Poisonous Snakebites

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Background: little evidence-based medicine available on treatment of snakebites; majority of poisonous snakes do not inject venom at time of bite; 70% of victims deliberately handling snakes at time of bite (some occur during gardening)

Physiologic consequences of snakebites: tissue loss, hemolysis, neurologic paralysis, respiratory arrest, and coagulopathy; complications of treatment exceed all other risks combined

Overview of treatment: traditional “cut and suck,” electric shock, and cryotherapy probably have no role; treatment with antivenin usually suggested early, but, per speaker, “ought to be thought of last”; antivenins expensive (sold by manufacturer for $1000 per vial, and resold by hospitals to patient for $5000)

Crotalidae polyvalent immune fab (Crofab): currently, only antivenin in United States; recommended only for Crotalidae bites; according to package insert, indicated for severe envenomation with extensive local swelling and progression (almost never seen), extensive coagulopathy, and some systemic effects; not recommended for non-rattlesnake bites; administration of 7 to 10 vials recommended; complications — risk for serum sickness (immediate or delayed) 30% after administration of one vial; risk increases with previous exposures; if immunoglobulin measured, reaction detected in almost 100% of patients

Clinical approach to snakebite: obtain information about snake and patient, history of allergies, and tetanus immunization status; physical examination — record extent of localized swelling and progression by marking skin (envenomation typically minor or absent)

Determining whether treatment required: draw complete blood count and clotting studies; provide tetanus prophylaxis (wound at risk for tetanus); measure and record amount of swelling; give broad-spectrum antibiotics; measure compartment pressures; do not give antivenin unless truly indicated; evaluate articular surfaces (when involved, open and irrigate); evaluate depth of bite; observe patients for breathing and urologic complications, and monitor clotting

Speaker’s experience: over 45 yr, only 2 patients received antivenin (given by transferring hospital in both cases); morbidity included one lost digit (necrotic on admission); 10% underwent some treatment for coagulopathy; 15% underwent limited fasciotomy of hands; 6 patients admitted to intensive care unit (ICU); no patients intubated; both patients who received antivenin developed delayed serum sickness; similar results reported in 4 studies of patients in Texas, including pediatric population

Delirium and Altered Consciousness in the ICU: Why Surgeons Should Know About It

Alison Wilson, MD, Associate Professor of Surgery, Director, Jon Michael Moore Trauma Center, and Chief, Trauma, Emergency Surgery and Surgical Critical Care, West Virginia University, School of Medicine, Morgantown

Definition of delirium: acute onset of cerebral dysfunction with altered consciousness; may be hyperactive, hypoactive, or mixed; hypoactive type associated with poorer outcomes and more frequently misdiagnosed; other characteristics — reduced focus and attention; change in cognition; deficits in memory and language; disorientation and delusions

Clinical importance of delirium: associated with increases in length of ICU and hospital stays, days on ventilator, risk for infection, and mortality rates at 6 and 12 mo; risk for mortality increases 10% for each day of delirium; cognitive functional state decreased at 6 mo; expensive

Risk factors: nonmodifiable — preexisting dementia; hypertension; alcoholism; high severity of illness at admission; modifiable — ambient noise in ICU; immobilization; administered and withheld medications; lack of sleep; mechanical ventilation; electrolyte abnormalities; pain

Medications associated with delirium: opioids; promethazine (eg, Phendoz, Phenergan, Promethegan); anticholinergics; medications for seizure prophylaxis; benzodiazepines (should be avoided); withheld medications — selective serotonin reuptake inhibitors should not be stopped abruptly (patients can enter catatonic-like state; medications for Parkinson disease or dementia; acute withdrawal of anxiolytic medications can be life threatening

Sleep deprivation: rapid eye movement (REM) and non-REM 2 major cycles of sleep; non-REM sleep — characterized by active brain activity but decreased metabolism, with 3 stages of progressively deeper sleep; detected as slow-wave sleep; REM sleep — brain active but skeletal muscle atony present; considered restorative sleep; multiple studies of ICU show sleep fragmented, with little or no REM component

Educational Objectives

The goal of this program is to improve the nonsurgical care of surgical patients. After hearing and assimilating this program, the clinician will be better able to:

1. Recommend appropriate management for patients with snakebites.
2. Cite major risk factors for the development of delirium in the intensive care unit.
3. Assess evidence on the effects of hyperglycemia in surgical patients.
4. Outline approaches to achieve glycemic control in surgical patients.
5. Recognize the role of biologic agents in the treatment of inflammatory bowel disease.

