Trauma, Transfusion & Tribulation

Andrew Clark, BSc, MB, ChB, FRCP(C)
Associate Professor Anaesthesia, Dalhousie University
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Objectives

Discuss:

- The impact of trauma
- The effects of trauma on body fluid
- Traditional & novel resuscitative strategies
- Which fluids to transfuse
The Impact of Trauma

- Early trauma death most often due to:
  - Head injury 40%
  - Hemorrhage 30%
- Mortality from massive hemorrhage 50%
- 50% of trauma deaths occur pre-hospital
- Mortality of shock is 50-75%
The Impact of Trauma

- Kirkpatrick Can J Surg 2008;51:57
- “Once airway & breathing are secured, the first priority in trauma care is definitive control of bleeding, much more important than fluid resuscitation”
- “Hypotensive patients with abdominal injury needing laparotomy have an increase in mortality of 1% for every 3 minutes spent in resuscitation”
The Usefulness of War

- **WWII** – Crystalloid solutions thought to be bad
- **Korean War** - Crystalloid solutions beginning to be used
- **Vietnam War** - $\uparrow$ use of crystalloids directly $\downarrow$ renal failure in wounded troops
- **Desert Storm** – Balanced fluids better resuscitated gunshot trauma
- **Iraq/Afghanistan** – Massive Transfusion Protocols (MTPs)
‘Da Shock Traumatique
Dans les Blessures de Guerre’
(Bull.Med.Soc.Chir; 1918; 44:205)

<table>
<thead>
<tr>
<th>Time From Injury</th>
<th>Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 hour</td>
<td>10%</td>
</tr>
<tr>
<td>4 hours</td>
<td>33%</td>
</tr>
<tr>
<td>8 hours</td>
<td>75%</td>
</tr>
</tbody>
</table>
History of Resuscitation

- Coined the phrase ‘damage control’
- 2011: Hydroxyethyl Starch (HES) in low-volume is now the standard of care in U.S. battlefield resuscitation (average transport time to trauma centre 17 minutes)
History of Resuscitation

- Lessons learned from combat:
  - 20% of combat casualties die on battlefield
  - Major cause = hemorrhage
  - Thus, major therapy = fluid.

WRONG!
Novel Perspectives

- 70% of blood volume is in venous circuit
- Catecholamines increase blood pressure
- Catecholamines *may* not increase tissue perfusion
- Shock induces hormone/cytokine release that alters *both* macro and microcirculation
- Cells deprived of O2 anaerobically produce lactate
Accurate clinical signs are crucial for early diagnosis but very difficult to obtain.

4 classes of hypovolemic shock:

- <15% loss = normal vital signs
- 15-30% loss = tachycardia, ↓ pulse pressure
- 30-40% loss = ↓ BP, ↓ LOC, cool
- >50% = unrousable
Novel Perspectives

- ‘Normal’ BP does NOT mean normal organ perfusion
- BP is almost useless as an early indicator or a monitoring tool of shock state
- ‘Modern’ ATLS recommendation – 20-30ml/kg Ringer’s Lactate in a 3:1 ratio of estimated blood loss
- The tide is turning....dry is good
Novel Perspectives

- Shock = coagulopathy
- Shock = acidosis
- Shock = hypothermia

The LETHAL TRIAD
Novel Perspectives

- The problem with research in trauma:
  - Randomized - NOT
  - Blinded – NOT
  - Controlled – NOT
  - Human - NOT
Yorkshire swine simulated polytrauma to 50% hemorrhage

Divided into 4 groups:

<table>
<thead>
<tr>
<th>Fluid</th>
<th>Survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>6% Hetastarch</td>
<td>25%</td>
</tr>
<tr>
<td>Fresh whole blood</td>
<td>100%</td>
</tr>
<tr>
<td>‘Spray dried’ plasma</td>
<td>83%</td>
</tr>
<tr>
<td>Valproate</td>
<td>50%</td>
</tr>
</tbody>
</table>
Colloids Make You Bleed??

NO! Trauma Makes You Bleed!
Volume Status Assessment in Trauma

Clarke J Trauma 2002;52:420

“During the first 90 minutes in ER, in hypotensive patients with abdominal injury needing laparotomy, every three minutes spend in resuscitation increases mortality by 1%.”

