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Rush University Medical Center

REVIEW OF SURGERY

SIXTH EDITION

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FOREWORD

The 6th edition of the *Rush University Medical Center Review of Surgery* is dedicated to our current and former General Surgery residents who have been an integral part of our program since the book's inception in 1988. This book is intended to address the needs of those preparing for the board examination as well as those who need to maintain an up to date knowledge for the maintenance of certification examination. We thank all of you for motivating us to become better surgeons and for helping us to deliver the best care for our patients. We hope you benefit from this book.

DEDICATIONS

This book is dedicated to my wife, Beth, and my children, Jack and Megan, for their ongoing love and support and keeping me focused on the important things in life.
Jonathan A. Myers, MD

To my lovely wife, Kristin, and our twins, Henry and Emma.
Minh B. Luu, MD

To my parents, John and Joan, for making it all possible.
To my wife, Janet, for her never-ending understanding and support of my career.
To my children, Keith, Michael, Kyle, Kameron, Samantha, and John, for inspiring my optimism for the future.
Keith W. Millikan, MD

To my wonderful and supportive wife, Ethel Seltzer, and our children, Roxanne, Daniel, David, Peter, and Nora.
Bruce A. Orkin, MD

For SAKER5
Steven D. Bines, MD

To my parents, Ed and Lois, my wife, Michelle, and my children, Andrew, David, and Luke.
Edward F. Hollinger, MD, PhD

PREFACE

The editors of the *Rush University Medical Center Review of Surgery* are pleased to present the 6th edition of this book.

This edition includes 35 chapters divided into 9 sections. Four chapters that were deemed less relevant to board preparation were eliminated, and several sections were reconfigured. All remaining chapters were updated and enhanced to impart the most up-to-date knowledge to the reader. Each subject was once again based on current practice and referenced with widely read textbooks of surgery.

Contributions for this text were solicited from more than 60 active clinicians, all presently or formerly affiliated with Rush University. Topics cover current knowledge in the rapidly evolving field of medicine, incorporating surgical care, basic science, patient safety, core competencies, and multispecialty disease-driven care.

We are confident that the 6th edition of the *Rush University Medical Center Review of Surgery* will continue to provide a basis for the reader to gain the knowledge needed in general surgery and associated specialties and serve as a primer to those preparing for certification exams.

ACKNOWLEDGMENTS

The editors wish to recognize the achievements of the outstanding group of contributors whose efforts were invaluable to the completion of this book. The associate editors provided tremendous energy in selecting authors, maintaining deadlines, and delivering stellar work.

This edition could not have been completed without the tireless work of Kathy Martin, who led the charge to piece together all components of this text and seamlessly coordinate our efforts. Thank you to Skye Unrein and Shannon Patrick for their administrative assistance and to the excellent staff at Elsevier for their direction.

We would not be here today were it not for the groundwork laid by former editors of the previous editions of this book including Steven Economou, Daniel Deziel, Thomas Witt, Theodore Saclarides, Edgar Staren, Richard Prinz, Walter McCarthy, and Linnea Hauge. Finally, a heartfelt thanks to Jose Velasco, the 5th edition senior editor, for his mentorship and guidance on this project.

HOW TO USE

The topics in the 6th edition have been divided into 35 chapters, split into 9 sections, which should facilitate a review of the material for certification, or maintenance of certification, in general surgery.

Each section contains a variable number of chapters, encompassing questions, and the corresponding comments and references attached to each question. Most questions are followed by one or more references that link them to a relevant textbook and to selected articles. Authors sought evidence-based material as appropriate. A select best answer format is utilized. At the end of each question, a letter indicates the preferred answer, followed by comments elaborating on the topic. A list of references is included at the end of each chapter.

Words and phrases appearing in boldface type within the text indicate links to facilitate a search of the material to be reviewed.

TABLE OF CONTENTS

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SECTION I

SURGICAL FUNDAMENTALS

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CHAPTER 1

PHYSIOLOGIC RESPONSE TO INJURY

Gillian Alex, M.D., and Ami Shah, M.D.

1. Cytokines involved in the initial proinflammatory response include all of the following except:

A. Interleukin-6
B. Interleukin-10
C. Tumor necrosis factor-α
D. Interleukin-1
E. Interleukin-8

ANSWER: B

COMMENTS: The complement cascade is the earliest humoral system activated in response to injury. C3a and C5a, the biologically active anaphylatoxins, induce the release of proinflammatory cytokines. Tumor necrosis factor-α (TNF-α) and interleukin-1 (IL-1) are the key mediators of this cascade. IL-6 induces T and B cells, and IL-8 recruits and activates inflammatory cells at the site of injury. IL-10, in contrast, is one of the key mediators of the antiinflammatory response and acts to inhibit the aforementioned cytokines.

Ref.: 1

2. Which of the following is true regarding the role of TNF-α release in the inflammatory response?

A. It can be effectively blocked by anti–TNF-α antibodies to halt systemic inflammatory response syndrome (SIRS).
B. It does not have any beneficial effects in the early phases of the inflammatory response.
C. It is primarily from leukocytes.
D. It promotes polymorphonuclear (PMN) cell adherence and further cytokine release.
E. It is always deleterious.

ANSWER: D

COMMENTS: TNF-α is a vital component of the early inflammatory response, especially locally, at the site of injury. It is released when the biologically active anaphylatoxins C3a and C5a are stimulated by the humoral system. Infusion of low doses of TNF-α in rats simulates the septic response, resulting in fever, hypotension, fatigue, and anorexia. TNF-α promotes adherence of PMN cells to endothelium, production of prostaglandins by fibroblasts, and activation of neutrophils and stimulates the release of multiple other cytokines from lymphocytes. TNF-α becomes deleterious when the proinflammatory stimuli are unchecked, leading to cellular damage and multiorgan system failure. TNF-α is released by macrophages and natural killer cells, but not leukocytes. Trials involving anti–TNF-α antibodies (NORASEPT, INTERSEPT) have not shown statistically significant improvement in patient outcomes.

Ref.: 1

3. A 56-year-old female is admitted to the intensive care unit (ICU) with a diffuse axonal injury after a motor vehicle crash. The nursing staff notices coffee ground material coming from her orogastric tube. What is the best intervention to prevent this complication?

A. Enteral feeding
B. Oral sucralfate
C. Oral proton pump inhibitor (PPI)
D. Intravenous (IV) H_2 blocker
E. IV PPI drip

ANSWER: D

COMMENTS: Stress-related gastritis can cause clinically significant bleeding in up to 5%–10% of ICU patients; therefore stress ulcer prophylaxis is now routinely administered in the ICU. Ulcers and bleeding are thought to be secondary to mucosal damage caused by low-flow states and subclinical hypoperfusion to the gastric mucosa. Patients with the following criteria should receive stress ulcer prophylaxis:

- coagulopathy defined as platelets < 50,000 cells per mcl (microliter); INR > 1.5; or PTT > two times the normal reference range
- mechanical ventilation > 48 h
- history of gastrointestinal ulcer or bleed
- traumatic brain/spinal cord injury or burn
- two or more of the following minor criteria:
  - Sepsis
  - ICU admission
  - Occult gastrointestinal bleed > 6 days
  - Glucocorticoids > 250 mg

Clinical data suggest that if enteral access is possible,the best agent is an oral PPI. If enteral access is not feasible, an IV PPI or H_2 antagonist is an alternative. IV PPIs are costly, so most centers favor an IV H_2 antagonist. Sucralfate has been studied and is effective in protecting against stress gastritis, but a disadvantage is its interference with the absorption of other medications such as antibiotics, warfarin, and phenytoin. Previously, it was thought that the use of H_2 blockers was associated with nosocomial pneumonia because of gastric bacterial colonization and subsequent aspiration. However, more recent trials have not

demonstrated any difference between other protective agents and H_2 receptor antagonists in the rate of ventilator-associated pneumonia. Antacids have not shown efficacy in preventing stress-related mucosal lesions in the ICU patients and are not considered as appropriate prophylactic agents.

Ref.: 2

4. A 64-year-old male with severe pancreatitis is transferred to the ICU from an outside hospital. A report is given to the nurse that the patient has received "large-volume resuscitation." Upon reaching the ICU, he is afebrile, tachycardic to 127, and has a BP of 120/60 mmHg. His abdomen is tense and full; he has a Foley in place but no urine in the bag. You suspect abdominal compartment syndrome (ACS). What is the mechanism of his oliguria?

