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Crush injuries and crush syndrome – a review. Part 1: the systemic injury

Nikolas A Jagodzinski, Charitha Weerasinghe and Keith Porter

Crush injuries can occur in large numbers following natural disasters or acts of war and terrorism. They can also occur sporadically after industrial accidents or following periods of unconsciousness from drug intoxication, anaesthesia, trauma or cerebral events. A common pathophysiological pathway has been elucidated over the last century describing traumatic rhabdomyolysis leading to myoglobinuric acute renal failure and a systemic 'crush syndrome' affecting many organ systems. If left unrecognised or untreated, then mortality rates are high. If treatment is commenced early and the systemic effects are minimised then patients are often faced with significant morbidity from the crushed limbs themselves. We have performed a thorough review of the English language literature from 1940 to 2009 investigating crush injuries and crush syndrome and present a comprehensive, two-part summary. Part 1: The systemic injury: In this part we concentrate on the systemic crush syndrome. We determine the pathophysiology, clinical and prognostic indicators and treatment options such as forced alkaline diuresis, mannitol therapy, dialysis and haemofiltration. We discuss more controversial treatment options such as allopurinol, potassium binders, calcium therapy and other diuretics. We also discuss the specific management issues of the secondary 'renal disaster' that can occur following earthquakes and other mass disasters. Part 2: The local injury: Here we look in more detail at the pathophysiology of skeletal muscle damage following crush injuries and discuss how to minimise morbidity by salvaging limb function. In particular we discuss the controversies surrounding fasciotomy of crushed limbs and compare surgical management with conservative techniques such as mannitol therapy, hyperbaric oxygen therapy, topical negative pressure therapy and a novel topical treatment called gastric pentadecapeptide BPC 157.

Key words: crush syndrome; acute renal failure; alkaline diuresis; mannitol; rhabdomyolysis; mass disasters

Introduction

Man-made disasters such as war, acts of terrorism and mining accidents create large numbers of crush victims (Better, 1999). In civilian life, crush injuries occur most commonly after collapse of structures

during natural disasters such as earthquakes, hurricanes, tsunamis and land-slides. Crush injuries are rare in Great Britain and are usually caused by road traffic collisions and industrial accidents.

Crush syndrome can develop from a variety of mechanisms and not just from trauma. Unconscious patients following strokes or intoxication can lie in the same position for long periods and may develop rhabdomyolysis if pressure areas are not protected (Porter and Greaves, 2003). Surgeons and intensivists are well aware of the dangers of positioning anaesthetised patients (Reis and Better, 2005). Certain drugs (alcohol, cocaine), bites and toxins

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can also cause rhabdomyolysis and a crush-type syndrome, as can heat-stroke, burns, electrocution, seizures, severe exercise and some viral and bacterial infections (Gabow *et al.*, 1982; Ward, 1988; Brody *et al.*, 1990; Sinert *et al.*, 1994; Sahjian and Frakes, 2007).

Traumatic crush syndrome is usually caused by a static compressive force on skeletal muscle. A pseudo-crush syndrome has also been reported in victims of abduction, starvation and persistent, intermittent blunt trauma with weapons such as chains and other metal and wooden objects (Bloom *et al.*, 1995). Repeated minor fracture of muscle mass, rhabdomyorhexis, has a cumulative effect equivalent to major crush injury, especially if compounded by forced dehydration.

Studies from disaster areas around the globe, whether natural or man-made, have provided us with most of our knowledge of the crush syndrome over the last two centuries. A Napoleonic Army surgeon first described a crush syndrome in 1812 in a comatose soldier who developed muscle and skin necrosis in pressure areas (Reis and Better, 2005). German physicians during the First World War also recognised the crush syndrome, as did physicians in 1909 after the Messina earthquake (Welbourn, 1991). An American physiologist, WB Cannon recognised the lethal effects of reperfusion in the case of 'A lieutenant caught in a dugout after a shell burst' who died 32 h after extrication (Cannon, 1923). His rapid deterioration and shock developed 'on permitting the circulation to return to the damaged tissue'.

Bywaters and Beall (1941) were the first to describe the pathophysiological processes in the English language in 1941 after studying patients extricated from collapsed buildings during the London Blitz. They reported a case series of similar patients who, despite correction of their haemodynamic instability, rapidly deteriorated over several days with renal failure and 'tea-coloured' urine. They all died in hospital and their post-mortem findings revealed similar pathological processes in the kidneys. Their subsequent research in 1944 identified myoglobin as the cause of the obstructive renal failure (Bywaters and Stead, 1944).

Numerous case series along with clinical and laboratory studies have developed our knowledge of this complex, and inherently reversible, syndrome. Clinicians currently working in Haifa, Israel have published extensively on this topic over the last

30 years due to their regular influx of crush victims from their close proximity to conflicts in Beirut and Lebanon. Following the Armenian earthquake in 1988, the International Society of Nephrologists (ISN) set up a Renal Disaster Relief Task Force (RDRTF) to coordinate treatment for the secondary 'renal disaster' that inevitably ensues following geological disasters all around the globe (Lamiere *et al.*, 2003; Vanholder *et al.*, 2007a).

One of the most effective tools for decreasing the death toll after disasters is successful treatment of the crush syndrome and related acute renal failure (ARF) (Sever *et al.*, 2006). Clinicians should be aware of the potential causes, clinical signs and pathophysiological processes involved in the crush syndrome. Early recognition and aggressive treatment can prevent a lethal downwards spiral. Various treatment algorithms have been suggested but certain aspects remain controversial. In order to improve our management, we have performed a review of all available literature in the English language from Medline, Embase, Ovid and Cinahl from 1950 to July 2009 searching for 'Crush Syndrome,' 'Crush injury' and 'crush injuries' in the title. We have also reviewed the British Nursing Index (BNI), the Database of Abstracts of Reviews of Effects (DARE) and the Health Technology Assessment (HTA) Database with the same search terms. Our search produced 1371 articles of which 624 were duplicates. Our aims in Part 1 are to review the pathophysiology of the systemic effects of crush injuries and to determine the best methods of assessment, treatment and prevention. We excluded articles relating to nerve crushes and the 'double crush syndrome' and analysed the remaining 396 abstracts for relevance. We have included reviews of 111 articles in Part 1 and 94 articles in Part 2 including appropriate cross-references. In Part 2, we look in more detail at the localised injury to crushed limbs and what treatment options are available to minimise morbidity.

Pathophysiology

Torso crush injuries

A compressive force to the thorax can cause death by several potential mechanisms including pneumo-haemothorax, transection of the aorta, pericardial tamponade or cardiac contusion, multiple rib

fractures, flail chest and massive lung contusions (Martin, 1993; Wyse and Mitra, 2000). Even if the initial force is insufficient to cause one of these life-threatening injuries then splinting of the ribs by a static compressive force will lead to traumatic asphyxia. Furuya (1981) found that no animal would survive a force of more than five times its body weight for longer than 10 min. Blood is forced back up the valveless superior vena cava and jugular veins resulting in rapid dilation and rupture of capillaries and venules in the neck, head and face. Using autopsies of mob victims in Paris in 1837, Dr Ollivier described the syndrome of subconjunctival haemorrhages, bluish discolouration of the face and neck and oedema coining the term 'Masque Ecchymotique' (Ollivier, 1837; Stewart, 1999). Periorbital haematomas have also been described following blunt thoracic injury in the absence of fractures involving the base of skull and face (Deakin, 1995).

Another hypothesis for the mechanism of traumatic asphyxia is the 'fear response' (Williams *et al.*, 1968). Deep inspiration, glottic closure and constriction of the abdominal muscles accompany the sense of impending doom when the victim realises the situation is hopeless. This increases the intrathoracic pressure further compounding the compression (Lee *et al.*, 1991). Traumatic asphyxia has been experimentally induced in dogs and the classical findings did not occur until the endotracheal tube was occluded (Williams *et al.*, 1968).

Near fatal haemorrhage from crush-avulsion injuries to female breasts have been reported in the literature as part of the 'seat belt syndrome' (Majeski, 2001).

Crush injuries to the abdomen can cause a spectrum of organ damage with associated haemorrhage and splinting of the diaphragm. The abdominal aorta can be crushed against the lumbar spine causing thrombus, intimal tears or rupture with retroperitoneal haematoma and arterial insufficiency (Edwards *et al.*, 1990). A sudden rise in intra-abdominal pressure can also cause bowel evisceration through the anus with stripping of the mesentery (Rechner and Cogbill, 2001). A pregnant trauma victim presents a serious challenge to the trauma team and the needs of the foetus should be considered as well as the complex physiological needs of the mother (Schoenfield *et al.*, 1995). Early input from an obstetrician should be sought.

Exsanguination is the primary cause of early death in patients with pelvic crush injuries (American College of Surgeons, 2004). If they survive the initial trauma, patients are still at high risk of sepsis and multi-organ failure (Fleming and Bowe, 1973; Tscherne *et al.*, 2000). Urethral and rectal injuries have also been reported (Tomkins *et al.*, 1988; Dixon *et al.*, 1992).

Crush injuries to the head can cause instant death from raised intracranial pressure from bleeding or from skull fracture and direct brain injury. Traumatic injuries following progressive compression to the head are more unusual and can have a distinctive clinical picture depending on the direction of the compressive force (Tortosa and Poza, 1996). Static forces applied in a transverse axis produce fractures in the skull base without producing significant cerebral damage. Stretching of the cranial nerves occurs universally in bitemporal head crush injuries and the increase in vertical diameter of the skull causes diabetes insipidus (Tortosa *et al.*, 2004). People who survive the acute period of a crush injury to the head have a good long-term neuropsychologic prognosis, reflecting the ability of the brain and cranium to withstand quasi-static loading, especially in childhood (Duhaime *et al.*, 1995; Prasad *et al.*, 1999).

Crush syndrome

Traumatic rhabdomyolysis, or the crush syndrome, is the consequence of prolonged continuous pressure on the limbs (Michaelson, 1992). When applied to the head or torso, the prolonged pressure necessary to cause crush syndrome is thought to be too much to survive (Oda *et al.*, 1997b). Major crush injuries damaging more than one organ system are often fatal, especially if rescue is delayed (Stewart, 1987). Head and torso trauma are often immediately fatal but injury to the limbs alone is often survivable even with amputations, multiple fractures and massive mutilating wounds. Late mortality from crushing of limbs is generally attributable to rhabdomyolysis resulting in the crush syndrome which affects many organ systems if left untreated (Santangelo *et al.*, 1982; Michaelson, 1992). Hyperkalaemia and acute renal failure are cardinal features compounded by hypovolaemic shock, acute cardiomyopathy, disseminated intravascular coagulation, hypothermia,

acute respiratory distress syndrome, sepsis and psychological trauma.