- Trauma is a common problem
- Frequently lethal
- Time is of the essence
### Volume Status Assessment in Trauma

**ITACCS Seminar 2003 (Am Coll Surg)**

4 Classes of hemorrhage:

<table>
<thead>
<tr>
<th>Class</th>
<th>I</th>
<th>II</th>
<th>III</th>
<th>IV</th>
</tr>
</thead>
<tbody>
<tr>
<td>% blood volume loss</td>
<td>15%</td>
<td>15-30%</td>
<td>30-40%</td>
<td>&gt;40%</td>
</tr>
<tr>
<td>Pulse Rate</td>
<td>&lt;100</td>
<td>&gt;100</td>
<td>&gt;120</td>
<td>&gt;140</td>
</tr>
<tr>
<td>Blood Pressure</td>
<td>Normal</td>
<td>Normal</td>
<td>Decreased</td>
<td>Decreased</td>
</tr>
<tr>
<td>Pulse Pressure</td>
<td>Normal</td>
<td>Decreased</td>
<td>Decreased</td>
<td>Decreased</td>
</tr>
<tr>
<td>Urine Output</td>
<td>&gt;30</td>
<td>20-30</td>
<td>5-15</td>
<td>0</td>
</tr>
<tr>
<td>Mental Status</td>
<td>Slightly anxious</td>
<td>Anxious</td>
<td>Confused</td>
<td>Lethargic</td>
</tr>
</tbody>
</table>
Volume Status Assessment in Trauma
Predictors of Massive Bleeding

*Nunez J Trauma* 2009;66:2:346

- 4 factors
  - Penetrating mechanism
  - Trauma sonography
  - Blood pressure <90
  - Pulse >120

- Score >2 is 75% sensitive and 86% specific
Volume Status Assessment in Trauma
Predictors of Massive Bleeding

*McLaughlin J Trauma 2008;64 (s)57*

- Retrospective analysis 3442 patients
- Four factors:
  - Pulse >105
  - BP <110
  - pH <7.25
  - HCT <32
- 66% of these patients will require massive transfusion
Assessment of Volume Status in Trauma

- Vital signs poor predictors of extent of bleeding
- SV02 is better
- Base deficit correlates with:
  - Transfusion requirements
  - ICU Length of Stay
  - Mortality
- Ability to normalize lactate within 24 hours predicts survival
# Common Injuries & Associated Hemorrhage

<table>
<thead>
<tr>
<th>Injury</th>
<th>Volume (mls)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unilateral hemothorax</td>
<td>3000</td>
</tr>
<tr>
<td>Hemoperitoneum/distension</td>
<td>2000-5000</td>
</tr>
<tr>
<td>Pelvic fracture</td>
<td>2000</td>
</tr>
<tr>
<td>Femur fracture</td>
<td>1200</td>
</tr>
<tr>
<td>Tibia/fibula fracture</td>
<td>600</td>
</tr>
<tr>
<td>5cm diameter soft tissue defect</td>
<td>500</td>
</tr>
</tbody>
</table>
Traditional Approach to Trauma Resuscitation

(As taught to me 1984-1988 Anesthesia Residency)

1. Aggressive crystalloid resuscitation with 20ml/kg NS (repeated PRN)
2. Delay surgery until pulse and BP normal
3. Avoid plasma re ARDS
4. Avoid platelets until 2 blood volumes of PRBCs given
5. Avoid colloid – expensive & coagulopathic
6. Delay surgery until patient normothermic/normal pH
Traditional Approach to Trauma Resuscitation

(As taught to me 1984-1988 Anesthesia Residency)

1. Wrong
2. Wrong
3. Wrong
4. Wrong
5. Wrong
6. Wrong

Rong, Dammit!
Because

1. Trauma patients bleed to death more quickly than you can transfuse them

2. Trauma causing **shock** causes a **coagulopathy**

3. Non-blood fluid resuscitation worsens the coagulopathy by:
   - Diluting factors & platelets
   - Washing off tenuous plugs
   - Worsening hypothermia
   - Worsening acidosis
Acute Coagulopathy of Trauma: A New Disease Entity