A. Extrinsic compression of abdominal organs on the kidneys, leading to reduced GFR

B. Elevated renal venous pressure, leading to reduced GFR

C. Decreased arterial flow to the kidney, leading to reduced glomerular filtration rate (GFR)

D. Extrinsic compression of the ureters, causing an obstructive oliguric renal failure

E. Compression of the bladder, causing an obstructive oliguric renal failure

ANSWER: B

COMMENTS: Intraabdominal hypertension can be defined as intraabdominal pressure greater than or equal to 20 cm H_2O. ACS occurs in the setting of intraabdominal hypertension and evidence of abdominal hypoperfusion. ACS reduces the GFR secondary to elevated renal venous pressure and causes oliguria. Other physiologic derangements that can be seen are elevation of the diaphragms impeding oxygenation and ventilation raising the central intrathoracic, venous, and intracranial pressures. All of these issues can be treated with decompressive laparotomy. Decompressive laparotomy should be employed as a treatment for ACS when there is evidence of end-organ dysfunction.

Ref.: 2

5. For the patient in Question 4, which of the following parameters would necessitate a decompressive laparotomy for treatment?

A. Peak airway pressures of 30 mmHg

B. Systemic vascular resistance of 1400 dyn/s/cm^5

C. Pulmonary capillary wedge pressure of 18 mmHg

D. Urine output of 0 ml

E. Requirements of Fraction of inspired oxygen $(FiO)_2$ of 80% with positive end-expiratory pressure (PEEP) of 12

ANSWER: D

COMMENTS: Decompressive laparotomy should be performed only when there is evidence of end-organ dysfunction. Of all the answer choices provided, only decreased urine output indicates end-organ dysfunction. The rest of the parameters may be seen in ACS but do not indicate organ damage secondary to ACS; however, laparotomy would improve all of the parameters above.

Ref.: 2

6. A patient is brought to the emergency department after being found unresponsive. Electroencephalography (EEG) indicates status epilepticus. A potential secondary clinical consequence is:

A. Meningitis

B. Hypothermia

C. Myoglobinuria

D. Cerebrovascular accident

E. Hypoglycemia

ANSWER: C

COMMENTS: Status epilepticus is an entity that should be considered in any patient with recurrent or persistent seizure activity or in those who do not wake up after seizure activity. One of the potential systemic complications is rhabdomyolysis, which would result in myoglobinuria, elevated serum creatinine kinase, and pigmented granular urinary casts. The other options are potential primary causes of seizure activity. Rhabdomyolysis is a direct result of muscle injury and can be caused by prolonged seizure activity; major trauma; drug overdose; vascular embolism; extremity compartment syndrome; malignant hyperthermia; neuroleptic malignant syndrome; myositis; severe exertion; alcoholism; and medications such as statins, macrolide antibiotics, and cyclosporine.

Ref.: 2

7. Euthyroid sick syndrome is diagnosed in a patient in the surgical ICU. All of the following are part of this clinical phenomenon except:

A. The patient behaves as though clinically hypothyroid

B. Normal or decreased total serum thyroxine (T_4) level

C. Increased serum reversed triiodothyronine (rT_3) level

D. Decreased thyroid stimulating hormone (TSH) level

E. Decreased total serum T_3 level

ANSWER: A

COMMENTS: The hallmark of this diagnosis is that the patient behaves neither clinically hypothyroid nor hyperthyroid. The other choices are the expected laboratory findings in patients with this syndrome. Referred to alternatively as euthyroid sick syndrome, low T_3 syndrome, low T_4 syndrome, and nonthyroidal illness, considerable debate exists regarding whether this syndrome represents a pathologic process or an adaptive response to systemic illness that allows the body to lower its tissue energy requirements. In light of this controversy, no consensus has been reached on how to treat this entity or whether any treatment at all is necessary. Because the interpretation of thyroid function tests in critically ill patients is complex, these tests should not be done in an ICU setting unless a thyroid disorder is strongly suspected.

Ref.: 2

8. Acute respiratory distress syndrome (ARDS) develops in an acutely injured patient. If an alveolar biopsy specimen were taken within the first 24 h, the histologic examination would demonstrate:

A. Influx of protein-rich fluid and leukocytes

B. Preservation of type II pneumocytes

C. Bacterial colonization

D. Alveolar hemorrhage

E. High levels of collagen and fibronectin

ANSWER: A

COMMENTS: ARDS involves three distinct phases. The early, exudative phase is characterized by disruption of the alveolar epithelium with an influx of protein-rich fluid and leukocytes. Type II pneumocytes are damaged, and therefore surfactant production is halted. The second fibroproliferative phase includes the arrival of mesenchymal cells that produce collagen and fibronectin. The third, or resolution, phase involves gradual remodeling and clearance of edema.

Ref.: 2 and 3

9. An obese patient with a body mass index (BMI) of 50 underwent a laparoscopic gastric bypass. Because of a technical difficulty in the case, the procedure lasted for 8 h. The patient was doing well postoperatively until 4 h, when the nurse noted a change in the urine color from yellow to dark brown. She also reported that the patient's urine output decreased and his creatinine increased from 1.0 to 1.5. Which test would confirm the cause of these findings?

A. Renal ultrasound
B. Haptoglobin
C. Serum creatinine kinase
D. Complete blood count
E. Urine electrolytes

ANSWER: C

COMMENTS: Rhabdomyolysis can occur postoperatively in obese patients whose back and buttock muscles were compressed against the operating table for a prolonged time. Preventive measures include the use of larger tables to better distribute body weight, effective padding at all pressure points, intraoperative changing of patient position, and limitation of operative times. Physicians should have a high index of suspicion for rhabdomyolysis in this patient population so that early recognition and treatment can prevent the potentially devastating consequence of acute renal failure (ARF) in this already high-risk group. Creatinine kinase should be measured in any patient complaining of muscle pain or in whom dark urine, oliguria, or rising plasma creatinine develops.

Ref.: 4

10. The **primary** algorithm to treat the patient in Question 9 includes all of the following except:

A. Loop diuretics
B. Mannitol
C. Aggressive intravenous fluid resuscitation
D. Sodium bicarbonate
E. Serial basic metabolic panels

ANSWER: A

COMMENTS: The goal of the treatment algorithm for rhabdomyolysis is to prevent ARF. The cause of rhabdomyolysis-induced ARF is multifactorial and includes hypovolemia, ischemia, direct tubule toxicity caused by the heme pigment in myoglobin, and intratubular obstruction by casts. Treatment of rhabdomyolysis is to induce prompt polyuria with sufficient intravenous fluid resuscitation to produce 1.5 to 2 mL/kg/h of urine. Concurrently, urine alkalinization with a goal urine pH greater than 6.5 should be instituted with sodium bicarbonate to prevent precipitation of casts and obstruction of nephrons. Mannitol may also act as a free radical scavenger in addition to a diuretic, although this is somewhat controversial. Loop diuretics can be used as an alternative if brisk urine output cannot be achieved with the aforementioned measures, but they have the disadvantage of acidifying the urine.

Ref.: 4

11. An 82-year-old female with multiple prior abdominal surgeries presents with a small bowel obstruction. She undergoes an exploratory laparotomy with an extensive lysis of adhesions for 7 h. She receives 2 L of crystalloid during the case and has 200 cc of urine output. Her creatinine increases by 0.6 mg/dL the next day. All of the following are appropriate treatments except:

A. Rule out causes of outflow obstruction
B. Recheck hemoglobin
C. Calculate fractional excretion of sodium (FeNa)
D. Give a bolus of fluid
E. Start vasopressors for a mean arterial pressure (MAP) goal of 65 mmHg

ANSWER: E

COMMENTS: The most common cause of postoperative acute kidney injury (AKI) is renal hypoperfusion secondary to hypovolemia. Nephrogenic injury in patients with hypovolemia occurs when the renal arteries constrict in response to increased levels of epinephrine, angiotensin II, and vasopressin and the nephrons receive inadequate delivery of oxygen. The goal of the treatment is to quickly reverse shock and restore renal blood flow. The primary treatment is always intravenous fluid resuscitation. Active bleeding and obstruction should be ruled out. FeNa should be calculated to confirm your cause. Vasopressors should be avoided whenever possible because the resultant vasoconstriction may exacerbate the ischemic insult to the kidneys.

Ref.: 4

12. A 52-year-old diabetic male presents to the emergency department with chest pain, diaphoresis, and an elevated troponin. He is taken to the cardiac catheterization lab. Which of the following is true of contrast-induced AKI (CIAKI)?

