chest acceleration** to monitor chest compression rate, depth, release, and duty cycle
- **Audio recording** to monitor audible events

3. Project Updates: CPR Process Monitoring



Measurement of CPR Process:

- Rate of chest compressions
- Rate of ventilation
- CPR flow fraction
 - ▶ proportion of pulseless resuscitation time with chest compressions
- First five minutes



3. Project Updates: CPR Process Monitoring



Devices

■ ALS:

- ▶ LP-12 – Medtronic ERS Inc
- ▶ MRX – Philips Inc and Laerdal Inc
- ▶ M- and E-Series – Zoll Inc

■ BLS:

- ▶ LifePak 500 – Medtronic ERS Inc
- ▶ Heartstart & MRX – Philips Inc and Laerdal
- ▶ AED Pro BLS – Zoll Inc

3. Project Updates: CPR Process Monitoring



Performance Standards

Parameter	Target	Min-Max
Ventilation / min	10-12	6 - 16
Chest Compression / min	100	80 -120
CPR Flow Fraction	0.85	0.5 -

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 - ▶ Others



3. Project Updates: ROC PRIMED for Cardiac Arrest



A Factorial Design of “An Active Impedance Threshold Valve versus Sham Valve” and “Analyze Later versus Analyze Early”

- Incorporates 2 interventions to improve hemodynamics during CPR:
 1. Impedance threshold device (ITD)
 2. Chest compressions before rhythm analysis



3. Project Updates: ROC PRIMED for Cardiac Arrest



1. Impedance Threshold Device (ITD)

- Enhances venous return and cardiac output by increasing negative intrathoracic pressure during decompression phase of CPR
- Promising results in preliminary clinical trial [Aufderheide]
- Randomize real valve vs. sham valve
- **ResQPod** – Advanced Circulatory Systems