Muscle can survive ischaemia for up to 4 h but violent crushing destroys muscle immediately (Reis and Better, 2005). Even if the force is insufficient to mangle the muscle tissue, the combination of mechanical force and ischaemia will cause muscle death within an hour (Heppenstall *et al.*, 1986; Reis and Better, 2005). Any intramuscular mechanical force which acts continually above the diastolic blood pressure causes this combination of pressure-stretch myopathy and ischaemic myopathy (Heppenstall *et al.*, 1986). These mechanisms of muscle injury are described further in our sequel paper: Crush injuries and crush syndrome – a review. Part 2: The local injury.

Skeletal muscles make up the largest organ system in the body approaching 40% of body weight and containing approximately 75% of body potassium. When they are crushed, the degree of redistribution of fluids and solutes of the intracellular and extracellular compartments may reach the most extreme degree as seen in clinical practice in salvageable patients, except, perhaps after extensive burns (Better, 1990; Better *et al.*, 1992). Increased permeability of the myocytes' sarcolemmal membranes allows influx of sodium and calcium creating a pressure head for water to follow by osmosis. The entire extracellular fluid volume (around 12 L in an average 75 kg man) may penetrate into the injured muscles within hours to days of injury. This is termed 'third spacing' and leads to a rapid depletion of intravascular fluid, hypovolaemic shock and cardiac arrest (Better, 1990, 1999). Hypovolaemic shock is compounded by local activation of the nitric oxide system in crushed muscle causing extreme vasodilatation (Rubinstein *et al.*, 1998). Renal ischaemia is caused by activation of constrictor hormones such as angiotensin II, catecholamines, vasopressin and intrarenal thromboxane (Odeh, 1991).

Crushed muscle also releases myoglobin, urate and phosphate into the circulation. In the presence of acidic urine in the distal convoluted tubule of the kidney, these substances precipitate into tubular casts causing an obstructive post-renal failure (Bywaters and Stead, 1944; Better, 1999). Phosphate can react with calcium causing metastatic calcification which damages the renal parenchyma. Myoglobin readily forms hydroxyl free-radicals, which

produce a direct oxidant injury to the kidney (Sahjian and Frakes, 2007). The combination of pre-renal, renal and post-renal failure leads to a severe metabolic acidosis. Acidic urine further precipitates tubular casts and sets up a vicious cycle of worsening ARF. Anaerobic respiration of injured muscle produces lactic acidosis. Multiple organ failure (MOF) and death ensues.

Crushed, dead muscle bleeds profusely and sets up a consumption coagulopathy leading to disseminated intravascular coagulation (DIC) (Better, 1990; Kracun and Wooten, 1998; Better, 1999; Reis and Better, 2005). Microthrombi block capillaries in the glomerular apparatus compounding the pre-renal failure. Fibrinolysis is activated by clotting in order to clear thrombi from the microvasculature setting up a cycle resulting in uncontrolled fibrinolysis (Gentilello and Pierson, 2001). Further exsanguination from both injured and non-injured body parts worsens hypovolaemic shock. Platelet inhibitors such as prostaglandin I₂ (PGI₂) and antithrombin III are released from endothelial cells during shock which exacerbates the vicious cycle (Reed *et al.*, 1986).

Acidosis, coagulopathy and hypothermia have been coined the 'lethal triad of trauma'. Their interlinking pathophysiologies set up a vicious cycle and their concurrence carries a grave prognosis for trauma victims (Ferrara *et al.*, 1990; Cosgriff *et al.*, 1997; Gentilello and Pierson, 2001). Mortality from moderate hypothermia (28–32°C) due to exposure is less than 25%, with virtually all deaths attributable to underlying diseases, rather than to hypothermia itself. In contrast, in trauma patients, a core temperature less than 32°C is associated with 100% mortality, and any decrease in temperature below 35°C is a poor prognostic sign (Jurkovich *et al.*, 1987).

A crushed patient is susceptible to both primary and secondary hypothermia. Prolonged exposure awaiting rescue can cause excessive heat loss (primary hypothermia). Diminished heat production in shocked trauma patients causes a secondary hypothermia even in the absence of environmental cooling (Gentilello and Pierson, 2001). Hypothermia can prolong clotting times to the same extent as a severe clotting factor deficiency (Johnston *et al.*, 1989). This is often grossly underestimated in laboratory tests as samples are usually warmed to 37°C before testing. This corrects the

inhibition of enzymatic reaction rates in the coagulation cascade that hypothermia usually causes. Hypothermia also has an inhibitory affect on platelet function. Acidosis and clotting factor deficiencies from DIC further impede the coagulation cascade and exsanguination can be rapid (Valeri *et al.*, 1987).

Muscle damage occurs at three distinct stages: at the time of the initial mechanical crushing force, during the period of ischaemia and during the period of reperfusion (Walker *et al.*, 1987). In fact, studies of enzyme release suggest that most damage to myocytes occurs during reperfusion rather than ischaemia (Presta and Ragnotti, 1981). All three stages are discussed further in Part 2: The local injury. Briefly, Odeh's 'oxygen paradox' theory proposes that reperfusion of ischaemic tissue provides oxygen as a substrate for xanthine oxidase and other enzymes to produce hydroxyl free-radicals (Odeh, 1991). These reactive oxygen metabolites directly damage the microvasculature and parenchyma of skeletal muscle and set up a cascade of free-radical propagation (Walker *et al.*, 1987; Krost *et al.*, 2008). Reperfusion of ischaemic kidneys and heart can cause secondary damage to their vasculature by similar mechanisms meaning they are subjected to a double hit of free-radical attack (Odeh, 1991). Odeh also proposes the 'calcium paradox' theory of tissue damage on reperfusion whereby sodium is exchanged for calcium causing cell damage by several mechanisms as discussed in Part 2.

Reperfusion of crushed limbs can cause pulmonary embolus by sudden release of marrow, fat and thrombus. Embolised fat can also pass through the lungs back into the systemic circulation. Sudden drops in conscious level, focal neurological signs and seizures can occur after extrication from crushing objects through this mechanism (Gurd and Wilson, 1974).

Hypovolaemic shock causes splanchnic vasoconstriction which can manifest as stress-induced gastritis, bowel ischaemia, pancreatitis, acalculous cholecystitis and ischaemic hepatitis (Odeh, 1991). Increased endotoxin from gram-negative bowel flora enters the circulation when hepatic filtration is already reduced. Tumour necrosis factor α , and other cytokines, are released from the monocyte-macrophage system stimulating a systemic inflammatory response, shock, acute respiratory distress

syndrome (ARDS) and eventual MOF. An increase in pulmonary capillary permeability intrinsically associated with the crush syndrome can cause a delayed ARDS, even when complications such as sepsis and MOF are prevented (Nishihara *et al.*, 1997).

Crush victims are susceptible to developing overwhelming sepsis. Both ARF and a catabolic state from injury independently render crushed patients immunocompromised, yet they face infection from traumatic wounds, surgical wounds, ventilators, urinary catheters, venous cannulas and invasive monitoring (Cossio, 1977; Kracun and Wooten, 1998). Compartment syndrome is a frequent cause of morbidity and mortality in patients who survive crush syndrome and its controversial treatment is discussed in Part 2: The local injury.

Clinical picture and prognostic indicators

Crush syndrome can be caused by a multitude of mechanisms; so a good history is important in creating a clinical suspicion. Unconscious trauma victims, therefore, pose a particular clinical challenge. Michaelson and Better have deduced that when an eight-storey concrete building collapsed in Lebanon in 1982 containing roughly 100 people, around 80% were killed in the first few minutes from head or torso trauma. Out of the 20% who survived, half were completely unscathed but most of the other half, that is 10% of the total victims, suffered traumatic rhabdomyolysis from crushed limbs (Michaelson *et al.*, 1984; Ron *et al.*, 1984; Reis and Michaelson, 1986; Better, 1990, 1999).

Victims who are trapped by any mechanism are usually afraid and extremely emotionally distressed (Stewart, 1999). Those who are conscious do not commonly complain of pain (Michaelson, 1992). Their vital signs are frequently normal or near to it. Crushed limbs almost universally have good pulses and are not swollen (Stewart, 1987). Direct arterial injury is uncommon in crush injuries but limbs frequently have patchy numbness (Michaelson, 1992; Reis and Better, 2005). The skin can be bruised and discoloured but is usually intact (Stewart, 1999). The combination of all of these initial clinical signs can be falsely reassuring.

Extrication of patients can take several hours. Release of the crushing force can cause sudden haemodynamic collapse and cardiac arrest due to the various mechanisms of the reperfusion syndrome. Patients usually survive extrication ('rescue death') if resuscitative treatment and monitoring has commenced whilst the patient is still trapped (Michaelson *et al.*, 1984; Oda *et al.*, 1997b; Sahjian and Frakes, 2007). Limbs begin to swell only several hours after extrication but the progression over several days causes excruciating pain and enormous, turgid, brawny limbs at high risk of compartment syndrome (Michaelson, 1992). Crushed limbs have been misdiagnosed as thrombophlebitis and paraplegia in patients unable to give a history (Reis and Michaelson, 1986; Better, 1990; Reis and Better, 2005). A coexisting spinal injury should be excluded, however.

We know that patients with torso trauma have higher mortality rates as do patients with the lethal triad of trauma: acidosis, coagulopathy and hypothermia (Oda *et al.*, 1997b; Gentilello and Pierson, 2001). The development of ARF is also associated with a poor survival. The likelihood of developing ARF is proportional to the mass of skeletal muscle crushed, the magnitude of the crushing force and the length of time it is crushed for (Michaelson, 1992; Shigemoto *et al.*, 1997; Kracun and Wooten, 1998; Porter and Greaves, 2003). Patients crushed very briefly by a large force, such as pedestrians run over by vehicles, do not often go on to develop crush syndrome (Michaelson, 1992; Porter and Greaves, 2003). The time from injury to cell death varies with the compressing force involved. Skeletal muscle can tolerate ischaemia for up to 2 h without permanent injury. From 2–4 h, some reversible cell damage occurs and by 6 h irreversible tissue necrosis generally sets in (Malinoski *et al.*, 2004).