A. It is the most common form of iatrogenic AKI in hospitalized patients.
B. CIAKI is characterized by oliguria.
C. Evidence of CIAKI occurs within 6 to 24 h of contrast administration.
D. The creatinine returns to normal within 1 month of insult for most patients.
E. The 1-year mortality associated with CIAKI is < 5%.

ANSWER: A

COMMENTS: CIAKI is the most common cause of iatrogenic AKI in hospitalized patients. It generally presents as a nonoliguric injury, with an increase in creatinine seen 48 to 72 h after the dye load was administered. Patients' creatinine returns to baseline within 7 to 10 days. The 1-year associated mortality is 30%.

Ref.: 5

13. Which of the following interventions reduces the likelihood of CIAKI?

A. *N*-acetylcysteine administration before giving the dye load

B. A one-time dose of prednisone 40 mg before administration of dye load

C. 0.9% normal saline for 12 h before and after giving the dye load

D. 0.45% normal saline for 12 h before and after giving the dye load

E. 1 L bolus of 0.9 normal saline at the time of giving the dye load

ANSWER: C

COMMENTS: The pathogenesis of CIAKI is primarily an ischemic form of injury caused by the vasoconstrictive properties of contrast media. In addition, contrast media can potentially have direct toxic effects on endothelial cells and renal tubules. Patients with diminished renal vasodilatory capacity (i.e., diabetic nephropathy) have an increased risk of CIAKI. Hydration is the only intervention proven to prevent CIAKI, with oral hydration more efficient than PO. Randomized controlled trials have found a small superiority in treatment, with 0.9% over 0.45% saline. There have also been multiple smaller studies demonstrating that 12 h of rehydration before and after dye load is more beneficial than a single bolus before the contrast load. *N*-acetylcysteine has been used for the prevention of CIAKI, with mixed results in the literature. However, due to the low cost and low side-effect profile, some authors still advocate its use.

Ref.: 5

14. A 47-year-old male with Crohn's colitis maintained on 40 åmg prednisone daily for the past year presents for elective colectomy. The procedure was uncomplicated, and he was adequately resuscitated. In the postanesthesia care unit (PACU) the patient is noted to be febrile and hypotensive with MAPs in the 50s. What is your next step in management?

A. IV dobutamine

B. Hydrocortisone

C. 1 unit of packed red blood cells

D. Antibiotics

E. Epinephrine

ANSWER: B

COMMENTS: The patient in the above scenario has been exposed to prolonged steroids and, as a result, has relative adrenal insufficiency. These patients may experience shock when they do not receive glucocorticoid replacement during times of relative corticoid and mineralocorticoid deficiencies. Signs and symptoms of acute insufficiency include fever, nausea, vomiting, refractory hypotension, and lethargy. Intravenous volume replacement with isotonic fluids and immediate IV steroid treatment with hydrocortisone are essential.

Ref.: 6

15. You are called by a PACU nurse for a patient who just underwent an elective splenectomy for idiopathic thrombotic purpura. The patient is afebrile, tachycardic, and hypotensive. What is your next step in management?

A. Check hemoglobin

B. IV fluid resuscitation

C. Electrocardiogram

D. Antibiotics

E. Start vasopressors

ANSWER: A

COMMENTS: Anytime a patient in the immediate postoperative period becomes unstable, evaluation for bleeding is critical. Hemoglobin should be checked, and if necessary, the patient should be returned to the operating room. The other steps may ultimately be required; however, bleeding must be ruled out first.

Ref.: 6

16. Which of the following metabolic changes occur during times of physiologic stress?

A. Increase in growth hormone (GH) release

B. Increase in TSH

C. Increased levels of T4 and T3

D. Initial insulin increase and then suppression

E. Increase in cortisol excretion

ANSWER: E

COMMENTS: There are many metabolic changes in times of stress. Cortisol is a major effector of metabolism and is the main hormone increased in the stress response. Cortisol inhibits growth hormone (GH) release, decreasing GH levels. Insulin-like growth factor levels are decreased in these times as well. Injury decreases TSH and conversion of T4 into T3, resulting in decreased levels of both T4 and T3. There are two patterns of insulin release, initial suppression followed by elevated release but increased peripheral resistance, leading to hyperglycemia.

Ref.: 6

17. Which of the following patients most likely has sepsis and should have prompt evaluation for transfer to an ICU?

A. A 27-year-old female after lithotripsy for nephrolithiasis who is afebrile with a heart rate (HR) of 102, BP 90/40 mmHg, altered mental status, and white blood cell (WBC) count of 9

B. A 72-year-old male with pancreatitis and a temperature of 102 degrees Farenheit, HR 110 beats/min, BP 110/60 mmHg, and WBC count of 14 cells per mcl

C. A 53-year-old female at postoperative day 0 from a colon resection who is tachycardic to 120 s and requires intubation in the PACU

D. An 84-year-old nursing home resident with a urine culture positive for Proteus spp.

E. An 18-year-old male who presented with a gangrenous appendicitis, is now at postoperative day 0 from a laparoscopic appendectomy, and is febrile to 103 and tachycardic to 130 s with BP of 140/70

ANSWER: A

COMMENTS: In 2016, the consensus guidelines on the definitions of sepsis and septic shock were revised for the first time since 2001. The aim of the consensus committee was to change the definitions to reflect the change in understanding of the pathophysiology and natural history of sepsis. The committee defined sepsis as a life-threatening organ dysfunction caused by dysregulated host

responses to infection. The prior definition of sepsis included two or more SIRS criteria plus a possible source of infection. SIRS may reflect a host response that is merely adaptive; therefore the old definition did not adequately identify all patients who may benefit from intensive therapies. Through examination of large data sets, the quick sepsis-related organ failure assessment (qSOFA) was developed to help promptly identify patients with suspected infection who are likely to have a prolonged ICU stay or die in the hospital. Criteria for the qSOFA are altered mental status, respiratory rate > 22/min, or systolic BP < 100 mmHg. Patients who screen positive warrant a higher level of care and intervention. Of the patients listed above, only patient A meets the criterion for qSOFA. While several of the others may meet criteria based on the former definition of sepsis, their conditions may be physiologic responses to injury and not suggestive of impending life-threatening injury and therefore do not need intensive monitoring.

Ref.: 7

18. Which of the following is the best parameter for monitoring septic shock?

A. Central venous pressure (CVP)
B. Vasopressor requirement
C. Urine output
D. Serum lactate
E. Mental status changes

ANSWER: D

COMMENTS: Septic shock is a subset of sepsis in which underlying circulatory and cellular/metabolic abnormalities are profound enough to substantially increase mortality. Patients with septic shock can be identified with a clinical construct of sepsis with persistent hypotension requiring vasopressors to maintain a MAP > 65 mmHg and a serum lactate level > 2 mmol/L despite adequate volume resuscitation. With these criteria, hospital mortality is in excess of 40%. Serum lactate is a good indicator of global perfusion. By definition, patients with sepsis suffer global hypoperfusion. CVP is often unreliable and can be affected by patient positioning, catheter positioning, and other physiologic derangements. Vasopressor requirements are often needed in septic shock to help improve perfusion but cannot be used as a direct measure of perfusion. Oliguria and altered mental status are signs of end-organ damage.

Ref.: 7

19. All of the following are negative outcomes that have been directly associated with perioperative hypothermia except:

A. Coagulopathy
B. Wound infections
C. Nosocomial pneumonia
D. Myocardial ischemia
E. Delayed wound healing

ANSWER: C

COMMENTS: Preservation of normothermia in surgical patients is important and is one of the goals of the Surgical Care Improvement Project (SCIP). Hypothermia results in peripheral vasoconstriction, which leads to decreased subcutaneous oxygen tension and antibiotic delivery. Both neutrophil activity and leukocyte chemotaxis are impaired. All of these sequelae give rise to an increased incidence of wound infections. Globally reduced enzyme function leads to coagulopathy. Collagen cross-linking and therefore wound healing is affected by hypothermia. An increased risk for myocardial ischemia in patients with known coronary artery disease has been associated with hypothermic states. There has not been a direct correlation between the development of nosocomial pneumonia and hypothermia. The SCIP measures aim to achieve a target temperature of 36.0°C in perioperative patients using active warming methods.