Impedance Threshold Device



**Endotracheal Tube
Set-up**

**Bag Valve Mask
Set-up**

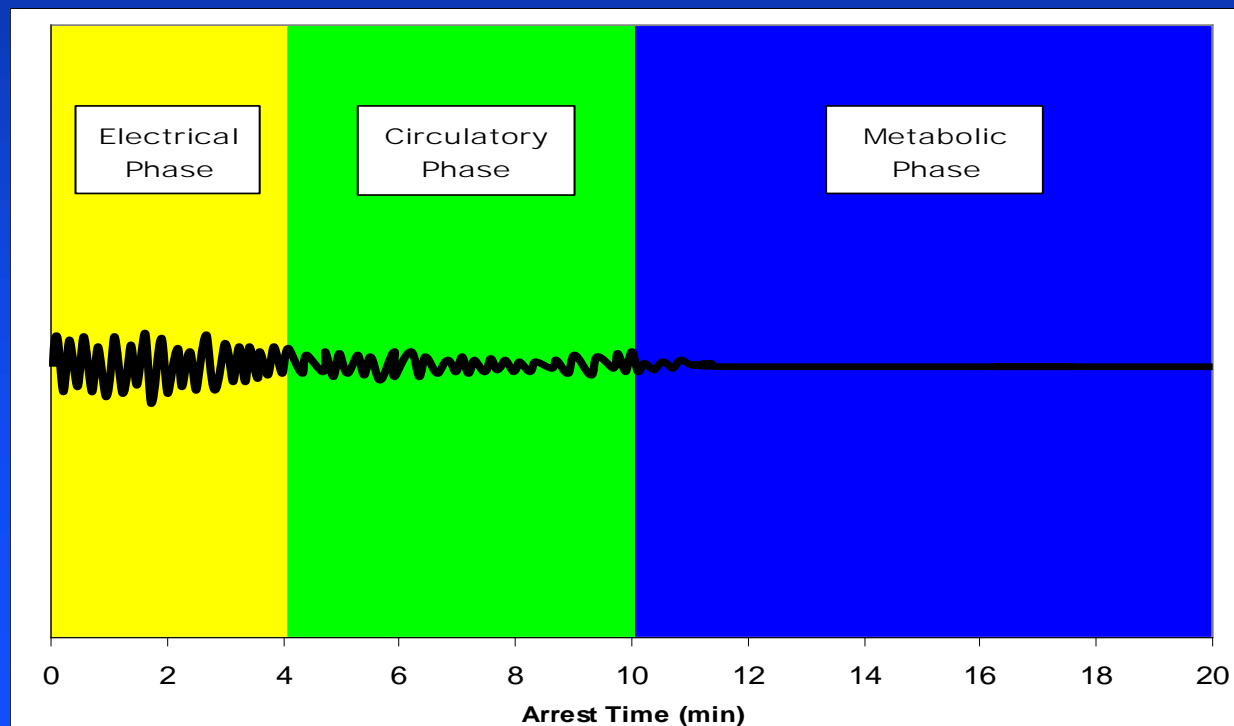


3. Project Updates: ROC PRIMED for Cardiac Arrest

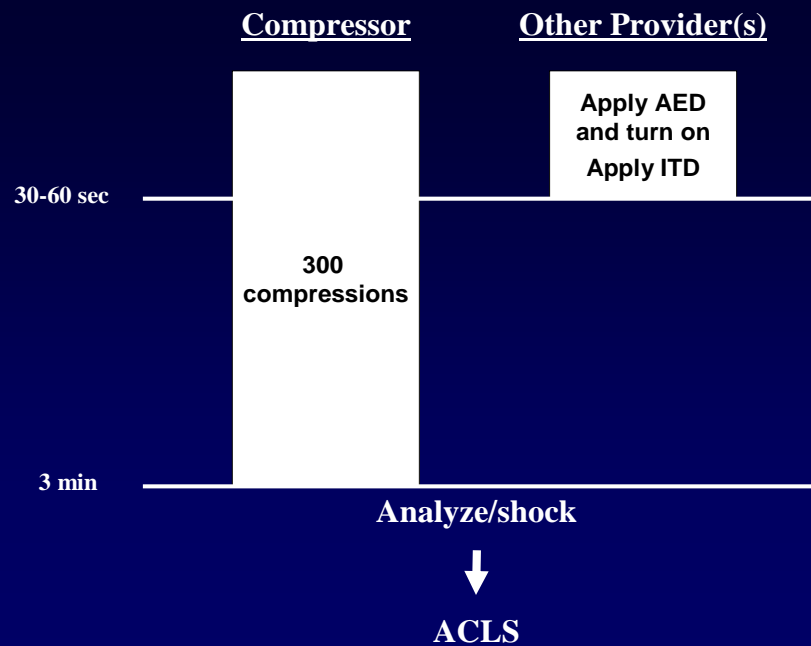


2. Analyze Later Vs. Analyze Early

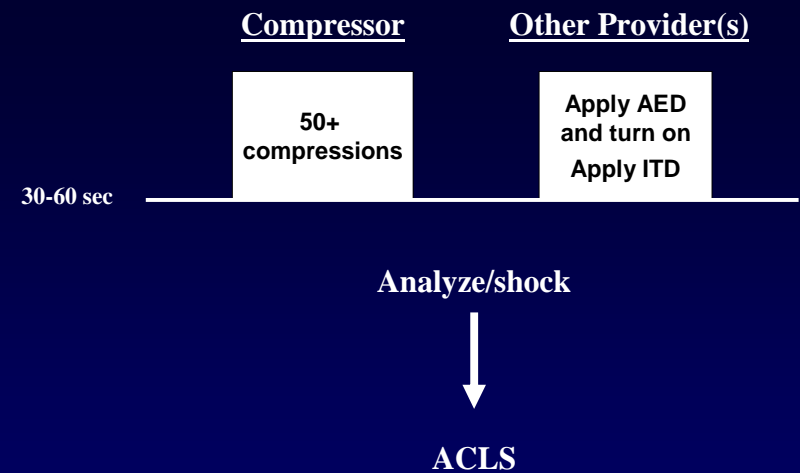
- Defibrillation may be more effective if CPR is given prior to shock for patients in circulatory phase of VF (prime the pump)