Coagulopathy is present on admission in 25% of patients

500% increase in mortality

Only patients in shock are coagulopathic on admission
Acute Coagulopathy of Trauma: A New Disease Entity

- **Mechanisms**
  - **Primary**
  - Shock causes increase in thrombomodulin
  - Thrombomodulin has 2 effects:
    - Binds thrombin, preventing it from cleaving fibrinogen
    - TM-T Complex activates thrombin-activatable fibrinolysis inhibitor (TAFI) via activated protein C
  - Activated protein C is a de-inhibitor of fibrinolysis
Brohi, J. Trauma, 2008

Platelet → THROMBIN

Shock → Thrombomodulin

VIIa IXa Xa VIII V 

Fibrinogen → Fibrin 

FDPs → Plasmin 

Protein C 

TM/T Complex 

APC → TAFI 

Plasminogen
Acute Coagulopathy of Trauma: A New Disease Entity

- Secondary
- Acidosis
- Hypothermia
- Dilution
Effects of Acidosis

- Coagulation proteases optimum pH 8
- Xa/Va complex activity reduced
  - 50% at pH 7.20
  - 70% at pH 7.0
  - 90% at pH 6.8
- Base deficit predicts shock; shock predicts death
- Calcium binding to factors ↓ with acidosis
- Base deficit < 6 = 2% of patients with ↑ PTT and INR
- Base deficit >6 = 20% of patients with ↑ PTT/INR
Effects of Hypothermia

- 9% incidence in trauma
- Serine proteases activity ↓ 5% per 1 degree C
- Platelet activation ↓ 10% per degree C
- Platelet TXA2 release ↓ 15% per degree C
- Clinical bleeding obvious < 34 degrees C
Effects of Hypothermia

Mortality 7% if temperature > 34
Mortality 40% if temperature < 34
Mortality 70% if temperature < 33
Mortality 99% if temperature < 32
Effects of Dilution of Clotting Factors

- Coagulopathy present in:
  - 50% of patients resuscitated with > 3L of non-blood fluid
  - 10% of patients resuscitated with 500ml of non-blood fluid
- Unusual to give warmed fluids in the past
- Amount of fibrinogen in fluid is critical
# Fibrinogen in Fluids

<table>
<thead>
<tr>
<th>Fluid Type</th>
<th>Fibrinogen Content</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 unit fresh whole blood</td>
<td>1000 mg</td>
</tr>
<tr>
<td>1 bag (10u) cryoprecipitate</td>
<td>2500 mg</td>
</tr>
<tr>
<td>1 dose (6u) platelets</td>
<td>480 mg</td>
</tr>
<tr>
<td>1 unit FFP (250ml)</td>
<td>400 mg</td>
</tr>
<tr>
<td>1 unit PRBCs</td>
<td>&lt;100 mg</td>
</tr>
<tr>
<td>Colloid/crystalloid</td>
<td>Nada</td>
</tr>
</tbody>
</table>
Effect of Hematocrit

- Platelet adhesion occurs around margins of vessels.
- Platelet adhesion 5X better at HCT 40 than HCT 10.
- Goal HCT >30 (i.e. HGB 100).
- *NB* – red cells donate ADP to help platelet activation.
Shock makes thrombomodulin
Thrombomodulin/thrombin complex activates Protein C
APC De-inhibits fibrinolysis

Thus shock unleashes fibrinolysis
New Approaches to Shock Resuscitation
Damage Control Resuscitation

McCunn, University of Pennsylvania, 2009

- “Hemostatic” resuscitation
- 1:1:1 red cells, plasma, platelets

Consider using plasma as primary resuscitative fluid

- Borgman J Trauma 2007;63:801
- Spinella Crit Care Med 2007;35:2576
- Stinger J Trauma 2008;64:(s)79
Hemostatic Resuscitation

- Studies show from both military and civilian populations that patients who are resuscitated with high ratios of fibrinogen to red blood cells do much better

- Mortality in low fibrinogen ratio group: 52-60%
- Mortality in high fibrinogen ratio group: 24-30%

- Optimum BP to perfuse the patient but not wash off plugs:
  - MAP 65
  - Systolic 90
Survival Associations