Ref.: 8

20. An obese 21-year-old male suffers multiple fractures and a liver injury; 21 days later, he develops acute dyspnea, diaphoresis, and desaturates to 86% at room air. A computed tomography (CT) of the chest is positive for pulmonary embolus. All of the following are risk factors for venous thromboembolic events except:

A. Severity of injury
B. BMI
C. Smoking
D. Pelvic fractures
E. Hypertriglyceridemia

ANSWER: E

COMMENTS: Venous thromboembolic disease (VTE), which can manifest as deep venous thrombus (DVT) or pulmonary embolism (PE), is common and can have serious or fatal consequences. Risk factors for VTE frequently encountered by surgeons include increased severity of injury, increased BMI, history of smoking, intraabdominal cancers, pelvic fractures or surgery, lithotomy positioning, and operative times longer than 2 h. Hypertriglyceridemia and hypercholesterolemia have been examined as risk factors for VTE, but no statistically significant association has been established.

Ref.: 2, 9

21. Which of the following patients should receive prolonged prophylaxis (28 days) for VTE?

A. Female with a newly diagnosed DVT in her right popliteal vein
B. Male with chronic pulmonary embolus who undergoes a laparoscopic cholecystectomy
C. Female with gastric cancer who undergoes a total gastrectomy
D. Female with uterine fibroids undergoing total abdominal hysterectomy
E. Female with breast cancer undergoing bilateral mastectomy

ANSWER: C

COMMENTS: Continued prophylaxis after surgery should be based on the assessment of risk of VTE. In patients with abdominal cancer, VTE is an important cause of death. About 29% of patients with abdominal cancer will develop a complication of VTE during their disease course. Continuing chemical prophylaxis for 28 days postoperatively decreases the incidence of thromboembolic events and has a risk reduction of >50% in mortality, which persists for greater than 3 months. Patients A and B both require therapeutic treatment and not prophylaxis.

Ref.: 9

22. Which of the following is a contraindication to enteral feeding?

A. Ileus

B. Small bowel anastomosis

C. Hemodynamic instability requiring vasopressors

D. Pancreatitis

E. Pneumonia

ANSWER: C

COMMENTS: Enteral feeding should be initiated early in the course of critical illness or injury. The intestine plays a role in digestion and absorption of nutrients and acts as a barrier to enteric flora, preventing host invasion by microorganisms or their toxins. This intestinal barrier can be impaired during critical illness, making patients susceptible to bacterial translocation. Enteral feeding is protective against microvilli atrophy and impairment of the intestinal barrier. Patients can and should be fed in all of the scenarios above with the exception of hemodynamic instability. In times of global hypoperfusion there is a risk of intestinal ischemia caused by enteral feedings. Patients with pancreatitis may receive enteral feedings; however, postpyloric feedings are preferred.

Ref.: 10

23. A patient with a previous history of ischemic bowel requiring extensive bowel resection, now with only 100 cm of bowel remaining and dependent on total parenteral nutrition (TPN), presents to your office complaining of hair loss, rash on the extremities, and dry skin. Which nutrient deficiency is this patient most likely suffering from?

A. Copper

B. Selenium

C. Vitamin D

D. Essential fatty acids

E. Zinc

ANSWER: D

COMMENTS: Short gut as a result of small bowel loss and or dysfunction of the remaining bowel is characterized by malabsorption of nutrients, diarrhea, and weight loss. Essential fatty acids are not part of TPN formulas, and deficiency causes dermatitis, diarrhea, alopecia, patchy red areas on the skin, brittle nails, easy bruising, bleeding tendencies, and delayed wound healing.

Ref.: 11

24. Strategies that have been suggested to decrease the risk for postoperative pulmonary complications include all of the following except:

A. Routine nasogastric tube decompression

B. Lung expansion maneuvers

C. Preoperative smoking cessation

D. Postoperative epidural anesthesia

E. Use of intraoperative short-acting neuromuscular blocking agents

ANSWER: A

COMMENTS: Postoperative pulmonary complications include atelectasis, pneumonia, prolonged mechanical ventilation, bronchospasm, and exacerbation of the underlying lung disease. Aggressive pulmonary toilet, smoking cessation, epidural analgesia, and minimal neuromuscular blockade have been shown to be effective means of reducing postoperative respiratory complications. In contrast, because systemic reviews have found that routine use of nasogastric decompression increases pulmonary complications, nasogastric tubes should be used postoperatively only when specifically indicated for the operative procedure. An early postoperative fever is most likely due to atelectasis causing a respiratory shunt secondary to alveolar collapse. This results in varying degrees of hypoxemia. Persistent collapse leaves alveoli prone to bacterial colonization. Aggressive pulmonary toilet with incentive spirometry, forced coughing, and frequent turning is the best prevention.

Ref.: 12

25. A patient with resolving ARDS requires a tracheostomy. The family wants to know the benefit of early tracheostomy compared with prolonged intubation. Which of the following is correct?

A. There is no difference in overall mortality between patients receiving prolonged endotracheal (ET) intubation and those receiving tracheostomy.

B. There is increased sedation and pain requirement with a surgically placed tracheostomy.

C. There is an increased risk of pneumonia with ET intubation.

D. There is a decrease in the time required for mechanical ventilation with tracheostomy.

E. ICU stays are the same for both ET intubation and tracheostomy.

ANSWER: A

COMMENTS: There is no mortality difference between patients receiving prolonged endotracheal intubation and those receiving a tracheostomy. Patients with a tracheostomy do have shorter stays in the ICU and decreased sedation and pain requirements. There are equivocal rates of pneumonia and days requiring mechanical ventilation in both tracheostomy and ET intubation.

Ref.: 13

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CHAPTER 2

WOUND HEALING AND CELL BIOLOGY

Steven D. Bines, M.D.

1. Which of the following statements regarding the role of collagen in wound healing is true?

A. Collagen synthesis in the initial phase of injury is the sole responsibility of endothelial cells.

B. Net collagen content increases for up to 2 years after injury.

C. At 3 weeks after injury, more than 50% of the tensile strength of the wound has been restored.

D. Tensile strength of the wound increases gradually for up to 2 years after injury; however, it generally reaches a level of only about 80% of that of uninjured tissue.

E. Tensile strength is the force necessary to reopen a wound.

ANSWER: D

COMMENTS: Synthesis of collagen by fibroblasts begins as early as 10 h after injury and increases rapidly; it peaks by day 6 or 7 and then continues more slowly until day 42. Collagen continues to mature and remodel for years. Its solubility in saline solution and the thermal shrinkage temperature of collagen reflect the intermolecular cross-links, which are directly proportional to collagen age. After 6 weeks, there is no measurable increase in the net collagen content. However, synthesis and turnover are ongoing for life. Historical accounts of sailors with scurvy (with impaired collagen production) who experienced reopening of previously healed wounds illustrate this fact. Tensile strength correlates with the total collagen content for approximately the first 3 weeks of wound healing. At 3 weeks, the tensile strength of the skin is 30% of normal. After this time, there is a much slower increase in the content of collagen until it plateaus at about 6 weeks. Nevertheless, tensile strength continues to increase because of intermolecular bonding in collagen and changes in the physical arrangement of collagen fibers. Although the most rapid increase in tensile strength occurs during the first 6 weeks of healing, there is a slow gain for at least 2 years. Its ultimate strength, however, never equals that of the unwounded tissue, with a level of just 80% of the original skin strength being reached. Tensile strength is measured as the load capacity per unit area. It may be differentiated from burst strength, which is the force required to break a wound (independent of its area). For example, in wounds of the face and back, burst strength is different because of differences in skin thickness, even though tensile strength may be similar. Corticosteroids affect wound healing by inhibiting fibroblast proliferation and epithelialization. The latter effect can be reversed by the administration of vitamin A.

Ref.: 1–3, 6

2. A 34-year-old man sustained a gunshot wound to his abdomen that necessitated exploratory laparotomy and small bowel resection. Two weeks after the initial operation, he was reexplored for a large intraabdominal abscess. Which of the following will result in the most rapid gain in strength of the new incision?

A. A separate transverse incision is made.

B. The midline scar is excised with a 1-cm margin.

C. The midline incision is reopened without excision of the scar.

D. The midline incision is left to heal by secondary intention.

E. The rate of gain in strength is not affected by the incision technique.

ANSWER: C

COMMENTS: When a normally healing wound is disrupted after approximately the fifth day and then reclosed, the return of wound strength is more rapid than that with primary healing. This is termed the secondary healing effect and appears to be caused by the elimination of the lag phase present in normal primary healing. If the skin edges more than about 7 mm around the initial wound are excised, the resulting incision is through essentially uninjured tissue, so accelerated secondary healing does not occur.

Ref.: 2, 3, 6

3. A 29-year-old black woman is scheduled for incision and drainage of a breast abscess that has recurred three times despite ultrasound-guided needle drainage. The patient has a history of keloid formation and is concerned about an unsightly scar on her breast. Which of the following statements concerning wound healing is true?