The incidence of ARF in 372 patients with crush syndrome caused by the Hanshin-Awaji earthquake was 50.5%, 74.7% and 100% for those with one, two and three crushed limbs respectively (Oda *et al.*, 1997b). The incidence of ARF as a result of rhabdomyolysis from different causes has been reported to range from 0–67% in various clinical settings but most quote figures of around 15–20% (Ward, 1988; Brody *et al.*, 1990; Sinert *et al.*, 1994; Goldfarb and Chung, 2002; Fernandez *et al.*, 2005). These figures worsen considerably following mass disasters due to the inevitable delay in rescue.

The presence of sepsis is associated with extremely poor survival rates if compounding a crush syndrome with ARF (Cossio, 1977; Rainford, 1978; Ward, 1988).

The diagnosis of crush syndrome can be made where rhabdomyolysis causes systemic manifestations such as hypovolaemia, electrolyte and mineral disturbances, myoglobinuria and oligo-anuria (urine output <20 mL/h, urea >40 mg/dL and creatinine >2 mg/dL) (Ensari *et al.*, 2002). Most papers reviewed used a serum creatine kinase (CK) greater than 1000 U/L (or five times their maximal normal laboratory limit) to clinically diagnose rhabdomyolysis.

Basic observations should be monitored in all crush victims including blood pressure, heart rate, respiratory rate and oxygen saturations. Urine output and continuous cardiac monitoring should be commenced as early as possible (Sahjian and Frakes, 2007). Hyperkalaemia (with levels of potassium (K⁺) over 7–9.5 mEq/L), hypocalcaemia and oliguria are early clinical signs which can precipitate arrhythmias and cardiac arrest within 1–2 h of extrication (Allister, 1983; Better *et al.*, 1992; Better, 1999). Serum potassium levels should be measured 3–4 times daily in the first few days following admission as most early deaths are caused by either hyperkalaemia or hypovolaemia (Oda *et al.*, 1997b; Sever *et al.*, 2003). Michaelson *et al.* (1984) recommend measuring blood and urine electrolytes and osmolality, as well as blood gases, every 6 h.

Anaerobic respiration of skeletal muscle and other organs causes a metabolic acidosis with a raised serum lactate. Myoglobin released from crushed muscles is filtered in the kidney and has a half-life of only 3 h (compared with CK which has a half-life of 1.5 days). The concentration of myoglobin in the blood can be compared with that in the urine to track the course of crush syndrome by measuring myoglobin production versus clearance (Sahjian and Frakes, 2007). Muckart *et al.* (1992) postulated that a venous bicarbonate level <17 mmol/L in the presence of myoglobinuria is associated with the development of ARF (Shigemoto *et al.*, 1997).

Several studies have looked into the prognostic values of serum CK. Measurements greater than 500, 5000, 16 000 and 75 000 U/L have all been reported to be associated with development of ARF

(Ward, 1988; Oda *et al.*, 1997a, b; Brown *et al.*, 2004). A retrospective review of CK levels in 2083 trauma patients by Brown *et al.* (2004) identified a peak CK level of over 5000 U/L as statistically the best marker. A historical cohort design by Ward in 1988 developed a model predictive of ARF in rhabdomyolysis (from all causes) by means of multiple logistic regression analyses based on 171 patients (Ward, 1988). It was postulated that peak serum CK, potassium and phosphorus levels reflect the degree of muscle damage rather than renal clearance as they are grossly raised at presentation and before ARF develops, generally by day two. Serum albumin levels reflect the general health of the patient and, therefore, the susceptibility to ARF. The presence of dehydration at presentation was also included in the model and they recommend monitoring pulmonary capillary wedge pressures for an accurate assessment. A haematocrit over 50% at presentation is another good measure of the level of dehydration and susceptibility to ARF.

A retrospective chart review by Fernandez *et al.* (2005) showed that no patient developed ARF if their initial serum creatinine was less than 1.7 mg/dL. They also suggested that serum potassium, initial CK, urine pH and specific gravity were not statistically significant predictors of developing ARF, whereas a low serum bicarbonate, raised serum urea and creatinine, hypocalcaemia and haematuria on dipstick were independently good predictors. In a study by Gabow *et al.* (1982), the peak creatinine, peak potassium, peak phosphorous, peak uric acid and trough calcium levels were statistically different between patients with rhabdomyolysis who did, and did not, develop ARF.

The presence of microalbuminuria can also be a poor prognostic indicator in the development of ARF (Porter and Greaves, 2003). A raised serum amylase can indicate splanchnic vasoconstriction; so may be able to predict the development of a systemic inflammatory response syndrome (SIRS), ARDS and MOF (Odeh, 1991; Porter and Greaves, 2003).

Many scoring systems have been developed to predict outcome and guide management of trauma patients. Physiologically based systems include the Glasgow Coma Score (GCS), the Revised Trauma Score (RTS), the Acute Physiology and Chronic Health Evaluation score (APACHE), the Sequential Organ Failure Assessment score (SOFA) and the

Systemic Inflammatory Response Syndrome (SIRS) score. Anatomically based scoring systems include the Abbreviated Injury Score (AIS), the Injury Severity Score (ISS), the New Injury Severity Score (NISS), the Anatomic Profile (AP), the Penetrating Abdominal Trauma Index (PATI) and the International Classification of Disease (ICD)-based Injury Severity Score (ICISS). Scoring systems that combine physiological and anatomical concepts include A Severity Characterisation of Trauma (ASCOT) and TRISS, which is a combination of the RTS and ISS (Pohlman and Bjerke, 2007). All of these scoring systems can be valuable adjuncts to management but with the insidious onset and progression of symptoms and signs in crush syndrome, unless scores are frequently revised, clinicians should not rely on them alone. Brown *et al.* (2004) found that the combination of age >55, ISS >16 and CK >5000 is associated with a 41% probability of renal failure compared with a probability of 3% in the absence of these three risk factors.

One recent study by Amoros *et al.* (2007) tried to compare NISS classifications of patients arriving in hospital with injury classifications previously performed by Police. They demonstrated that misclassifications by Police were too frequent to reliably use national data on road traffic crashes to predict outcome.

The various potential prognostic indicators reported in the literature are summarised in Table 1. A combination of a good history, basic monitoring and trends in laboratory tests on serum and urine can provide adequate prognostic information and guide treatment.

Treatment

The systemic affects of the crush syndrome are preventable if clinicians have a high index of suspicion, are aware of the pathophysiological processes and clinical course and start appropriate treatment early enough. If treatment is delayed and the vicious cycles have begun then it is more difficult to treat but still reversible (Ensari *et al.*, 2002). Nephrologists and intensivists should be involved early, even if initial prognostic indicators are favourable (Michaelson, 1992).

Table 1 Prognostic indicators used in management of crush syndrome

Prognostic indicator	Value	Significance
Crushed torso		Increases mortality rates
Presence of 'lethal triad of trauma'	Acidosis + coagulopathy + hypothermia	Increases mortality rates
Development of ARF	urine output <20 mL/h, urea >40 mg/dL and creatinine >200 µmol/L	Increases mortality rates
Physiological + anatomically based scoring systems		Increases mortality rates
Number of Limbs Crushed	1 = 50%, 2 = 75%, 3 = 100%	Likelihood of developing ARF
Initial serum CK	>5000 U/L (or >30 000 to benefit from bicarbonate + mannitol)	Likelihood of developing ARF + need for haemodialysis
Dehydration at presentation	Haematocrit >0.5	Likelihood of developing ARF
Serum phosphorus		Likelihood of developing ARF
Serum bicarbonate	<17 mmol/L	Likelihood of developing ARF
Raised urea + creatinine on presentation		Likelihood of developing ARF + need for haemodialysis
Hypocalcaemia		Likelihood of developing ARF
Raised peak serum uric acid		Likelihood of developing ARF
Serum albumin	Below normal	General health status + susceptibility to ARF
Hyperkalaemia (+hypocalcaemia)	K ⁺ > 7 mEq/L	Risk of arrhythmias + cardiac arrest (early sign) + predictor of developing ARF
Serum Lactate	Above normal	Presence of lactic acidosis
Serum vs Urine myoglobin/time		Clinical course of the crush syndrome
Microalbuminaemia		Likelihood of developing ARF
Serum amylase		Gut ischaemia + possible development of SIRS

Extrication

Patients have survived being trapped for 5 days and occasionally longer (Better, 1990; Stewart, 1999). Search and rescue attempts should not be delayed or abandoned until after this period at least. Once a victim is found, extrication should not be delayed as the likelihood of developing crush syndrome is proportional to the amount of time a limb is crushed for (Porter and Greaves, 2003).

If a crushed limb is trapped and preventing extrication then amputation at scene should be considered a life-saving measure (Stewart *et al.*, 1979; Stewart, 1999). In a similar way to tourniquet application, limb amputation before release of the crushing force may prevent the sequelae of the reperfusion syndrome and minimise the systemic insult (Stewart *et al.*, 1979). In order to prevent morbidity from amputation, however, all attempts should be made to preserve crushed limbs, as discussed in Part 2: The local injury. The systemic insult is treatable and preventable with adequate fluid resuscitation and appropriate intensive therapy. Advances in reconstructive surgical techniques can restore some limb function (Porter and Greaves, 2003).

The initial component of any rescue effort is a safe approach as damaged buildings and structures are prone to further collapse. In some western countries such as the United Kingdom, New Zealand and the United States of America, civilian fire brigades and military forces have formed full-time Urban Search and Rescue (USAR) teams to be able to deploy rapidly and efficiently. These usually consist of components for digging, lifting and cutting heavy masonry and steelwork, for providing temporary support of buildings, sniffer-dogs, sonic devices, fibre-optic scopes and infra-red cameras for locating victims and basic first-aiders (Better, 1999).