- Increased survival associated with:
  - Temperature $> 34$ degrees
  - Blood pressure $> 65$ mean
  - Hematocrit $> 30$
  - Base deficit $< 6$
Survival Associations

- The only independent predictor of mortality is low fibrinogen ratio

- High fibrinogen ratio \(\uparrow\) survival and:
  - \(\downarrow\) Blood loss
  - \(\downarrow\) Blood product usage
  - \(\downarrow\) ICU LOS
Cytokines and Trauma

- Trauma is a potent cause of elevated cytokines
- Cytokine elevation beyond 3 days is predictive of MOF, ARDS and death
- Therefore, potentially useful indicators of the degree of cellular damage and success of resuscitation

Injury 2007: 38(12); 1336-1341
Trauma, Cytokines & Coagulopathy

- K Mattox (Baylor College):
  - 750 ml of saline will promote cytokine release and thrombomodulin
- J. Trauma 2008: 64(5);1211-1217

Brohi et al:

- Thrombomodulin mechanism of acute coagulopathy of trauma
- Tissue injury releases thrombin which binds to thrombomodulin
- Bound thrombin cannot catalyse fibrinogen to fibrin
Trauma, Cytokines & Coagulopathy

- Thrombin/thrombomodulin complex inhibits 2 inhibitors of fibrinolysis:
  - Thrombin activatable fibrinolysis inhibitor (TAFI)
  - Plasminogen Activator Inhibitor (PAI)

Trauma = Coagulopathy!!
Resuscitation Strategies

- Krausz: J Trauma 2003:54(5);539-42
  In the Israeli Army, the issue of ‘scoop and run’ or ‘stay and stabilize’ HAS BEEN RESOLVED
  - If evacuation time < 1 hour, then GO
  - If evacuation time > 1 hour then start IV and give colloid, then go

- “In uncontrolled hemorrhagic shock, where bleeding has stopped because of hypotension, vasoconstriction and thrombus formation, aggressive fluid resuscitation with Ringer’s Lactate to achieve normal hemodynamics is PROHIBITED”
Resuscitation Strategies

- Brisebois; J Trauma 2003: 54(5);536
- In the Canadian Army, ATLS guidelines (20 ml/kg Ringer’s Lactate) are followed but emphasis is placed on bleeding control and rapid evacuation
Resuscitation Strategies

- Vandromme: J Trauma 2011: 70:384-90
- Massive transfusion risk identified by PREHOSPITAL SHOCK INDEX (SI):
  - SI = HR/SBP
  - Normal SI = < 0.7
- 8011 patients studied, 276 massively transfused
## Resuscitation Strategies

<table>
<thead>
<tr>
<th>Shock Index (SI)</th>
<th>Risk of Mortality (field)</th>
<th>Risk of Mortality (ER)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 0.9</td>
<td>1.5</td>
<td>2.5</td>
</tr>
<tr>
<td>&gt; 1.1</td>
<td>5</td>
<td>8</td>
</tr>
<tr>
<td>&gt; 1.3</td>
<td>8</td>
<td>20</td>
</tr>
</tbody>
</table>
Resuscitation Strategies
Other methods to predict massive transfusion risk:

- **ABC** (assessment of blood consumption)
  - FAST ultrasound
  - BP <90
  - P >120
  - Penetrating Mechanism

- **TRASH** (trauma associated severe hemorrhage)
  - ABC plus HGB <100 and base excess

- **McLaughlin Score**:
  - BP < 110
  - Pulse >105
  - pH < 7.25
  - HCT < 32
Resuscitation Strategies

- Morrison: J Trauma 2011:70(3); 652-663
- The first randomized control trial of hypotensive resuscitation strategy
Resuscitation Strategies
Morrison

- **Method:**
- 90 patients studied
- No fluid bolus given in the field (as is standard in Texas)
- 2 groups were resuscitated to a goal of: 65 mmHg mean arterial pressure vs 50 mmHg pressure
- Baseline demographics, transport time and injury severity were comparable between the two groups
Results:

- No differences found in the amount of fluids given, measured blood loss or anesthetic and pressor drugs used
- The low mean arterial pressure group received less blood products
- The high mean arterial pressure group had greater mortality of which virtually all was due to coagulopathy
Resuscitation Strategies

Nirula (J Trauma, 2010; 69:595-601)