A. Keloids contain an overabundance of fibroblasts.

B. A hypertrophic scar extends beyond the boundaries of the original wound.

C. Improvement is usually seen with keloid excision followed by intralesional steroid injection.

D. An incision placed perpendicular to the lines of natural skin tension will result in the least obvious scar.

E. Hypertrophic scars occur most commonly on the lower extremities.

ANSWER: C

COMMENTS: Keloids are caused by an imbalance between collagen production and degradation. The result is a scar that extends beyond the boundaries of the original wound. The

absolute number of fibroblasts is not increased. Treatment of keloids is difficult. There is often some improvement with excision and intralesional steroid injection. If this technique is not successful, excision and radiation treatment can be used. Hypertrophic scars contain an overabundance of collagen, but the dimensions of the scar are confined to the boundaries of the original wound. Hypertrophic scars are often seen in the upper part of the torso and across flexor surfaces. Scar formation is affected by multiple factors, including the patient's genetic makeup, wound location, age, nutritional status, infection, tension, and surgical technique. In planning for surgical incisions, an effort to parallel natural tension lines will promote improved wound healing.

Ref.: 2, 3, 6

4. A 30-year-old man is scheduled for definitive management of his open wounds after undergoing embolectomy and fasciotomies on his left lower extremity. Which of the following statements is true regarding the use of split- and full-thickness skin grafts?

A. A split-thickness skin graft undergoes approximately 40% shrinkage of its surface area immediately after harvesting.

B. A full-thickness skin graft undergoes approximately 10% shrinkage of its surface area immediately after harvesting.

C. Secondary contraction is more likely to occur after adequate healing of a full-thickness skin graft than after adequate healing of a split-thickness skin graft.

D. Sensation usually returns to areas that have undergone skin grafting.

E. Skin grafts may be exposed to moderate amounts of sunlight without changing pigmentation.

ANSWER: D

COMMENTS: Skin grafts are considered to be full thickness when they are harvested at the dermal–subcutaneous junction. Split-thickness skin grafts are those that contain epidermis and variable partial thicknesses of the underlying dermis. They are usually 0.018 to 0.060 inch in thickness. Cells from epidermal appendages deep to the plane of graft harvest resurface on the donor site of a split-thickness skin graft in approximately 1 to 3 weeks, depending on the depth. The donor site requires a moist environment to promote epithelialization, and such an environment is maintained by using polyurethane or hydrocolloid dressings. Because a full-thickness graft removes all epidermal appendages, the defects must be closed primarily. When a skin graft is harvested, there is immediate shrinkage of the surface area of the graft. This process, known as primary contraction, is due to recoil of the elastic fibers of the dermis. The thicker the skin graft, the greater the immediate shrinkage, with full-thickness grafts shrinking by approximately 40% of their initial surface area and split-thickness grafts shrinking by approximately 10% of their initial surface area. Shrinkage must be considered when planning the amount of skin to harvest for covering a given wound size. Secondary contraction occurs when contractile myofibroblasts in the bed of a granulating wound interact with collagen fibers to cause a decrease in the wound's surface area. Secondary contraction is greater in wounds covered with split-thickness grafts than in those covered with full-thickness grafts. The amount of secondary contracture is inversely proportional to the amount of dermis included in the graft rather than the absolute thickness of the graft. Dermal elements hasten the displacement of myofibroblasts from the wound bed.

Sensation may return to areas that have been grafted if the bed is suitable and not significantly scarred. Although sensation is not completely normal, it is usually adequate for protection. This process begins at about 10 weeks and is maximal at 2 years. Skin grafts appear to be more sensitive than the normal surrounding skin to melanocyte stimulation during exposure to ultraviolet sunlight. Early exposure to sunlight after grafting may lead to permanently increased pigmentation of the graft and should be avoided. Dermabrasion or the application of hydroquinones may be beneficial in reducing this pigmentation.

Ref.: 2, 3, 6

5. A 21-year-old graduate student has a large hypertrophic scar on the lower part of her face. The patient had sustained a laceration on her face 2 years previously after hitting her face on the side of a swimming pool. Which of the following statements regarding scar revision is true?

A. Scar maturation refers to the change in size of the wound in the first 1 to 2 months.

B. Scar revision should have been performed in the first 3 months after injury to minimize fibrosis.

C. Revision should be performed earlier in children than in adults.

D. It corrects undesirable pigmentation.

E. Scar revision should be delayed for approximately 1 year to allow maturation.

ANSWER: E

COMMENTS: Changes in pliability, pigmentation, and configuration of a scar are known as scar maturation. This process continues for many months after an incision; therefore it is generally recommended that revision not be carried out for approximately 12 to 18 months because natural improvement can be anticipated within this period. In general, scar maturation occurs more rapidly in adults than in children. Most erythematous scars show little improvement after revision; therefore scar revision should not be undertaken for correction of undesirable scar color alone.

Ref.: 2, 3, 6

6. A 68-year-old diabetic man undergoes a below-knee amputation. The patient's postoperative course is complicated by severe depression and anorexia. Before discharge, the patient is started on a multivitamin regimen. Which of the following statements regarding wound healing is true?

A. Vitamin A is needed for hydroxylation of lysine and proline in collagen synthesis.

B. High doses of vitamin C improve wound healing.

C. Vitamin E is involved in the stimulation of fibroplasia, collagen cross-linking, and epithelialization.

D. Zinc deficiency results in delayed early wound healing.

E. Iron deficiency has been linked to defects in long-term wound remodeling.

ANSWER: D

COMMENTS: Vitamin A is involved in the stimulation of fibroplasia and epithelialization. Although there has been no conclusive evidence of its efficacy in humans, in animal studies vitamin A has been shown to reverse the inhibitory effects of glucocorticoids in the inflammatory phase of wound healing and epithelialization.

Vitamin C is a necessary cofactor in the hydroxylation and cross-linking of lysine and proline in collagen synthesis. Deficiencies in vitamin C (scurvy) can lead to the production of inadequately hydroxylated collagen, which either degrades rapidly or never forms proper cross-links. Doses higher than physiologic doses do not improve wound healing. Vitamin E is applied to wounds and incisions by many patients, but there is no evidence to support the role of vitamin E in wound healing. Large doses of vitamin E have been found to inhibit wound healing. Zinc is a necessary cofactor of RNA and DNA polymerase, and deficiencies have been linked to poor early wound healing. Iron (specifically, the ferrous iron) is necessary for converting hydroxyproline to proline. However, chronic anemia and iron deficiency have not been linked to delayed or impaired wound healing.

Ref.: 2, 3, 6

7. Which of the following statements regarding wound epithelialization is true?

A. Integrins act as a key modulator of the interaction between epithelial cells and the surrounding environment.

B. Structural support and attachment between the epidermis and dermis are provided by tight cell junctions.

C. Early tensile strength of the wound is a direct result of collagen deposition.

D. A reepithelialized wound develops hair follicles and sweat glands like those seen in the normal skin.

E. Contact inhibition can prevent collagen deposition and result in a chronic (nonhealing) wound.

ANSWER: A

COMMENTS: Migration of epithelial cells is one of the earliest events in wound healing. Shortly after injury and during the inflammatory phase, basal epithelial cells begin to multiply and migrate across the defect, with fibrin strands being used as the support structure. Integrins are the main cellular receptors involved in epithelial migration; they act as sensors and integrators between the extracellular matrix and the epithelial cell cytoskeleton. Tight junctions within the epithelium contribute to its impermeability, whereas the basement membrane contributes to structural support and attachment of the epidermis to the dermis. Surgical incisions seal rather promptly and after 24 h are protected from the external environment. Early tensile strength is a result of blood vessel ingrowth, epithelialization, and protein aggregation. After covering the wound, the epithelial cells keratinize. The reepithelialized wound has no sweat glands or hair follicles, which distinguishes it from the normal skin. Control of the cellular process during wound epithelialization is not completely understood, but it appears to be regulated in part by contact inhibition, with growth being arrested when two or more similar cells come into surface contact. Derangements in the control of this process can result in epidermoid malignancy. Malignancy is more frequently observed in wounds resulting from ionizing radiation or chemical injury, but it can occur in any wound when the healing process has been chronically disrupted. For example, squamous cell carcinoma may develop in patients with chronic burn wounds or osteomyelitis (Marjolin's ulcer).