Faculty Disclosure

In adherence to ACCME Standards for Commercial Support, Audio Digest requires all faculty and members of the planning committee to disclose relevant financial relationships within the past 12 months that might create any personal conflicts of interest. Any identified conflicts were resolved to ensure that this educational activity promotes quality in health care and not a proprietary business or commercial interest. For this program, the following has been disclosed: Dr. Dellinger receives grant support from, serves on the advisory boards for, and/or lectures for honoraria for Merck & Co, Baxter, Janssen Pharmaceuticals, Targanta Therapeutics, Astellas Pharm US, CareFusion, Durata Therapeutics, Pfizer, Applied Medical Resources, Rib-X Pharmaceuticals, Affinium Pharmaceuticals, Tetraphase Pharmaceuticals, and 3M. Dr. Mattox reported nothing to disclose. Dr. Wilson reported nothing to disclose. Dr. Hyman reported nothing to disclose. The planning committee reported nothing to disclose.
Physiologic consequences of sleep deprivation: decreased immune response; altered metabolic and endocrine responses; increased sensitivity to pain; altered cardiac modulation

Sedation: decreases N3 (deep non-REM sleep) and REM sleep; excessive sedation linked to morbidity, mortality, and increased cost, even after 48 hr; Society of Critical Care Medicine states that harm likely from iatrogenic coma; use of benzodiazepines represents independent predictor of delirium; appropriate use of sedation — goal should be light sedation (defined as awakening to voice) with scheduled awakenings; fewer ventilation days and lower rates of morbidity and mortality seen with light sedation than with heavier sedation

Assessment of sedation: objective measurement with, eg, Sedation Agitation Scale, Richmond Agitation-Sedation Scale recommended (have high interrater reliability; validated); implement protocol-driven sedation practices; incorporate sedation holidays

Choice of medications for sedation: several studies have shown non-benzodiazepines associated with lower ICU and ventilator days; intermittent administration of benzodiazepines linked to fewer days on ventilator and shorter ICU stays, compared with continuous infusion

Environmental modifications: control noise; have lights turned on during day and turned off at night; minimize sedation (instead, focus on pain control); cluster activities and procedure times; modify position of patient; encourage early mobilization

Early mobilization: randomized trial (Schweickert et al, 2009) — associated with decreases in incidence of delirium, need for deep sedation, and length of ICU and hospital stays; ventilator-free days increased; cognition and function after discharge improved; mobilization of ICU patients — possible with patients on mechanical ventilation or vasopressors; patients with open abdomens can be mobilized if adequate abdominal support provided (requires cooperation with physical and occupational therapists)

Monitoring patients for delirium: should be documented at least once per shift; validated ICU tool should be used; because delirium can occur within 24 hr of admission to ICU, monitoring should be part of nursing assessment from onset of ICU stay

Treatment of delirium: no pharmacologic prevention available; avoid benzodiazepines for treatment; haloperidol — ability to prevent delirium not supported by strong level 1 evidence; however, practice of substituting atypical antipsychotic medication (AAP; eg, quetiapine [Seroquel]) for haloperidol to avoid prolonged QT interval illogical because AAPs associated with greater risk of producing this effect (and have much higher cost)

Perioperative Glucose Control: Is It Only for Cardiac Surgery?

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Glucose control in cardiac surgery patients: National Surgical Quality Improvement Project (NSQIP) requires glucose management; Vanderbilt study (2000) — risk for infection increased with increasing postoperative glucose, but no association seen with preoperative hyperglycemia or elevated hemoglobin A1c (HbA1c); risk increased in those with diagnosed or undiagnosed diabetes, and in any patient with postoperative glucose >200 mg/dL; 47% of patients with postoperative hyperglycemia not diabetic; report by Furnary et al demonstrated that risk for infection increased 27% for every 20 mg/dL increase in mean glucose; mean of glucose measurements over entire hospitalization much higher than single measurement; HbA1c not associated with complications; for patients undergoing bariatric surgery with poor glucose control, speaker admits 1 day prior to surgery and administers insulin drip to achieve tight glucose control