- “Scoop & Run to the Trauma Centre or Stay & Play at the Local Hospital: Hospital transfer Effects on Mortality”

- 1112 patients – 318 initially triaged to non-trauma centre
## Resuscitation Strategies

**Nirula** *(J Trauma, 2010; 69:595-601)*

<table>
<thead>
<tr>
<th></th>
<th>Non-Trauma Centre</th>
<th>Trauma Centre</th>
</tr>
</thead>
<tbody>
<tr>
<td>Crystalloid</td>
<td>4200</td>
<td>400</td>
</tr>
<tr>
<td>Risk of Blood</td>
<td>12 (60%)</td>
<td>1 (5%)</td>
</tr>
<tr>
<td>Transfusion</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mortality Risk</td>
<td>3.8</td>
<td>1.0</td>
</tr>
</tbody>
</table>
Resuscitation Strategies

Nirula (J Trauma, 2010; 69:595-601)

- The group initially triaged to a trauma centre had worse hemodynamics and base deficit but normalized much faster than patients initially triaged elsewhere.

- 2 confirmatory studies:
  - Sampalis (Quebec) – J Trauma (1999) marked ↓ in mortality when trauma care regionalized.
Resuscitation Strategies

Ley (J Trauma, 2011; 20:398-400)

- “Emergency Department Crystalloid Resuscitation of 1.5 Litres or More is Associated With Increased Mortality…”
- 3137 patients – Cedars Sinai Los Angeles from 2000-2008, retrospective review
- Mathematical modeling of the ideal fluid bolus (logistic regression)
# Resuscitation Strategies

Ley (J Trauma, 2011; 20:398-400)

<table>
<thead>
<tr>
<th>Fluid Volume</th>
<th>Odds Ratio</th>
<th>Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;1500 in Elderly</td>
<td>2.89</td>
<td></td>
</tr>
<tr>
<td>&gt;1500 in Young</td>
<td>2.09</td>
<td></td>
</tr>
<tr>
<td>&gt;3000 in Elderly</td>
<td>8.6</td>
<td></td>
</tr>
<tr>
<td>&gt;3000 in Young</td>
<td>2.7</td>
<td></td>
</tr>
</tbody>
</table>
Resuscitation Strategies
Ley (J Trauma, 2011; 20:398-400)

- Patients receiving > 1500 mls fluid also had ↑ risk of:
  - Exsanguination
  - Coagulopathy
  - Poor indices of organ perfusion (lactate)

- Predictors of mortality included:
  - Increased INR
  - Decreased HGB
  - Increased lactate
  - But NOT pulse, blood pressure or shock index

- 80% of patients with normal BP still had ↑ lactate
What Should Be End-Points of Resuscitation?
Permissive hypotension

Limited fluid resuscitation

Many large animal model studies have been performed to discover “when does the clot pop off”?

= 80 mmHg systolic BP

“Well-informed resuscitationists will DISALLOW blood pressure cuffs as a measure of success of fluid therapy
Kenneth Mattox, Baylor College
Houston, Texas (2005)

DO THEY HAVE A RADIAL PULSE?
Thromboelastography studies show that trauma patients who are hypotensive (therefore coagulopathic) recover much faster if they are given little or no fluid than if they are aggressively resuscitated with crystalloid.

- “25 ml colloid boluses Q5 Min until return of radial pulse” THEN NO MORE FLUID UNTIL BLEEDING CONTROLLED
Hence

Damage Control

Resuscitation
Damage Control Resuscitation

3 Principles:

- Permissive Hypotension
- Aggressive control of acidosis and hypothermia
- Early blood product use
Permissive Hypotension

- Dr. Beecher, 1942:
  - “Systolic blood pressure of 70 to 80 is adequate. It is wasteful of time and blood products to attempt to get blood pressure up to normal levels”

- Clark ‘the fluid guy’ says stop killing rats, sheep, pigs and other animals – we know that normal blood pressure kills!!!!

- The tide has turned against ‘20ml/kg of saline’

So, which fluid and how much?
How Much Fluid?

GOAL-DIRECTED:

Blood Pressure?  NO

Urine output?  NO

Hemoglobin?  NO
How Much Fluid?