Ref.: 2, 4–6

8. In DNA replication, what type of mutation is specifically associated with the generation of a stop codon?

A. Point mutation

B. Missense mutation

C. Nonsense mutation

D. Frameshift mutation

E. Neutral mutation

ANSWER: C

COMMENTS: A change in a single base pair is known as a point mutation. A single amino acid change resulting from a point mutation is known as a missense mutation. A missense mutation may cause changes in the structure of the protein that lead to altered biologic activity. Nonsense mutations occur if a point mutation results in the replacement of an amino acid codon with a stop codon. Nonsense mutations lead to premature termination of translation and often result in the loss of encoded protein. Frameshift mutations occur when a few base pairs are added or deleted and lead to the introduction of unrelated amino acids or stop codons. A neutral mutation occurs when the change results in the substitution of a different but chemically similar amino acid. Frequently, the amino acids are similar enough that little or no change occurs in the resultant protein.

Ref.: 7

9. Which of the following is correct regarding cell signaling?

A. Cytokines are exclusively peptide mediators.

B. Autocrine mediators are secreted by a cell and act on adjacent cells of a different type.

C. Cytokines are usually produced by cells specialized for only that purpose.

D. The effects of hormones are generally local rather than global.

E. Growth factors are frequently mediated by second messenger systems such as diacylglycerol (DAG) and cyclic adenosine monophosphate (cAMP).

ANSWER: E

COMMENTS: Cytokines are proteins, glycoproteins, or peptides that bind to target cell surface receptors to stimulate a cellular response. They are important mediators of wound healing. Cytokines can reach target cells by paracrine, autocrine, or intracrine routes. Paracrine mediators are produced by one cell and act on an adjacent target cell. Autocrine mediators are secreted by a cell and act on cell surface receptors on the same cell. Intracrine mediators act within a single cell. Hormones are released by cells and act on a distant target (endocrine route). Although the distinction between cytokines and hormones has blurred, in general, hormones are secreted from specialized glands (e.g., insulin, parathyroid hormone) and cytokines are secreted by a wide variety of cell types. Hormones typically induce body-wide effects, whereas the effects of cytokines may be more localized (e.g., wound healing at the site of an injury). Generally, growth factors are named according to their tissue of origin or their originally discovered action. Growth factors interact with specific membrane receptors to initiate a series of events that ultimately lead to stimulation of cell growth, proliferation, or differentiation. The intermediate events activate a variety of second messenger systems mediated by agents such as inositol 1,4,5-triphosphate (IP_3), DAG, and cAMP.

Ref.: 7–9

10. A 25-year-old man presents to the office with complaints of contracture of his left index finger after a burn injury. Which of the following statements is true about growth factors?

A. Epidermal growth factor (EGF) stimulates the production of collagen.

B. Vascular endothelial growth factor (VEGF) and platelet-derived growth factor (PDGF) both stimulate angiogenesis by binding to a common receptor.

C. Fibroblast growth factor (FGF) stimulates wound contraction.

D. Transforming growth factor-β (TGF-β) is stored in endothelial cells.

E. Tumor necrosis factor-α (TNF-α) inhibits angiogenesis.

ANSWER: C

COMMENTS: EGF was the first cytokine described. It is a potent mitogen for epithelial cells, endothelial cells, and fibroblasts. EGF stimulates the synthesis of fibronectin, angiogenesis, and collagenase activity. PDGF is released from the alpha granules of platelets and is responsible for the stimulation of neutrophils and macrophages and for increasing the production of TGF-β. PDGF is a mitogen and chemotactic agent for fibroblasts and smooth muscle cells and stimulates angiogenesis, collagen synthesis, and collagenase activity. VEGF is similar to PDGF but does not bind to the same receptors. VEGF is mitogenic for endothelial cells. Its role in promoting angiogenesis has led to an interest in anti-VEGF therapies for cancer. FGF has acidic and basic forms whose actions are identical but whose strengths differ (basic FGF is 10 times stronger than acidic FGF). FGF is mitogenic for endothelial cells, fibroblasts, keratinocytes, and myoblasts; stimulates wound contraction and epithelialization; and induces the production of collagen, fibronectin, and proteoglycans. It is an important mediator of angiogenesis. TGF-β is released from the alpha granules of platelets and has been shown to regulate its own production in an autocrine manner. TGF-β stimulates fibroblast proliferation and the production of proteoglycans, collagen, and fibrin. It is an important mediator of fibrosis. Administration of TGF-β has been suggested as an approach to reduce scarring and reverse the inhibition of wound healing by glucocorticoids. TNF-α is a mitogen for fibroblasts and is produced by macrophages. It stimulates angiogenesis and the synthesis of collagen and collagenase.

Ref.: 3, 6, 10, 11

11. An 85-year-old nursing home patient is found to have a worsening stage III sacral pressure ulcer. The ulcer is debrided and tissue for culture obtained. Tissue cultures reveal 10^8 organisms per gram of tissue after operative debridement. What is the next most appropriate step in the management of the patient's wound?

A. Muscle flap coverage

B. Wound vacuum-assisted closure (VAC)

C. Intravenous antibiotics

D. Repeat debridement

E. Debridement with immediate application of a split-thickness skin graft

ANSWER: D

COMMENTS: The National Pressure Ulcer Advisory Panel has recommended a staging system for pressure sores that is useful in planning treatment. Stage I is represented by the presence of nonblanching erythema of intact skin. Stage II is characterized by partial-thickness skin loss involving the epidermis or dermis. Clinically, the ulcer is manifested as a blister, abrasion, or shallow crater. Stage III is full-thickness skin loss with involvement of the underlying subcutaneous tissue. Stage III wounds may extend down to but not through the underlying fascia. Stage IV represents full-thickness skin loss with extensive destruction or tissue necrosis of underlying structures, which may include muscle and bone. Studies have shown that wounds with quantitative cultures revealing more than 10^6 organisms per gram of tissue that undergo reconstruction with skin or even muscle flaps have a significantly greater risk for complications, including infection, accumulation of fluid, and wound dehiscence. Similarly, a skin graft is unlikely to survive in an environment with such a high bacterial inoculate. Negative-pressure wound therapy, such as with the wound VAC system, involves the use of a sponge and an occlusive dressing connected to a suction apparatus in a closed system. In patients with large wounds, a wound VAC may serve as a bridge to reduce the wound size for definitive reconstruction. It has been shown to be effective in reducing wound edema, controlling wound drainage, encouraging diminution of wound size, and facilitating the formation of granulation tissue. Although studies have shown that wound VAC therapy may reduce bacterial counts over time, the most appropriate management of such patients is repeat debridement of the wound. Intravenous antibiotics may be recommended to treat the underlying osteomyelitis.

Ref.: 2, 3, 6, 12

12. A 45-year-old woman undergoes bilateral transverse rectus abdominis muscle (TRAM) breast reconstruction after modified radical mastectomy. The patient is scheduled for postoperative radiation therapy and is concerned that this will affect her wound-healing ability. Which of the following statements regarding wound healing in this patient is true?

A. Denervation has a profound effect on wound contraction and epithelialization.

B. A bacterial count of 1000 organisms per square centimeter retards wound healing.

C. Chemotherapy beginning 10 to 14 days after primary wound closure has little effect on the final status of a wound.

D. Tissue ischemia is the main component of tissue damage after irradiation.

E. Postoperative radiation therapy should be delayed for at least 4 to 6 months after surgery to decrease the incidence of wound complications.

ANSWER: C

COMMENTS: Denervation has no effect on wound contraction or epithelialization. Flap wounds in paraplegics heal satisfactorily when other factors, such as nutrition and temperature, are controlled. Subinfectious bacterial levels appear to accelerate wound healing and the formation of granulation tissue. However, when the level reaches 10^6 organisms per square centimeter of wound, healing is delayed because of decreased tissue oxygen pressure, increased collagenolysis, and a prolonged inflammatory phase. Various chemotherapeutic agents affect wound healing. Most antimetabolic agents (e.g., 5-fluorouracil) do not delay wound healing, although agents such as doxorubicin have been shown to delay wound healing. When chemotherapy begins 10 to 14 days after wound closure, little effect is noted on its final status despite a demonstrable early retardation in the wound strength. Tissue ischemia may not be the primary factor involved in chronic wound-healing problems associated with irradiation. Such problems are most likely related to changes within the nuclei and concomitant

cytoplasmic malformation. To decrease wound complications, it is usual to delay surgery until at least 3 to 4 weeks after full-dose irradiation and to avoid radiation therapy for at least 3 to 4 weeks after surgery.