Battlefield advanced trauma life support and the use of tourniquets

Basic life-support measures should be commenced as early as is safe and practical but all efforts should be made to transport crush victims to definitive secondary medical care as rapidly as possible. Advanced life-support measures, beyond the capabilities of basic first-aiders, are required to prevent or reverse the crush syndrome. The latest military

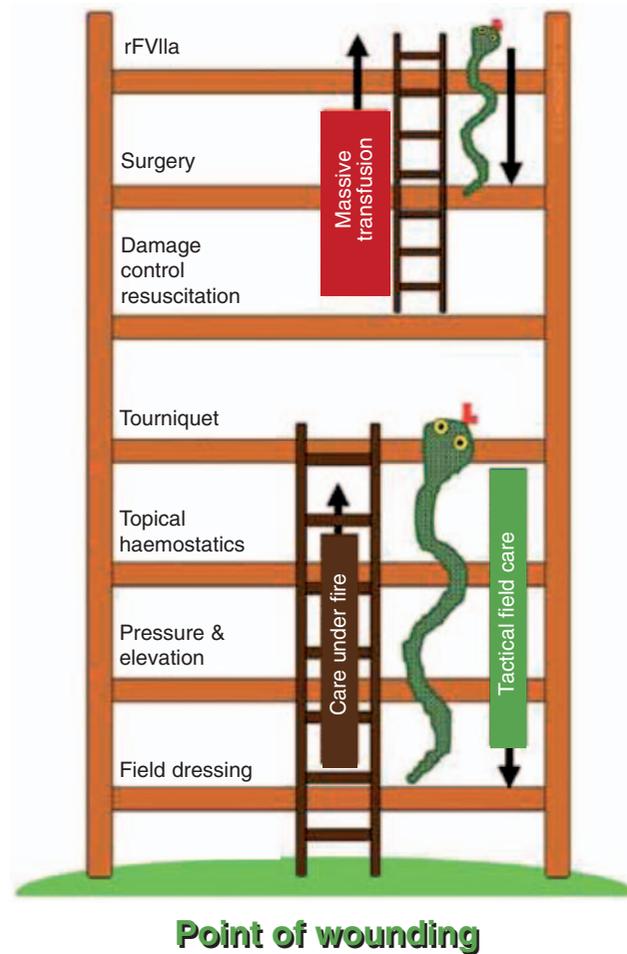


Figure 1 UK Defence Medical Services Haemostasis Ladder [Moorhouse I, Thurgood A, Walker N, Cooper B, Mahoney PF, Hodgetts TJ. 2007. A realistic model for catastrophic external haemorrhage training. *JR Army Med Corps* 153(2): 99–101. *Reproduced with kind permission of the Editor*]: Under normal circumstances there is progression from bottom to top of the large ladder considering each intervention sequentially. However, during 'Care Under Fire' (effective direct/indirect enemy fire) it is appropriate for catastrophic limb bleeding to immediately apply a tourniquet BUT to reassess its requirement during 'Tactical Field Care' (firefight won) the snake takes the user back to using a field dressing, pressure, and elevation at this point

teaching is based on the Battlefield Advanced Trauma Life Support (BATLS) protocol which works on a C-A-B-C-D-E paradigm (Hodgetts *et al.*, 2006). Recent statistics show that catastrophic haemorrhage is the overwhelming primary cause of death from military trauma, before airway or breathing compromise. If a crush victim has a problem with any of C-A-B-C then treatment should be started in conjunction with extrication

efforts. Ideally, medics with appropriate training should be involved.

British soldiers are taught basic medical techniques including a progressive treatment ladder for catastrophic haemorrhage following trauma to themselves or their colleagues (Figure 1) (Lakstein *et al.*, 2003; Moorhouse *et al.*, 2007). If the battle situation remains critical, tourniquets should be applied early, ignoring the lower rungs of the

ladder, and the situation should be reassessed once patients are moved to a safe zone. Tourniquets are now standard issue to all British soldiers and many lives have been saved by their use (Hodgetts *et al.*, 2006; Lee *et al.*, 2007; Moorhouse *et al.*, 2007).

There is a theoretical benefit in applying a tourniquet before releasing a crushed limb in order to prevent, or delay, the onset of the reperfusion syndrome (Weeks, 1968; Stewart *et al.*, 1979; Porter and Greaves, 2003; Krost *et al.*, 2008). There have been many studies suggesting that commencing aggressive fluid resuscitation and administering certain pharmacological agents prior to release of the compressive force on the limb may prevent the effects of the reperfusion syndrome. If intravenous or intra-osseous access cannot be gained whilst a patient is trapped, or if there are no trained medical personnel on scene, then a tourniquet may buy precious time until post-extrication. Stewart *et al.* (1979) suggest that a tourniquet should be applied before extrication of a crushed limb, especially if field amputations are to be performed (Stewart, 1987). They propose a two-fold benefit of preventing uncontrolled haemorrhage as well as preventing systemic release of toxins on reperfusion. If tourniquets are used, then they should not be released until hospital surgical facilities are available. We could not find objective evidence in the literature to support these proposals for crush injuries alone.

Appropriate help may be minutes, hours or days away depending on the circumstances and there are obvious dangers with tourniquet use. We know that the amount of muscle damage in a crushed limb is proportional to the compressing force and the length of time that it is compressed for. We also know that the mechanism of muscle damage in crushing is not solely due to ischaemia and reperfusion but also due to direct kinetic forces and to pressure-stretch mechanisms as discussed in Part 2: The local injury. Tourniquets are usually applied to a pressure greater than systolic blood pressure in order to occlude arteries and prevent haemorrhage. Applying a tourniquet for longer than 2 h causes further rhabdomyolysis, permanent neurovascular damage and skin necrosis (Lee *et al.*, 2007). Crush syndrome is reversible if treated early and aggressively and, for this reason, current consensus is to avoid using tourniquets on crushed limbs. Instead, patients should be extricated as quickly as possible

and transferred to definitive medical care whilst resuscitative measures continue.

Potassium binders

The most important and fatal medical complication of crush syndrome is hyperkalaemia (Sever *et al.*, 2003). Sodium polystyrene sulfonate (Kayexalate) can be given orally or rectally to patients to prevent fatal hyperkalaemia on reperfusion. Sever *et al.* (2006) recommend its administration to patients with crush injuries who face a prolonged transfer time to a trauma unit with dialysis facilities. A usual dose is 15 g per day per patient.

Rewarming

Patients crushed and trapped for a period of time have a very definite risk of developing hypothermia. As previously explained, hypothermia is a component of the 'lethal triad of trauma' and rewarming has become an essential component of resuscitation (American College of Surgeons, 2004). Hypothermia may be protective in delaying onset of cellular changes but extremely low core temperatures can cause hyperkalaemia and cardiac arrhythmias (Brattebo *et al.*, 1991; Campbell and Walker, 1992; Porter and Greaves, 2003; Lee *et al.*, 2007). Studies that compared slow versus rapid rewarming methods in trauma patients, including a randomised prospective trial, demonstrated a significant 7-fold increase in mortality during resuscitation of patients who were deliberately rewarmed less aggressively (Gentilello *et al.*, 1992, 1997). Aggressive active rewarming methods should be employed including warm intravenous fluid administration, warm air blankets, heat lamps, heated respiratory gases, bladder lavage, warm enemas and even peritoneal lavage and cardiopulmonary bypass if profound hypothermia is present (American College of Surgeons, 2004).

Analgesia

Crushed limbs are usually only mildly painful initially due to neurapraxias, the absence of swelling and the release of large amounts of endorphins relative to the large amount of tissue damage. This early lack of pain frequently masks a developing compartment syndrome until much later in the

course of treatment. Limbs become massively swollen and painful in the hours and days post-extrication requiring regional or general anaesthesia.

Patients are severely emotionally distressed during and after extrication; so analgesia and anxiolytics are frequently required (Stewart, 1999). Medications should be given parenterally if possible but oral administration is not contra-indicated if there is no limb available for intravenous or intra-osseous access (Porter and Greaves, 2003). Entonox, opiates, ketamine and benzodiazepines are all useful during a prolonged extrication process, especially if tourniquets are applied (Stewart *et al.*, 1979; Porter and Greaves, 2003; Lee *et al.*, 2007).

Fluid resuscitation

Aggressive fluid resuscitation is the mainstay of treatment for crush victims, even if vital signs are initially normal. Intravenous or intra-osseous access should be gained as soon as possible and fluid resuscitation should commence before extrication of crushed limbs and the reperfusion syndrome starts (Cossio, 1977; Michaelson *et al.*, 1984; Better, 1990; Oda *et al.*, 1997b; Reis and Better, 2005). Crystalloids such as normal saline (0.9% sodium chloride solution) should be given at a rate of 0.5–1.5 L/h to prevent sudden shock from hypovolaemia, pulmonary embolism and/or hyperkalaemic, hypocalcaemic cardiomyopathy (Better, 1990; Porter and Greaves, 2003). It is almost universally recognised in the literature that Ringer's lactate solution (Hartman's) should be avoided as it contains potassium (Porter and Greaves, 2003; Sever *et al.*, 2003). Aggressive administration of warmed crystalloid reverses metabolic acidosis, improves the coagulation cascade and prevents ARF by pre-renal, renal and post-renal mechanisms.

A mild 'permissive hypotension' may benefit survival rates by slowing exanguination in non-compressible haemorrhage (Revell *et al.*, 2002). In the presence of a crushed limb and haemorrhage, it is better to prevent crush syndrome with aggressive fluid therapy and direct control of bleeding than to permit mild hypotension.

Alternating normal saline with a 5% dextrose solution can prevent the development of hypernatraemia and hyperchloraemia but should not be used in the presence of established shock due to rapid metabolism of the dextrose component

dissipating pure water out of the intravascular compartment (American College of Surgeons, 2004). As well as having little effect on combating shock, it will cause more rapid limb oedema, pain and compartment syndrome.

Aggressive fluid resuscitation should continue through extrication and transfer to hospital. As mentioned previously, crushed muscle rapidly absorbs water down an osmotic gradient and the body's entire 12 L supply of extracellular fluid can be forced intracellularly over the first 12 h of reperfusion. Ideally, the rate of parenteral fluid administration should be guided by clinical response or central venous pressure measurements but the large volumes required are frequently underestimated. Reis and Better reported a treatment algorithm in 2005 that has proven benefits (Figure 2) (Reis and Better, 2005). Similar regimes have been adopted by the ISN's RDRTF (Better *et al.*, 1997). It should be continued until clinical and biochemical evidence of myoglobinuria has disappeared (usually by day 3) (Parry *et al.*, 1963; Better, 1990; Sever *et al.*, 2006).