- **GOAL-DIRECTED:**
  - Correct acidosis
  - Correct coagulopathy
  - Demonstrate tissue blood flow:
    - Esophageal doppler
    - Pulse Pressure Variation (FLOTRAC)
    - Side stream dark field imaging
    - SvO2
Which Fluid?

The ideal fluid:
Small volume
Cheap, easy and available
No side effects

Coagulation  Acidosis  Lung/Kidney
Inflammation
Caveats

1. In Scoop & Run model, there is no difference in mortality between small volumes and no fluid.
2. Small volume crystalloid (i.e. < 1000ml Ringer’s Lactate, not saline) would be acceptable but not optimal as only ¼ remains intravascular.
3. When the risk of massive transfusion is high, the best fluid is whole blood.
Albumin

JL Vincent ‘Nature’s Way’

- Still used
- No measureable coagulopathy or nephropathy
- Many biological actions
- Problems:
  - Expensive
  - Glass bottles
  - Contraindicated in head injury (SOAP)
Hydroxyethyl Starch (HES)
Many different compounds

- Made from waxy maize amylopectin
- Properties depend upon:
  - Molecular weight
  - Molar substitution
  - C2/C6 ratio
- Problems:
  - Older compounds (eg. Hetastarch & Pentaspan) caused nephropathy (VISEP) & coagulopathy

But Tetrastarch is similar to Albumin
(i.e. causes no coagulopathy and no nephropathy)
Current Management Principles

Massive Transfusion Protocols

1. Very early use of plasma/colloid
2. Minimal use of crystalloid
3. Goal is euvoelaemia
4. Avoid red cell storage lesions by using fresh product (<14 days old)
Current Management Principles

Massive Transfusion Protocols

5. Cell salvage wherever possible

6. “Transfusion packs” approximating whole blood as damage control

7. Evaluation of coagulation by thromboelastography
Advantages of MTPs

- Dramatic, life-saving results
- Mortality ↓ by 50%
- Avoidance of expensive and unproven magic bullets (O’Keefe, 2008)
  - Factor VIIa, Octoplex, FEIBA
- Overall decreased blood product usage
  - (O’Keefe Arch Surg 2008;143:686)
- Decreases ICU ventilator days, blood use & LOS
  - (Gonzalez, J Trauma, 2008;64:247)
Conclusions

1. Scoop & Run
2. Less is more
3. Saline is NOT normal
4. Ringer’s is all right… *but*...
5. Colloids are safe
6. Blood is the best therapy for bleeding
APPENDIX B: MASSIVE TRANSFUSION ALGORITHM

Massive Blood Loss Identified
MT Protocol Initiated
Initial Blood Work Drawn

SBP ≤ 90 or
100 with Head Injury &
GCS ≤ 13?
Yes

Avoid excessive crystalloid or
artificial colloid use.
Transfuse plasma as early as
possible for volume expansion
and correction of coagulopathy

Bolus 1-2 litres of
warmed Ringer’s
lactate * (10-20 mL/Kg)

SBP still ≤ 90
or 100 with Head Injury
& GCS ≤ 13?
Yes

Lab will provide universal** donor blood and products
until type specific is available

Ensure IV fluid is changed to NaCl prior to
administering blood/blood products

Consult Transfusion
Medicine Laboratory
for pediatric
doing

For adult patients with significant ongoing hemorrhage, consider tranexamic acid 1g IV
bolus over 10 minutes, then 1g IV infusion over 8 hours. Available from Pharmacy.
Aim to initiate within 3 hours of injury.

Level I, II and III Trauma Centres
RBC: 4 units
Plasma: 500 mL
Platelets: 1 dose when available

Level V Trauma Centres
RBC: 2 units
Plasma: 500 mL

q30 min, unless requested sooner

Level I, II and III Trauma Centres
RBC: 4 units
Plasma: 500 mL or as required
Platelets: 1 dose when available

Level V Trauma Centres
RBC: 2 units
Plasma: 500 mL

Initiate and continue transfusion and revert to goal
directed treatment once lab data becomes available.
The Priority of Plasma

<table>
<thead>
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<th>Level V Trauma Centres</th>
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</tr>
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</table>
An oasis of knowledge in the desert of ignorance...