Surgical Case Outcomes Assessment Program (SCOAP): examined 11,000 patients undergoing bariatric procedure or colectomy across state of Washington over 5-yr period; compared patients with glucose levels above and below 180 mg/dL on day of surgery or first 2 days postoperatively; 30% of hyperglycemic patients not diabetic; rates of infection and complications much higher in patients with glucose >180 mg/dL; in hyperglycemic patients, risk for infection higher in nondiabetic patients than in diabetic patients; in hyperglycemic patients, treatment with insulin beneficial even if glucose remains above 180 mg/dL

Cleveland Clinic study: examined 2500 nondiabetic patients undergoing colectomy; two-thirds of patients had blood glucose >125 mg/dL; mortality, sepsis, surgical site infection, and reoperation all substantially increased with glucose >125 mg/dL

Pathophysiologic effects of hyperglycemia: inactivates IgG; decreases complement activation; increases collagenase activity; impairs leukocyte function; impairs ischemic preconditioning; reduces collateral blood flow; has effects on blood pressure and cardiac rhythm; effects on platelets may lead to risk for cardiac complications in perioperative period; effects of insulin administration — inhibits lipolysis; inhibits inflammatory growth factors important in myocardial infarction; stimulates endothelial nitric oxide synthase, which improves perfusion of peripheral tissues

Optimum glucose level: not established; while hyperglycemia increases risk for surgical-site and other infections, tight glucose control may also be detrimental because hypoglycemia (especially in operating room and immediate postoperative period) increases risk for mortality

Establishing glucose control program: requires participation of endocrinology, pharmacy, surgery, anesthesiology, and nursing; extensive web resources with algorithms available

Managing Inflammatory Bowel Disease in the Era of Biologic Agents

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Two categories of biologic agents: monoclonal antibodies against tumor necrosis factor (TNF)-α — TNF-α increased in patients with inflammatory bowel disease (IBD); drugs include infliximab (Remicade), adalimumab (Humira), certolizumab pegol (Cimzia), and golimumab; leukocyte inhibitors — prevent adhesion of leukocytes to vascular endothelium or epithelium; natalizumab (Tysabri) nonselective blocker and associated with multifocal leukoencephalopathy (MLE); vedolizumab selective blocker (no cases of MLE reported)

Use of biologic agents for IBD: infliximab approved in 1998 for Crohn disease (CD) and in 2005 for ulcerative colitis (UC); biologic agents expensive

Infliximab: combination of human and mouse antibodies; antibody response to murine component attenuates effect; patients often receive immunomodulator (eg, 6-mercaptopurine or methotrexate) concurrently to prevent formation of antibodies; with postoperative glucose >150 mg/dL; same trends seen in general surgery; RABBIT 2 trial — randomized diabetic patients to basal bolus of insulin, followed by long-acting insulin for half of insulin needs and adjustments for measured glucose; vs insulin administration per sliding scale; results showed modest improvement in mean daily glucose; rates of infection and complications reduced to one-third of control arm; glucose control in bariatric surgery — Perna et al demonstrated that risk for infection increased 27% for every 20 mg/dL increase in mean glucose; mean of glucose measurements over entire hospitalization more significant than single measurement; HbA1c not associated with complications; for patients undergoing bariatric surgery with poor glucose control, speaker admits 1 day prior to surgery and administers insulin drip to achieve tight glucose control
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Adalimumab and certolizumab pegol human derived, so less anti-body response produced.

Clinical trials: in randomized placebo-controlled trial of patients with CD, rate of remission at 1 yr 28% with infliximab vs 14% in placebo arm; CHARM trial — compared weekly injection of adalimumab to placebo; rate of remission 41% in treatment arm; ENACT-2 — rate of remission with natalizumab 55% at 60 wk; certolizumab pegol trial — initial response rate 64% in treatment arm; among initial responders, 50% had sustained remission at 26 wk.

Toxicity: all patients should be tested for tuberculosis because biologic agents may reactivate latent disease; may reactivate hepatitis B; new onset of multiple sclerosis reported.