Ref.: 2–4, 6, 13

13. A 46-year-old man is evaluated shortly after undergoing radiation therapy and chemotherapy for primary laryngeal cancer. He also gives a history of long-term steroid use for rheumatoid arthritis. The patient complains of a chronic, nonhealing wound on his neck, just over his right clavicular head. Which statement regarding the treatment of this wound is true?

A. The wound should be treated with compression dressings.

B. The wound should be treated with injected steroids.

C. The patient should start taking vitamin A, and the wound should be covered with antimicrobial dressings.

D. The patient should start taking vitamin C, and the wound should be kept open to air.

E. The wound should be excised and a skin graft applied.

ANSWER: C

COMMENTS: Radiation results in progressive endarteritis obliterans and microvascular damage to the skin, which leads to skin ischemia and fibrotic interstitial changes. This leaves wounds in the skin particularly prone to infection. The use of antimicrobial dressings capable of maintaining a moist environment is ideal for these wounds. Research also supports the use of hyperbaric oxygen and growth factors to promote wound healing. Patients taking steroids should receive daily vitamin A supplements. Wounds in these patients show decreased rates of angiogenesis, collagen deposition, and cellular proliferation. Wounds should be kept free of bacterial contamination.

Ref.: 11, 14

14. A 25-year-old ballet dancer with a history of anorexia nervosa arrives at the emergency department with right lower quadrant pain. After an appendectomy, a wound infection at the surgical site requires debridement. The patient is placed on an antibiotic regimen, and the wound is packed with wet-to-dry dressings. Regarding wound healing and malnutrition, which of the following statements is true?

A. Hypoproteinemia leads to decreased levels of arginine and glutamine, which are essential in wound healing.

B. Cell membranes rapidly become dehydrated in the absence of vitamin E, resulting in delayed wound healing.

C. Zinc is essential to the fibroblast's ability to cross-link collagen.

D. Vitamin D serves an immunomodulatory role in wound healing.

E. The patient should be treated with high-dose vitamin C, vitamin A, and zinc.

ANSWER: D

COMMENTS: Adequate amounts of protein, carbohydrates, fatty acids, and vitamins are essential for wound healing. Hypoproteinemia results in decreased delivery of the essential amino acids used in the synthesis of collagen. Carbohydrates and fats provide energy for wound healing, and in their absence, proteins are rapidly broken down. Fatty acids are vital components of cell membranes. Vitamin C is a cofactor for hydroxylation of lysine and proline during collagen synthesis, and its deficiency leads to decreased collagen cross-linking by fibroblasts. Vitamin C is also effective in providing resistance to infection. Vitamin A is essential for normal epithelialization, proteoglycan synthesis, and enhanced immune function. Vitamin D is required for normal calcium metabolism, but it is also involved in promoting immune function in the skin. Vitamin E has not been shown to play a role in wound healing. Zinc deficiency leads to a deficient formation of granulation tissue and inhibition of cellular proliferation. Increased administration of vitamins and minerals does not accelerate wound healing and often has a deleterious effect.

Ref.: 2, 15

15. Which of the following statements regarding second messenger systems is true?

A. Most receptor proteins (such as G proteins) are completely extracellular.

B. Both the "first messenger" and "second messenger" mediators of cell signaling function within the cell cytoplasm.

C. Adenylate cyclase stimulates the conversion of cAMP to adenosine triphosphate (ATP).

D. IP_3 generally increases cytoplasmic calcium concentrations.

E. IP_3 and DAG together lead to inactivation of protein kinase C.

ANSWER: D

COMMENTS: The thyrotropin (TSH) receptor is a $G_{\alpha s}$ receptor found mainly on the surface of thyroid follicular cells. When activated, it stimulates increased production of thyroxine (T_4) and triiodothyronine (T_3).

Several families of receptor proteins have been identified. The most common is the G protein (guanine nucleotide–binding protein) family, a subset of guanosine triphosphatase (GTPase) enzymes. All G protein–coupled receptors have characteristic seven transmembrane domains. Binding of an extracellular ligand causes a conformational change in the receptor that allows it to exchange guanosine diphosphate (GDP) for guanosine triphosphate (GTP) on the intracellular portion of the G protein. The intracellular portion of the "large" (heterotrimeric) G protein–coupled receptor consists of three subunits, G_α, G_β, and G_γ. Other "small" (monomeric) G protein receptors have only a homologue of the G_α portion. There are several important subsets of the "large" G protein receptors, and they are classified according to the specific intracellular pathway that is activated.

$G_{\alpha s}$ stimulates membrane-associated adenylate cyclase to produce cAMP from ATP. cAMP is a second messenger that activates protein kinase A, which results in the phosphorylation of downstream targets. $G_{\alpha s}$ ligands include adrenocorticotropic hormone (ACTH), calcitonin, glucagon, histamine (H_2), TSH, and many others. $G_{\alpha i}$ inhibits the production of cAMP from ATP. $G_{\alpha i}$ ligands include acetylcholine (M_2 and M_4), dopamine (D_2, D_3, and D_4), and histamine (H_3 and H_4). $G_{\alpha q}$ activates phospholipase C, which cleaves phosphatidylinositol 4,5-bisphosphate (PIP_2) into IP_3 and DAG. IP_3 mediates the release of calcium from intracellular reservoirs, such as the endoplasmic reticulum (ER), sarcoplasmic reticulum (SR) in muscle, and mitochondria. IP_3 and DAG together work to activate protein kinase C, which can modulate membrane

permeability and activate gene transcription. $G_{\alpha q}$ ligands include histamine (H_1), serotonin ($5\text{-}HT_2$), and muscarinic receptors.

The most well-known "small" G protein receptors are the Ras family GTPases. The Ras receptors influence a wide variety of processes in the cell, including growth, cellular differentiation, and cell movement.

Ref.: 7, 8, 16

16. Inflammatory breast cancer is diagnosed in a 36-year-old woman. A decision is made to treat the patient with radiation, along with paclitaxel and doxorubicin. Which of the following statements regarding cellular motility and contractility is true?

A. Actin fibers are found mainly in muscle cells.

B. The interactions between actin and myosin that underlie the contraction of skeletal muscle require calcium but not ATP.

C. Intermediate filaments extend from the centrosome to the nucleus.

D. The proteins kinesin and dynein are required for directional transport of cellular components along the microtubules.

E. The microtubules used to form the spindle apparatus are synthesized de novo before each mitosis.

ANSWER: D

COMMENTS: The cytoskeleton provides the structural framework for the cell. It is composed of three main types of protein polymers: actin filaments, intermediate filaments, and microtubules. Actin filaments are found in nearly all types of cells. They form a cortical layer beneath the plasma membrane of most cells, the stress fibers of fibroblasts, and the cytoskeleton of microvilli of intestinal epithelial cells. In muscle cells, the interaction between the heads of myosin (thick filaments) and actin (thin filaments) requires hydrolysis of ATP to separate the filaments at the end of the power stroke. Calcium and troponin C (an actin-associated protein) are also required to expose the binding site for myosin on the actin filament. Intermediate filaments are a heterogeneous group of proteins that extend from the nucleus to the cell surface. They interact with other cytoskeletal filaments and binding proteins to produce their effects.

Microtubules arise from the centrosome, with the cell's microtubule-organizing center being located near the nucleus. Microtubules are in a constant dynamic equilibrium between assembly and disassembly. Movement of cellular components, such as vacuoles, along the microtubules requires ATP and either of two associated proteins: kinesin for movement away from the centrosome and dynein for movement toward it. Cilia and flagella contain columns of doublet microtubules in a 9–2 arrangement (nine doublets in a circle surrounding two central doublets). Movement is accomplished when the doublets slide along each other in a process mediated by dynein and fueled by hydrolysis of ATP. Microtubules also play an important role in cell division. Assembly of the mitotic spindle involves replication and splitting of the microtubule-organizing center into the two spindle poles and reorganization of the cytoskeletal microtubules to form the spindle apparatus.

Ref.: 8, 16

17. Regarding chemotherapeutic agents, which of the following statements is true?

A. Paclitaxel is a manmade taxane first manufactured in the polycarbon industry.

B. Taxanes unwind DNA thus preventing transcription.

C. Vinca alkaloids inhibit cell division by disrupting the mitotic spindle.

D. Doxirubicin intercalates between DNA base pairs thus disrupting transcription.

E. Taxanes impair the progression of topoisomerase ii.

ANSWER: C

COMMENTS: Taxanes function as mitotic inhibitors by inhibiting depolymerization of the mitotic spindle, which results in a "frozen" mitosis. Paclitaxel is a natural taxane that prevents depolymerization of cellular microtubules. The vinca alkaloids (e.g., vinblastine, vincristine) also inhibit cell division but by disrupting the mitotic spindle. Doxorubicin (Adriamycin) intercalates between DNA base pairs and impairs the progression of topoisomerase ii, which unwinds DNA for transcription.