Volume overload is a potential risk of aggressive fluid therapy, especially if a patient is elderly or severely oligo-anuric (potentially from delayed rescue) (Oda *et al.*, 1997b; Better, 1999; Sever *et al.*, 2006; Sahjian and Frakes, 2007). If monitoring is not available, it is recommended that less than 6 L of mannitol-alkaline solution should be infused daily (Vanholder *et al.*, 2000).

If blood transfusions are required to replenish lost blood, or treat a dilutional anaemia, then recent advances in military trauma have advocated the administration of 1:1:1 red cells: plasma: platelets (Malone *et al.*, 2006; Sahjian and Frakes, 2007). This protocol, along with preventing hypothermia by active rewarming, successfully prevents coagulopathy and the 'lethal triad of trauma' and has increased the rates of unexpected survival from military and civilian trauma since its introduction (Dente *et al.*, 2009). Blood transfusion without replacement of coagulation proteins contributes to the development of DIC (Kracun and Wooten, 1998).

Alkaline diuresis: bicarbonate and acetazolamide

The development of ARF is a crucial link in the progression of the crush syndrome. In 1941, Bywaters and Beall first described the 'tea-coloured

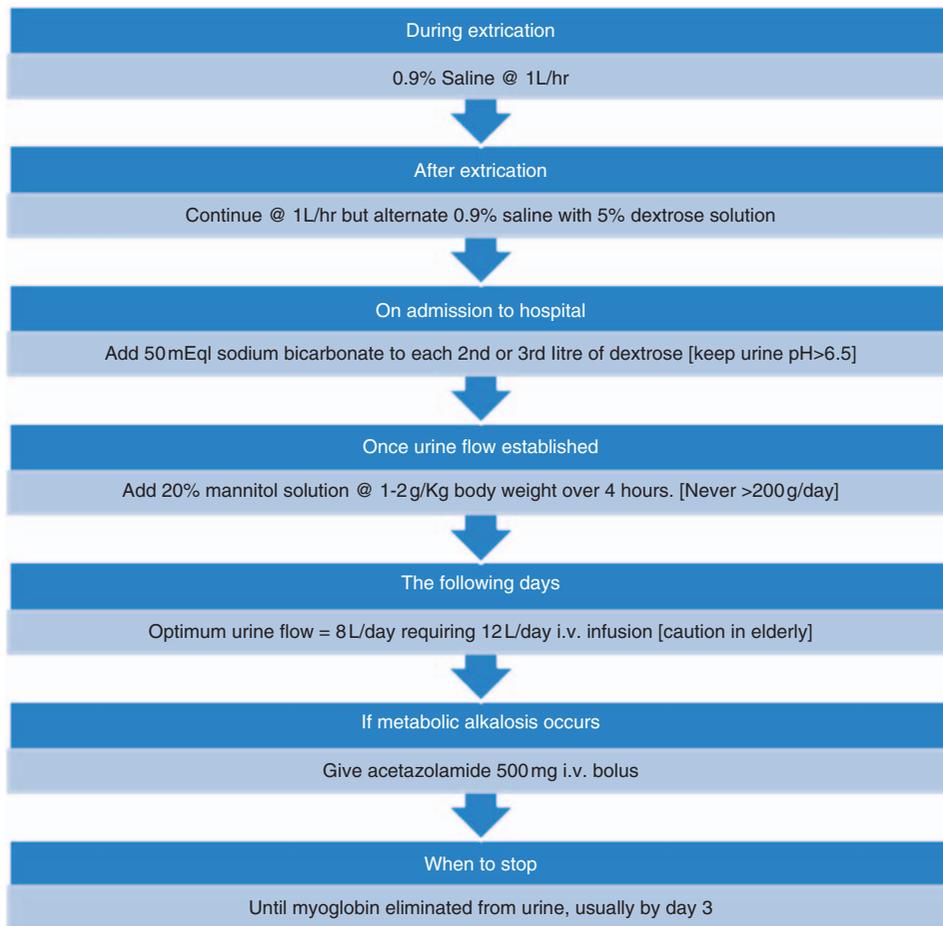


Figure 2 Recommended fluid therapy for crushed patients (adapted from Reis & Better, 2005)

urine' of crush victims (Bywaters and Beall, 1941). Bywaters and Stead (1944) later went on to implicate myoglobin as the nephrotoxic agent and they showed that alkalinisation of the urine using bicarbonate will abolish this nephrotoxicity. A forced alkaline diuresis is still advocated in today's practice (Figure 2).

It is generally accepted that urine pH should be kept above 6.5 to help prevent ARF (Better, 1990; Michaelson, 1992; Porter and Greaves, 2003). Although acidosis is known to protect kidneys against ischaemic ARF, alkalinisation will prevent the pigment nephropathy associated with crush syndrome (Better *et al.*, 1992). Bicarbonate can also counteract the hyperkalaemia produced after

crushing skeletal muscle. The earlier fluid resuscitation is started, the more likely ARF will be prevented. However, even if treatment is delayed, a forced alkaline diuresis can still prevent the need for dialysis (Oda *et al.*, 1997a; Ensari *et al.*, 2002).

Dangers with bicarbonate therapy include induction of metabolic alkalosis and metastatic calcification. Acetazolamide, a carbonic anhydrase inhibitor, can facilitate the alkalinisation of urine and can correct any metabolic alkalosis caused by overzealous use of bicarbonate (Better, 1990; Better *et al.*, 1992; Sahjian and Frakes, 2007). It can be given at a dose of 250 mg intravenously if the urine pH < 6.5 and the blood pH is alkaline (Michaelson *et al.*, 1984). Caution should be given, however, as metabolic

acidosis may be worsened. Administration of bicarbonate or acetazolamide should be titrated against urine output, urine pH and serum pH.

Mannitol

Mannitol is an osmotic diuretic and a free-radical scavenger. Its efficacy in prevention and treatment of ARF in dogs was first described in 1940, and then in 1961 in humans (Better *et al.*, 1992). By decreasing blood viscosity and dilating glomerular capillaries it can increase glomerular filtration rate and prevent obstruction in proximal tubules. Osmotic diuretics have a low molecular weight, are freely filterable and resist reabsorption creating an osmotic force in the tubules sufficient to retard the reabsorption of fluids and solutes (Better *et al.*, 1997). Inhibiting the reabsorption of sodium may also decrease the oxygen requirements of renal tubules and allow them to survive the metabolic insult. Increasing tubular flow rate dislodges and flushes obstructive, nephrotoxic myoglobin casts (Parry *et al.*, 1963).

By increasing extracellular and intravascular volume, venous return and cardiac output are improved. Mannitol is also positively inotropic and stimulates the release of atrial natriuretic factor and vasodilatory prostaglandins and inhibits the renin-angiotensin system (Better *et al.*, 1997).

Mannitol's ability to potently scavenge oxygen free-radicals prevents damage of renal parenchyma and cardiac and skeletal muscle caused on reperfusion (Walker *et al.*, 1987).

In the largest series of post-traumatic rhabdomyolysis patients studied to date, Brown *et al.* (2004) found that fluid therapy with mannitol and bicarbonate does not prevent ARF, the need for dialysis, or mortality in patients with a CK <30 000 U/L, but it did seem beneficial in patients with a CK >30 000 U/L. This article did not differentiate between rhabdomyolysis from different aetiologies. However, Oda *et al.* (1997b) postulated that patients with a crush injury to one limb of significant duration usually have a peak CK of $41\,143 \pm 4249$ U/L, two limbs of $109\,341 \pm 11\,566$ U/L and three limbs of $172\,524 \pm 36\,298$ U/L. Brown *et al.*'s (2004) theory would then suggest that mannitol is beneficial in crush injury.

Mannitol also has the ability to decrease intracompartmental pressure in crushed limbs and can

be used to prevent and treat compartment syndrome as discussed in Part 2: The local injury.

To treat oliguria between 20 and 300 mL/h 50–200 g (1–2 g/kg) mannitol may be used intravenously as a 15–20% solution over 24 h (Michaelson *et al.*, 1984; Better *et al.*, 1997). This should be given at a rate of 5/h added to each litre of infusate (Better, 1999). Anuric patients (<20 mL/h) should not routinely receive mannitol but a single test dose of 12.5 g may be given (Better *et al.*, 1997). Better *et al.* suggest that mannitol therapy should not be commenced until urine flow has been measured and documented (Better, 1999). However, in order to gain the maximum benefit as a potent scavenger of free-radicals, mannitol should be administered before, or as early after, reperfusion of the limb as possible (Walker *et al.*, 1987). Very high doses of mannitol appear to have a vasoconstrictive effect rather than its usual vasodilatory effects, and doses in excess of 200 g per day have, on rare occasions, produced ARF; so should be avoided (Dorman *et al.*, 1980). Mannitol-induced ARF is readily and rapidly reversible by haemodialysis (Better, 1999).

Allopurinol

Allopurinol is a xanthine oxidase inhibitor, so reduces the production of oxygen free radicals and protects against the 'oxygen paradox' and has been clinically proven to protect against myocardial necrosis. Free radical scavengers including allopurinol and mannitol should ideally be administered before crushed muscle is decompressed to protect against reperfusion syndrome and irreversible damage to ischaemic cells (Walker *et al.*, 1987). Allopurinol also reduces uric acid production which may cause further renal damage.

Other diuretics

In the first half of the 20th century, physicians used caffeine to raise the glomerular capillary pressure with a resultant increase in filtrate (Bywaters and Beall, 1941). Decapsulation of the kidney to reduce intra-renal pressures was also tried with varying success.

Loop diuretics such as furosemide have been postulated as possible means of restoring renal flow by renal vasodilation, prevention of obstruction and reducing renal oxygen demands (Better *et al.*, 1992;

Better, 1999). However, high-dose furosemide causes deafness, acidifies the urine promoting cast precipitation and does not obviate the need for dialysis (Brattebo *et al.*, 1991).

Dopamine can increase blood pressure and renal blood flow but prolonged use may result in the production of the neurotoxin 6-OH-dopamine (Better, 1999).