Use of biologic agents in presence of abscess: large abscesses should be drained before initiation of therapy; for small abscesses, biologic agents may be safe, but concomitant administration of antibiotics probably advisable.

Role of biologic agents in preventing surgery: 60% of cost of caring for IBD patients attributed to hospital costs (including surgery); therefore, even expensive medical therapy may be cost-effective if it prevents surgery; Fagen et al showed 7-fold reduction in need for surgery at 1 yr (however, this may represent delay rather than reduction in need for surgery).

Effects of biologic agents on operative morbidity: in one series of patients with CD treated with infliximab, no differences seen in leak or infection rates; however, Cleveland Clinic series demonstrated link between infliximab and postoperative complications; however, results may reflect bias (ie, sicker patients receive infliximab); half-life of infliximab 9 to 10 days, yet one report showed that higher complication rates seen in patients treated with biologic agents reported to persist for 1 yr; literature predominantly suggests that biologic agents increase complication rates, but more so in UC than in CD.

Use of biologic agents in perianal CD: obvious abscesses should be drained; in equivocal cases, perform examination under anesthesia and place drainage setons to control sepsis; infliximab may then be given at 0, 2, and 6 wk; setons removed at 6 wk; one-third of fistulas heal, one-third improve, and no efficacy seen in one-third.

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NONSURGICAL TOPICS FOR THE SURGEON

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To submit a test form by mail or fax, complete Pretest section before listening and Posttest section after listening.

1. What percentage of patients who receive Crotalidae polyvalent immune fab (Crofab) for snakebite develop serum sickness?
   (A) 5%  (B) 10%  (C) 20%  (D) 30%

2. Which of the following is not recommended for routine care of a patient admitted to the hospital for snakebite?
   (A) Measurement of compartment pressure
   (B) Administration of antivenin
   (C) Administration of broad-spectrum antibiotics
   (D) Performance of complete blood count and clotting studies

3. Acute withdrawal of which of the following medications can be life threatening?
   (A) Selective serotonin uptake inhibitors
   (B) Antiparkinson medications
   (C) Dementia medications
   (D) Anxiolytics

4. Patients in the intensive care unit often suffer physiologic consequences of:
   (A) Excessive rapid eye movement (REM) sleep
   (B) Insufficient REM sleep
   (C) Excessive non-REM sleep
   (D) Insufficient non-REM sleep

5. Which of the following has been shown to be an independent risk factor for delirium?
   (A) Use of benzodiazepines
   (B) Sleep deprivation
   (C) Sedation
   (D) All the above

6. Which of the following is a contraindication for mobilization of a patient?
   (A) Mechanical ventilation
   (B) Administration of vasopressors
   (C) An open abdomen
   (D) None of the above

7. Which of the following statements about glucose control in cardiac surgery patients is true?
   (A) Elevated hemoglobin A1c is associated with increased risk for postoperative infection
   (B) Preoperative hyperglycemia is associated with increased risk for postoperative infection
   (C) Postoperative hyperglycemia does not increase risk for infection in nondiabetic patients
   (D) Glycemic control reduces mortality rates in diabetic patients to rates typical of nondiabetic patients

8. Findings of the Surgical Case Outcomes Assessment Project (SCOAP), which investigated glycemic control in patients undergoing bariatric surgery or colectomy, included which of the following?
   (A) 80% of hyperglycemic patients were nondiabetic
   (B) The rate of infection was significantly higher in patients with blood glucose >130 mg/dL
   (C) Among patients with hyperglycemia, the risk for infection was higher in nondiabetic patients than in diabetic patients
   (D) When insulin failed to achieve glycemic control, there was no reduction in risk for infection

9. Which of the following biologic agents is associated with multifocal leukoencephalopathy?
   (A) Certolizumab pegol
   (B) Golimumab
   (C) Vedolizumab
   (D) Natalizumab

10. Which of the following biologic agents is derived from a combination of human and mouse antibodies?
    (A) Infliximab
    (B) Adalimumab
    (C) Certolizumab pegol
    (D) Vedolizumab

Answers to Audio Digest General Surgery Volume 61, Issue 21: 1-D, 2-C, 3-D, 4-C, 5-A, 6-B, 7-B, 8-B, 9-A, 10-C