2. Analyse Later vs. Analyse Early Cluster Randomization; EMS & Fire



Analyse Later



Analyse Early

3. Project Updates: **ROC PRIMED for Cardiac Arrest**



- **Primary outcome:** survival to hospital discharge with Modified Rankin Score ≤ 3
- **Sample size and timeline:** 15,000 patients over 16-18 months
- **Approvals:** ROC Protocol Review Committee, ROC DSMB, Health Canada, and FDA
- **IRB reviews** underway
- Detailed **training package** and **data entry** screens developed
- Expected launch: **early 2007**

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3. Project Updates: Other Projects



Ancillary studies will test physiological or mechanistic hypotheses or refine methodology:

- 1. In HSD Trial, will evaluate the effect of interventions on inflammatory response**
- 2. In ROC PRIMED, will test real-time auditory and visual feedback on the performance of CPR**
- 3. In ROC PRIMED, will evaluate the optimal assessment tool for functional status of survivors of cardiac arrest**

3. Project Updates: Other Projects



4. In Epistry, expanded data collection to refine **triage criteria of patients** to trauma centers
5. In Epistry, determine associations between **ventilation rate** and outcome in cardiac arrest and trauma
6. In HSD and ROC PRIMED, will collect data on time and effort required to perform **community consultation and notification** required to obtain waiver/exception from informed consent for emergency research

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4. Future Projects

In Cardiac Arrest:

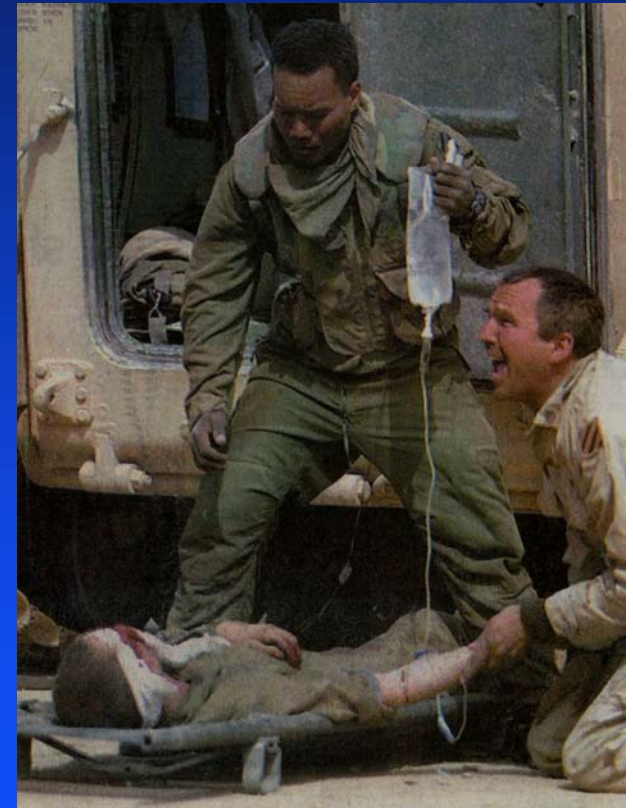
- The value of **ECG waveform analysis** to indicate shock or no shock
- The value of immediate **CPR performance feedback**
- Early **hypothermia**
- A number of **pharmacologic agents** including beta blockers, erythropoietin, and female hormones



4. Future Projects

In Traumatic Injury:

- The value of **controlled ventilation**
- Female **sex hormones**
- **Other solutions** as suggested by the current HSD Trial
- **Anti-oxidant agents** with a broad safety profile





Resuscitation Outcomes Consortium



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