Angiotensin converting enzyme (ACE) inhibitors suppress renal angiotensin II production but can aggravate ARF when renal perfusion is compromised (Better, 1999). ACE inhibitors and calcium channel blockers also worsen hyperkalaemia and hypotension so are best avoided.

Amiloride and benzamil are potassium sparing diuretics that protect against cellular damage by the 'calcium paradox' during reperfusion. Their use is discussed further in Part 2: The local injury.

Calcium

Hypocalcaemia is common in crush syndrome but tetany is rarely seen. Calcium administered during rhabdomyolysis is rapidly sequestered in the injured muscle, so is unable to correct hypocalcaemia (Better, 1990). Administration of calcium is not, therefore, indicated unless there is a threat of hyperkalaemic cardiac arrhythmia (Brattebo *et al.*, 1991). Metastatic calcification may be precipitated causing further muscle damage (Better *et al.*, 1992). Also, as the clinical course of the crush syndrome progresses and myocytes die, calcium is released back into the systemic circulation causing a rebound hypercalcaemia (Vanholder *et al.*, 2000).

Dialysis and haemofiltration

The percentage of patients with crush syndrome requiring blood purification to treat ARF varies in the literature from 4% to 94% (Gabow *et al.*, 1982; Shigemoto *et al.*, 1997; Viroja *et al.*, 2003; Fernandez *et al.*, 2005). Better *et al.* demonstrated that if appropriate fluid resuscitation is begun within 6 h of extrication, myoglobinuric ARF can be prevented (Better and Stein, 1990). If commencement of treatment is delayed due to entrapment or lack of appropriate resources, then aggressive fluid therapy under close monitoring may still prevent the development of ARF (Ensari *et al.*, 2002). Oligo-anuria unresponsive to aggressive mannitol-alkaline

fluid therapy, volume overload or a rising serum potassium (>7 mEq/L) are indicators of the need for dialysis (An, 1984; Sever *et al.*, 2006).

Fernandez *et al.* (2005) found that the most valuable predictors of the need for dialysis are the initial creatinine and blood urea nitrogen at presentation. Shigemoto *et al.* (1997) also found that serum creatinine on admission was a good indicator of the need for blood purification, but they felt that levels of serum CK and myoglobin on admission were more significant predictors. They also correlated the initial CK and myoglobin levels with the length of blood purification required to return a urine output of over 500 mL/day. Patients in Shigemoto *et al.*'s study were treated with either haemodialysis, plasma exchange or continuous haemodiafiltration depending on the availability of each method at the time. The randomised selection of blood purification method avoided clinical bias and allowed for a comparison to be made. They concluded that vigorous removal of myoglobin prior to the development of ARF would be effective in treating crush syndrome, but once ARF was established, all blood purification methods are relatively ineffective in removing myoglobin. The method employed should, therefore, be selected on its ability to treat ARF, rather than eliminating myoglobin.

For logistical reasons, especially in coordinating mass casualties, it is important to predict how long dialysis should be continued. On average, dialysis is usually required 2–3 times daily for 13–18 days to restore renal function and urine flow (Shimazu *et al.*, 1997). All types of renal-replacement therapy, intermittent haemodialysis, continuous renal-replacement therapy and peritoneal dialysis should be considered depending on the logistical challenges of local provision (Solez *et al.*, 1993; Sever *et al.*, 2006).

Sepsis

The major cause of mortality from crush injury reported in the literature is overwhelming sepsis from wound infections, peritonitis or pneumonitis (Cossio, 1977; An, 1984). Open injuries should, therefore, be treated aggressively and measures should be taken to avoid a systemic inflammatory response syndrome and multi-organ failure. Intensive care monitoring, early aggressive

treatment of sepsis and prevention of nutritional deficiencies with high-calorie feeding saves lives (Rainford, 1978; Kracun and Wooten, 1998; Demirkiran *et al.*, 2003). The debate as to whether a developing compartment syndrome should be treated conservatively or with fasciotomy or amputation to prevent sepsis is discussed in Part 2: The local injury.

Mass disaster management

Many earthquake-prone areas lie in densely populated regions such as California, the Mediterranean, the Middle East and Southeast Asia. There is a 62% probability that an earthquake with a magnitude greater than 6.7 will strike the San Francisco Bay area before 2031 (Sever *et al.*, 2006). Other types of natural disasters have also recently affected densely populated areas (e.g. the Southeast Asian tsunami and hurricanes Katrina and Rita in the USA.) Natural disasters are difficult to predict and impossible to prevent but, as they affect ever more people, contingencies for rescue and treatment of patients should be pre-planned. Similarly, victims of war and terrorist attacks have been commonplace throughout history and, as technologies improve, numbers of casualties multiply.

The number and severity of casualties with crush-related injuries depends on many variables including the timing of the disaster, geologic features, the population density, the quality of buildings, the effectiveness of rescue activities, the time victims spend under rubble and the affected region's health-care infrastructure (Sever *et al.*, 2006). Constructing high quality buildings and affixing furniture to the walls can reduce the impact. Medical professionals living in disaster-prone areas should be familiar with the pathophysiology and treatment of crush syndrome. Due to an increasing number of terrorist attacks on our home soil, medical professionals all over the world should be prepared to treat crushed patients and blast injuries (Riley *et al.*, 2002; Raynovich, 2006).

Early extrication, diagnosis and aggressive fluid management are crucially important in preventing ARF in crush injuries. However, difficulties in communication and transport in the wake of disasters often delay diagnostic and therapeutic interventions (Ensari *et al.*, 2002; Demirkiran *et al.*,

2003). Transport problems can often be solved by collaboration between military and civilian groups (Redmond *et al.*, 1991; Better, 1999). Aftershocks often damage hospitals that were initially operational, requiring evacuation of patients (Better, 1999). Patients who are treated locally in often inadequate conditions have a higher risk of death than those treated in appropriate surroundings (Kuwagata *et al.*, 1997; Sever *et al.*, 2006).

In the aftermath of the Armenian earthquake in 1988, in which reported deaths range from 25 000 to 190 000, nearly 600 people developed ARF of which at least 225 required dialysis (Richards *et al.*, 1989; Eknayan, 1992). This second catastrophe was later termed the 'renal disaster' (Sever *et al.*, 2006). The poorly organised relief effort with its influx of volunteers and materials from around the world only worsened the chaos, creating further disaster (Solez *et al.*, 1993). Global logistic coordination from countries removed from the disaster is probably the most effective solution (Vanholder *et al.*, 2007b). Lessons learnt from the Armenian earthquake have improved international effectiveness in managing such disasters (Sever *et al.*, 2006).

The International Society of Nephrology's (ISN) Renal Disaster Relief Task Force (RDRTF) have developed an algorithm for the global and local coordination of relief efforts (Sever *et al.*, 2006; Vanholder *et al.*, 2007a). A scouting team sent to a disaster area can assess the potential number of victims with crush syndrome, the local health care infrastructure and the need for dialysis support. Pre-prepared supplies stored in warehouses in disaster-prone regions can then be rapidly mobilised within 3–4 days anywhere in the world. A key person is identified locally who coordinates a hub-and-spoke triage service to evacuate patients to areas with sufficient water, electricity and medical care facilities. Internationally coordinated relief organisations, such as Medecins sans Frontieres, can then be deployed where necessary to supplement local authorities (Lamiere *et al.*, 2003). Mobile clinical analysers used to measure prognostic indicators on extricated patients can help with the triage process (Kubota *et al.*, 2003).

The efforts of the RDRTF have been tested and refined since its setup after the Armenian earthquake in 1988. Its most significant contribution was in the 1999 earthquake in Marmara, Turkey, where dialysis was provided to 477 patients out of 639

diagnosed with crush syndrome (Vanholder *et al.*, 2001; Kantarci *et al.*, 2002; Demirkiran *et al.*, 2003). They have also coordinated rescue efforts in the 2001 earthquake in Gujarat, India, in the 2003 earthquake in Bam, Iran, in the 2005 earthquake in Kashmir, Pakistan and in the 2007 earthquake in Peru as well as providing relief efforts in Algeria (Harjai, 2001; Lamiere *et al.*, 2003; Vanholder, 2006; Vanholder *et al.*, 2007a, b).

Discussion

Crush injuries are treated infrequently and sporadically in Britain and delayed or inappropriate treatment can be rapidly fatal. The pathophysiology of crush syndrome is well documented but there is no consensus on how to diagnose and treat it. A history of a sustained crush injury for over 2–4 h should alert clinicians to an impending crush syndrome. Patients who present unconscious following injury or drug or alcohol intoxication should also be screened for possible crush injuries.

Pre-hospital management should always be delivered at an appropriate level depending on the responding clinicians training. Resuscitation of patients should follow the ATLS or BATLS protocols. Tourniquets should only be used to control catastrophic haemorrhage and not to prevent the effects of reperfusion syndrome unless very experienced medical or surgical personnel are close at hand. If crush injuries are treated within 6 h of extrication then ARF can still be prevented. Intravenous or intraosseous access should always be sought prior to extrication if possible and an infusion of normal saline started to pre-empt the hypotension and arrhythmias that invariably occur on reperfusion of the crushed limb.

Although mannitol has proven benefits if given before reperfusing crushed limbs, it is unsafe to give in anuric patients, so should be withheld until monitoring has begun and urine flow has been documented. Likewise, allopurinol has theoretical benefits if given pre-extrication, but there are no clinical trials to this effect in humans, so should be avoided until further research clarifies the matter.

Kayexalate should be administered by appropriately trained medical personnel if transfer to

definitive medical facilities will be delayed. Patients should also be actively warmed if core temperatures are low.

Patients should be evacuated to definitive medical care as quickly and safely as possible. In the event of a large scale disaster, coordination of relief efforts by international civilian and military groups can dampen the effects of a secondary 'renal disaster' from having to treat multiple crush syndromes simultaneously. Much of our current knowledge on crush injuries is thanks to data obtained from such global relief.

There are many diagnostic and prognostic laboratory tests proposed in the literature and their use may be limited by local laboratory technical abilities. All patients need to have basic monitoring as per ATLS plus continuous cardiac monitoring and hourly urine measurements if a crush syndrome is suspected. ATLS guidelines also dictate that blood tests should be sent for urea and electrolytes, acid-base balance, FBC, clotting, LFTs, calcium and amylase levels. Crushed patients should also have their serum CK measured and their urine dipstick for pH and the presence of haem; usually indicative of myoglobinuria rather than haematuria in this instance.

Blood and urine may also be tested for osmolalities, myoglobin and albumin levels by intensivists or nephrologists to aid prognosis. However, these tests will not alter initial management and are inappropriate to request in an emergency.

There is overwhelming evidence to support the use of forced alkaline diuresis and mannitol therapy. Keeping urine alkali prevents myoglobin cast formation and the development of ARF which is central to crush syndrome. A serum CK of >1000 IU is indicative of rhabdomyolysis and patients may develop ARF at these levels, especially if dehydrated. A serum CK level >5000–10 000 is statistically more likely to produce ARF but local protocols should be followed as to the threshold at which to commence a forced alkaline diuresis. Brown *et al.* (2004) suggest that a forced alkaline diuresis plus mannitol therapy are only beneficial if initial serum CK levels are greater than 30 000 U/L. The regime proposed by Reis and Better in Figure 2 has proven benefits in patients with a sound diagnosis of crush syndrome. The use of other diuretics to treat crush syndrome have not been proven on such a large scale as mannitol.

Fluid resuscitation needs to be aggressive in young patients who have no pre-existing cause to be cautious. The target urine output is over 8 L in 24 h (>300 mL/h), which may require a huge positive balance if tolerated. Oligo-anuria or rising serum potassium despite these measures should prompt urgent haemofiltration or dialysis. A multi-disciplinary approach should be sought from first presentation of a crush injury including emergency doctors, surgeons, intensivists and physicians.

Hypocalcaemia will potentiate the risk of arrhythmias, especially in the presence of hyperkalaemia. However, calcium therapy will do little to raise serum levels acutely as it will be rapidly absorbed by crushed muscle, compounding the local tissue damage and possibly causing a rebound hypercalcaemia once myocytes die.

Management of the systemic effects of crush syndrome has improved immensely over the last century and many more patients are surviving. The overwhelming cause of mortality in patients reaching definitive medical care is now from the systemic inflammatory response and sepsis. The most appropriate treatment of the crushed limb itself is still in debate and is discussed in Part 2: The local injury.

References

- Allister C.** 1983. Cardiac arrest after crush injury. *Brit Med J* **287**: 531–2.
- American College of Surgeons.** 2004. Hypothermia. In: *Advanced trauma life support*, 7th edn. Chap 3, Chicago: ACS, 81–2.
- Amoros E, Martin JL, Chiron M et al.** 2007. Road crash casualties: Characteristics of police injury severity misclassification. *J Trauma* **62**: 482–90.
- An LC.** 1984. Acute renal failure due to crush syndrome. A clinical analysis of 23 cases. *World J Urol* **2**: 234–35.
- Better OS.** 1990. The crush syndrome revisited (1940–1990). *Nephron* **55**: 97–103.
- Better OS.** 1999. Rescue and salvage of casualties suffering from the crush syndrome after mass disasters. *Mil Med* **164**: 366–69.
- Better OS, Rubinstein I, Winaver J.** 1992. Recent insights into the pathogenesis and early management of the crush syndrome. *Sem Nephrol* **12**: 217–22.
- Better OS, Rubinstein I, Winaver JM et al.** 1997. Mannitol therapy revisited (1940–1997). *Kidney Int* **51**: 886–94.
- Better OS, Stein JH.** 1990. Early management of shock and prophylaxis of acute renal failure in traumatic rhabdomyolysis. *N Engl J Med* **322**: 825–9.
- Bloom AI, Zamir G, Muggia M et al.** 1995. Torture rhabdomyorhexis – A pseudo-crush syndrome. *J Trauma* **38**: 252–4.
- Brattebo G, Wisborg T, Fredriksen K.** 1991. Crush injuries in arctic off-shore fisheries: Initial treatment to prevent acute renal failure. *Arct Med Res* **50**: 104–7.
- Brody SL, Wrenn KD, Wilber MM et al.** 1990. Predicting the severity of cocaine-associated rhabdomyolysis. *Ann Emerg Med* **19**: 1137–43.
- Brown CVR, Rhee P, Chan L et al.** 2004. Preventing renal failure in patients with rhabdomyolysis: Do bicarbonate and mannitol make a difference? *J Trauma* **56**: 1191–6.
- Bywaters EGL, Beall D.** 1941. Crush injuries with impairment of renal function. *Br Med J* **1**: 427–32.
- Bywaters EGL, Stead JK.** 1944. The production of renal failure following injection of solutions containing myohaemoglobin. *Q J Exp Physiol* **144**: 277–80.
- Campbell DA, Walker MA.** 1992. Hypothermia and the crush syndrome. *JR Coll Surg Edinb* **37**: 257–8.
- Cannon WB.** 1923. *Traumatic shock*. New York: Appleton.
- Cosgriff N, Moore EE, Sauaia A et al.** 1997. Predicting life-threatening coagulopathy in the massively transfused trauma patient: Hypothermia and acidosis revisited. *J Trauma* **42**: 857–62.
- Cossio PM.** 1977. Crush injuries. *Br Med J* **2**: 1244.
- Deakin CD.** 1995. Bilateral periorbital hematoma (Raccoon Eyes) following thoracic crush injuries: Case reports. *J Trauma* **38**: 816–7.
- Demirkiran O, Dikmen Y, Utku T et al.** 2003. Crush syndrome patients after the Marmara earthquake. *Emerg Med J* **20**: 247–50.
- Dente CJ, Shaz BH, Nicholas JM et al.** 2009. Improvements in early mortality and coagulopathy are sustained better in patients with blunt trauma after institution of a massive transfusion protocol in a civilian level 1 trauma center. *J Trauma* **66**: 1616–24.
- Dixon CM, Hricak H, McAninch JW.** 1992. Magnetic resonance imaging of traumatic posterior urethral defects and pelvic crush injuries. *J. Urology* **148**: 1162–5.
- Dorman HR, Sondheimer JH, Cadnapaphornchai P.** 1980. Mannitol induced acute renal failure. *Medicine* **69**: 153–9.
- Duhaime A-C, Eppley M, Margulies S et al.** 1995. Crush injuries to the head in children. *J Neurosurg* **37**: 401–7.
- Edwards AT, Williams IM, Griffith GH.** 1990. Damage to the abdominal aorta following crush injury. *Injury* **21**: 408–9.
- Eknayan G.** 1992. Acute renal failure in the Armenian earthquake. *Ren Fail* **14**: 241–4.

- Ensari C, Tufekcioglu O, Ayli D et al.** 2002. Response to delayed fluid therapy in crush syndrome. *Nephron* **92**: 941–3.
- Fernandez WG, Hung O, Bruno GR et al.** 2005. Factors predictive of acute renal failure and need for hemodialysis among ED patients with rhabdomyolysis. *Am J Emerg Med* **23**: 1–7.
- Ferrara A, MacArthur FJ, Wright HK et al.** 1990. Hypothermia and acidosis worsen coagulopathy in the patient requiring massive transfusion. *Am J Surg* **160**: 515–8.
- Fleming WH, Bowe JC.** 1973. Control of hemorrhage in pelvic crush injuries. *J. Trauma* **13**: 567–70.
- Furuya Y.** 1981. Experimental traumatic asphyxia, grades of thoracic compression and mortality. *Igaku Kenkyu* **51**: 117–9.
- Gabow PA, Kaehny WD, Kelleher SP.** 1982. The spectrum of rhabdomyolysis. *Medicine* **61**: 141–52.
- Gentilello LM, Cobean R, Offner P et al.** 1992. Continuous arteriovenous rewarming: Rapid reversal of hypothermia in critically ill patients. *J Trauma* **32**: 316–27.
- Gentilello LM, Jurkovich GJ, Stark MS et al.** 1997. Is hypothermia in the major trauma victim protective or harmful? A randomized, prospective study. *Ann Surg* **226**: 439–49.
- Gentilello LM, Pierson DJ.** 2001. Trauma critical care. *Am J Respir Crit Care Med* **163**: 604–7.
- Goldfarb DS, Chung S.** 2002. The absence of rhabdomyolysis-induced renal failure following the world trade center collapse. *Am J Med* **113**: 260.
- Gurd AR, Wilson RI.** 1974. The fat embolism syndrome. *J Bone Joint Surg* **56B**: 408–16.
- Harjai MM.** 2001. Crush syndrome revisited; letter to editor. *Med J Armed Forces India.* **57**: 350.
- Heppenstall RB, Scott R, Sapega A et al.** 1986. A comparative study of the tolerance of skeletal muscle ischaemia: Tourniquet application compared with acute compartment syndrome. *J Bone Joint Surg* **68-A**: 820–8.
- Hodgetts TJ, Mahoney PF, Russell MQ et al.** 2006. ABC to <C>ABC: Redefining the military trauma paradigm. *Emerg Med J* **23**: 745–6.
- Johnston TD, Chen Y, Reed RL II.** 1989. Relative sensitivity of the clotting cascade to hypothermia. *Surg Forum* **40**: 199–201.
- Jurkovich GJ, Greiser WB, Luteran A et al.** 1987. Hypothermia in trauma victims: An ominous predictor of survival. *J Trauma* **27**: 1019–24.
- Kantarci G, Vanholder R, Tuglular S et al.** 2002. Acute renal failure due to crush syndrome during the Marmara earthquake. *Am J Kidney Diseases* **40**: 682–89.
- Kracun MD, Wooten CL.** 1998. Crush injuries: A case of entrapment. *Crit Care Nurs Q* **21**: 81–6.
- Krost WS, Mistovich JJ, Limmer DD.** 2008. Beyond the basics: Crush injuries and compartment syndrome. *Emerg Med Services* **37**: 67–73.
- Kubota M, Ishida H, Kojima Y et al.** 2003. Impact of mobile clinical analysers on disaster medicine: A lesson from crush syndrome in the 1995 Hanshin-Awaji earthquake. *Biomed Instrumentation Technol* **37**: 259–62.
- Kuwagata Y, Oda J, Tanaka H et al.** 1997. Analysis of 2702 traumatized patients in the 1995 Hanshin-Awaji earthquake. *J Trauma* **43**: 427–32.
- Lakstein D, Blumfield A, Sokolov T et al.** 2003. Tourniquets for hemorrhage control on the battlefield: A 4 year accumulated experience. *J Trauma* **54**: S221–5.
- Lamiere N, Mehta R, Vanholder R et al.** 2003. The organisation and interventions of the ISN Renal Disaster relief Task Force. *Adv Ren Replace Ther* **10**: 93–9.
- Lee C, Porter KM, Hodgetts TJ.** 2007. Tourniquet use in the civilian prehospital setting. *Emerg Med J* **24**: 584–7.
- Lee MC, Wong SS, Chu JJ et al.** 1991. Traumatic asphyxia. *Ann Thorac Surg* **51**: 86–8.
- Majeski J.** 2001. Shoulder restraint injury to the female breast: A crush injury with long-lasting consequences. *J Trauma* **50**: 336–8.
- Malinoski DJ, Slater MS, Mullins RJ.** 2004. Crush injury and rhabdomyolysis. *Crit Care Clinics* **20**: 171–92.
- Malone DL, Hess JR, Fingerhut A.** 2006. Massive transfusion practices around the globe and a suggestion for a common massive transfusion protocol. *J Trauma* **60**: S91–6.
- Martin LVH.** 1993. Crush injuries of the chest. An historical perspective in a single unit. *JR Coll Surg Edinb* **38**: 4–8.
- Michaelson M.** 1992. Crush injury and crush syndrome. *World J Surg* **16**: 899–903.
- Michaelson M, Taitelman U, Bshouty Z et al.** 1984. Crush syndrome: Experience from the Lebanon war, 1982. *Isr J Med Sci* **20**: 305–7.
- Moorhouse I, Thurgood A, Walker N et al.** 2007. A realistic model for catastrophic external haemorrhage training. *JR Army Med Corps* **153**: 99–101.
- Muckart DJJ, Moodley M, Naidu et al.** 1992. Prediction of acute renal failure following soft-tissue injury using the venous bicarbonate concentration. *J Trauma* **33**: 813–17.
- Nishihara G, Nakamoto M, Yasunaga C et al.** 1997. Adult respiratory distress syndrome associated with crush syndrome. *Nephron* **75**: 488–9.
- Oda Y, Shindoh M, Yukioka H et al.** 1997a. Crush syndrome sustained in the 1995 Kobe, Japan, earthquake; treatment and outcome. *Ann Emerg Med* **30**: 507–12.
- Oda J, Tanaka H, Yoshioka T et al.** 1997b. Analysis of 372 patients with crush syndrome caused by the Hanshin-Awaji earthquake. *J Trauma* **42**: 470–6.

- Odeh M. 1991. The role of reperfusion-induced injury in the pathogenesis of the crush syndrome. *New Eng J Med* **324**: 1417–21.
- Ollivier d-A. 1837. Relation medicale des envennements survenus au Champ-de-mars le 14 juin, 1837. *Ann D'hyg* **18**: 485.
- Parry WL, Schaefer JA, Mueller CB. 1963. Experimental studies of acute renal failure. 1. The protective effect of mannitol. *J Urol* **89**: 1–6.
- Pohlman TH, Bjerke HS. 2007. Trauma scoring systems. Available at: <http://emedicine.medscape.com/article/434076-overview> (accessed 16 July 2007).
- Porter K, Greaves I. 2003. Crush injury and crush syndrome: A consensus statement. *Emerg Nurse* **11**: 26–30.
- Prasad MR, Ewing-Cobbs L, Baumgartner J. 1999. Crush injuries in infants and young children: Neurologic and neuropsychologic sequelae. *J Child Neurol* **14**: 496–501.
- Presta M, Ragnotti G. 1981. Quantification of damage to striated muscle after normothermic or hypothermic ischemia. *Clin Chem* **27**: 297–302.
- Rainford DJ. 1978. Crush injuries. Letter to editor. *Br Med J* **1**: 51.
- Raynovich W. 2006. Crushed. How proper treatment of crush syndrome saved police Sgt. John McLoughlin after 22 hours under WTC rubble. *J Emerg Med Services* **31**: 58–65.
- Rechner P, Cogbill TH. 2001. Transanal small bowel evisceration from abdominal crush injury: Case report and review of the literature. *J Trauma* **50**: 934–6.
- Redmond AD, Watson S, Nightingale P. 1991. The south Manchester accident rescue team and the earthquake in Iran, June 1990. *Br Med J* **302**: 1521–3.
- Reed RL II, Ciavarella D, Heimbach DM *et al.* 1986. Prophylactic platelet administration during massive transfusion: A prospective, randomized, double-blind clinical study. *Ann Surg* **203**: 40–8.
- Reis ND, Better OS. 2005. Mechanical muscle-crush injury and acute muscle-crush compartment syndrome. *J Bone Joint Surg* **87-B**: 450–3.
- Reis ND, Michaelson M. 1986. Crush injury to the lower limbs: Treatment of the local injury. *J Bone Joint Surg (Am)* **68-A**: 414–18.
- Revell M, Porter K, Greaves I. 2002. Fluid resuscitation in prehospital trauma care: A consensus view. *Emerg Med J* **19**: 494–8.
- Richards NT, Tattersall J, McCann M *et al.* 1989. Dialysis for acute renal failure due to crush injuries after the Armenian earthquake. *Br Med J* **298**: 443–5.
- Riley D, Clark M, Wong T. 2002. World Trade Centre terror: Explosion trauma – blast, burns and crush injury. *Top Emerg Med* **24**: 47–59.
- Ron D, Taitelman U, Michaelson M *et al.* 1984. Prevention of acute renal failure on traumatic rhabdomyolysis. *Arch Intern Med* **144**: 277–80.
- Rubinstein I, Abassi Z, Coleman R *et al.* 1998. Involvement of nitric oxide system in experimental muscle crush injury. *J Clin Invest* **101**: 1325–33.
- Sahjian M, Frakes M. 2007. Crush injuries: Pathophysiology and current treatment. *Nurs Practitioner* **32**: 13–18.
- Santangelo ML, Usberti M, Di Salvo E *et al.* 1982. A study of the pathology of the crush syndrome. *Surg Gynecol Obstet* **154**: 372–4.
- Schoenfield A, Warchaizer S, Royburt M *et al.* 1995. Crush injury in pregnancy: An unusual experience in obstetrics. *Obstet Gynaecol* **86**: 655–6.
- Sever MS, Ereke E, Vanholder R *et al.* 2003. Serum potassium in the crush syndrome victims of the Marmara disaster. *Clin Nephrol* **59**: 326–33.
- Sever MS, Vanholder R, Lameire N. 2006. Management of crush-related injuries after disasters. *New Eng J Med* **354**: 1052–63.
- Shigemoto T, Rinka H, Matsuo Y *et al.* 1997. Blood purification for crush syndrome. *Renal Failure* **19**: 711–19.
- Shimazu T, Yoshioka T, Nakata Y *et al.* 1997. Fluid resuscitation and systemic complications in crush syndrome: 14 Hanshin-Awaji earthquake patients. *J Trauma* **42**: 641–6.
- Sinert R, Kohl L, Rainone T *et al.* 1994. Exercise-induced rhabdomyolysis. *Ann Emerg Med* **23**: 1301–6.
- Solez K, Bihari D, Collins AJ *et al.* 1993. International dialysis aid in earthquakes and other disasters. *Kidney Int* **1993**. **44**: 479–83.
- Stewart CE. 1999. Crush syndrome, traumatic asphyxia and compartment syndrome. *Emerg Med Services* **28**: 51–61.
- Stewart IP. 1987. Major crush injury. *Br Med J* **294**: 854–5.
- Stewart RD, Young JC, Kenney DA *et al.* 1979. Field surgical intervention: An unusual case. *J Trauma* **19**: 780–3.
- Tomkins RG, McCabe CJ, Burke JF *et al.* 1988. Rectal necrosis after pelvic crush injury. *J Trauma* **28**: 697–9.
- Tortosa JG, Martinez-Lage JF, Poza M. 2004. Bitemporal head crush injuries: Clinical and radiological features of a distinctive type of head injury. *J Neurosurg* **100**: 645–51.
- Tortosa JG, Poza M. 1996. Crush injuries to the head. *J Neurosurg* **39**: 877–8.
- Tscherne H, Pohlemann T, Gansslen A *et al.* 2000. Crush injuries of the pelvis. *Eur J. Surg* **166**: 276–82.
- Valeri CR, Feingold H, Cassidy G *et al.* 1987. Hypothermia induced reversible platelet dysfunction. *Ann Surg* **205**: 175–81.
- Vanholder R. 2006. Intervention of the renal disaster relief task force (RDRTF) in the Kashmir earthquake. *Nephrol Dial Transplant* **21**: 40.
- Vanholder R, Sever MS, De Smet M *et al.* 2001. Intervention of the RDRTF in the 1999 Marmara, Turkey earthquake. *Kidney Int* **59**: 783–91.

- Vanholder R, Sever MS, Ereik et al.** 2000. Rhabdomyolysis. *J Am Soc Nephrol* **11**: 1553–61.
- Vanholder R, Van Biesen W, Lameire N et al.** 2007a. The role of the ISN's RDRTF in the rescue of renal disaster victims. *Contrib Nephrol* **156**: 325–32.
- Vanholder R, van der Tol A, De Smet M et al.** 2007b. Earthquakes and crush syndrome casualties: Lessons learned from the Kashmir disaster. *Kidney Int* **71**: 17–23.
- Viroja D, Shah P, Trivedi HL et al.** 2003. Management of crush syndrome following Gujarat earthquake – Jan 2001. *Nephrol Dial Transplant* **18**: 659–60.
- Walker PM, Lindsay TF, Labbe R et al.** 1987. Salvage of skeletal muscle with free radical scavengers. *J Vasc Surg* **5**: 68–75.
- Ward MM.** 1988. Factors predictive of acute renal failure in rhabdomyolysis. *Arch Intern Med* **148**: 1553–7.
- Weeks RS.** 1968. The crush syndrome. *Surg Gynecol Obstet* **127**: 369–75.
- Williams JS, Minken SL, Adams JT.** 1968. Traumatic asphyxia – reappraised. *Ann Surg* **167**: 384–92.
- Welbourn CRB.** 1991. 50 years on: The crush syndrome. Letter to editor. *Br Med J* **302**: 238.
- Wyse MK, Mitra S.** 2000. Rapid onset pulmonary contusion after severe crush injury. *Pre-hosp Immed Care* **4**: 105–6.