Ref.: 8, 16

18. A 27-year-old woman sustains an incomplete T10 spinal cord injury after falling off a horse. The patient is given 30 mg/kg of methylprednisolone. Which of the following is true regarding steroid hormones and their receptors?

A. Steroid hormones are synthesized from proteins.

B. In the bloodstream, steroid hormones often dimerize to facilitate transport.

C. Steroid hormone receptors are found only in the cytoplasm.

D. Heat shock proteins (HSPs) are usually associated with cytosolic steroid hormone receptors.

E. Binding of the steroid hormone to a receptor induces a second messenger cascade to alter cellular metabolism.

ANSWER: D

COMMENTS: Steroid hormones are synthesized from cholesterol. Their lipophilic nature allows them to cross cell membranes easily. Steroid hormones can be divided into five groups based on their receptors: glucocorticoids, mineralocorticoids, androgens, estrogens, and progestogens. In the bloodstream, steroid hormones are generally bound to specific carrier proteins such as sex hormone–binding globulin or corticosteroid-binding globulin. Receptors for steroid hormones are most commonly located in the cytosol, although they are also found in the nucleus and on the cell membrane. After binding to the steroid hormone, steroid receptors often dimerize. For many cytosolic steroid receptors, binding of the ligand induces a conformational change and releases HSPs. Nuclear steroid receptors are not generally associated with HSPs. HSPs themselves have several roles, including functioning as intracellular chaperones for other proteins, serving as transcription factors, and facilitating antigen binding. They may also serve as targets for therapeutics. Ultimately, the activated steroid receptor must enter the nucleus to serve as a transcription factor for augmentation or suppression of the expression of particular genes. The resulting messenger RNA leaves the nucleus for the ribosomes, where it is translated to produce specific proteins.

Ref.: 16

19. A 55-year-old man with a history of hepatitis C cirrhosis has complaints of nausea, fever, and progressive lethargy. Part of his evaluation includes an assessment of his hepatitis C viral load. Which of the following tests would be most useful in assessing his hepatitis C viral load?

A. Western blot

B. Gel electrophoresis

C. Fluorescence microscopy
D. Polymerase chain reaction (PCR)
E. Expression cloning

ANSWER: D

COMMENTS: Western blot is a technique used to detect specific proteins in a sample. An antibody to the protein of interest is used as a probe. Gel electrophoresis is a method for separating proteins or nucleic acids according to their size, mass, or composition. It is based on the differential rate of movement of the molecules of interest through a gel when an electric field is applied. PCR is a technique by which DNA may be massively amplified. Primers or oligonucleotides are synthesized to complement one strand of the DNA to be amplified. Amplification involves three temperature-cycled steps: (1) heating for separation (denaturation) of the double-helix structure into two single strands, (2) cooling for hybridization of each single strand with its primer (annealing), and (3) heating for DNA synthesis (elongation). The steps are repeated with exponential amplification of the DNA of interest. When RNA is used, reverse transcriptase is employed initially to transcribe the RNA to DNA before amplification. Quantitative PCR can be used in real time to measure the starting concentration of DNA or RNA in a sample, for example, the amount of hepatitis C RNA in a blood sample. With expression cloning, DNA coding for a protein of interest is cloned into a plasmid (extrachromosomal DNA molecule) that can be inserted into a bacterial or animal cell. The cell expresses the protein, which allows the production of sufficient amounts for study. Fluorescence microscopy is performed by labeling a component of interest in a sample with a molecule that absorbs light at one wavelength and emits at another (fluorescence).

Ref.: 16

20. A 56-year-old man underwent total thyroidectomy for papillary cancer. On the first postoperative day, the patient complains of circumoral tingling and muscle weakness. Which of the following statements regarding the electrical properties of cell membranes is not true?

A. Ions flow through hydrophilic channels formed by specific transmembrane proteins.
B. Lipids provide the ability to store electric charge (capacitance).
C. Active pumps maintain the ionic gradients necessary for a resting membrane potential.
D. Initiation of an action potential depends on voltage-gated channels.
E. Large numbers of sodium ions rush in during the initial phase of a nerve action potential.

ANSWER: E

COMMENTS: This patient has clinical findings associated with hypocalcemia. Specific transmembrane proteins provide hydrophilic paths for the ions (primarily Na^+, K^+, Ca^{2+}, and Cl^-) involved in electrical signaling. The amino acid sequence in specific regions of these proteins determines the selectivity for ions. The lipid component of the plasma membrane provides the capability of storing electric charge (capacitance), and the protein component provides the capability of resisting electric charge (resistance). Establishment and maintenance of a resting cell membrane potential require the separation of charge maintained by membrane capacitance, selective permeability of the plasma membrane, concentration gradients (intracellular versus extracellular) of the permeant ions, and impermeant intracellular anions. Active pumping by the sodium [sodium-potassium adenosine triphosphatase (Na^+, K^+-ATPase)] or calcium pumps generally maintains the ionic concentration gradients. Action potentials are regenerative (self-sustaining) transient depolarizations caused by the activation of voltage-sensitive sodium and potassium channels. Only a small volume of Na^+ is necessary to initiate an action potential. In fact, the amount of Na^+ that flows into a typical nerve cell during an action potential would change the intracellular Na^+ concentration by only a few parts per million.

Ref.: 16, 17

21. Which cell junction acts as a transmembrane linkage without an intracellular communication function?

A. Tight junction
B. Gap junction
C. Desmosome
D. Connexon
E. All of the above junctions have an intracellular communication function

ANSWER: C

COMMENTS: Any patient undergoing abdominal surgery will sustain a certain amount of capillary leakage. A proposed mechanism involves increased release of nitric oxide (NO), which causes vasodilation in precapillary cells and vasoconstriction in postcapillary cells, ultimately resulting in increased third-spacing of fluids. There are three major types of cell junctions: gap junctions, desmosomes, and tight junctions. Gap junctions are the most common and function primarily in intercellular communication and cellular adhesion. The connection between cells maintained by a gap junction is not particularly stable; it depends on a variety of complexes on each cell but not on connecting proteins (hence the term gap). Gap junctions serve as a pathway of permeability between cells for many different molecules weighing up to 1000 daltons. Connexons are protein assemblies formed by six identical protein subunits. They span the intercellular gap of the lipid bilayer to form an aqueous channel connecting the bilayers. Desmosomes function as cellular adhesion points but do not provide a pathway of communication. They are linked by filaments that function as transmembrane linkers, but desmosomes are not points of true cell fusion. Tight junctions, in contrast, are true points of cell fusion and are impermeable barriers. They prevent leakage of molecules across the epithelium in either direction. They also limit the movement of membrane proteins within the lipid bilayer of the plasma membrane and therefore maintain cells in a differentiated polar state.

Ref.: 16, 18

22. A 42-year-old woman with a history of end-stage renal disease is being evaluated for cadaveric renal transplantation. Which of the following statements regarding cell surface antigens is true?

A. Cell surface antigens are generally glycoproteins or glycolipids.
B. Histocompatibility antigens are not cell surface antigens.
C. ABO antigens are glycoproteins.
D. ABO antibodies are present at birth.
E. Human leukocyte antigen (HLA) has an extracellular hydrophobic region and an intracellular hydrophilic region.

ANSWER: A

COMMENTS: Cell surface antigens are generally glycoproteins or glycolipids that are anchored to either a protein or a lipid. Common examples include the ABO blood group antigens and the histocompatibility antigens. Antigens of the ABO system are glycolipids whose oligosaccharide portions are responsible for the antigenic properties. The structures of the blood group oligosaccharides occur commonly in nature and lead to the stimulation needed to produce anti-A or anti-B antibodies after a few months of life. HLA antigens are two-chain glycoproteins that are anchored in the cell membrane at the carboxyl terminal. These antigens contain an extracellular hydrophilic region, a transmembrane hydrophobic region, and an intracellular hydrophilic region. This transmembrane structure allows extracellular signals to be transmitted to the interior of the cell.

Ref.: 19

23. Regarding chemical messengers, which statement is true?

A. They depend on cell surface–bound proteins to exert their effect.

B. They are limited to intracellular receptors to exert their effect.

C. First messengers bind directly to DNA to begin the protein synthesis process.

D. Extracellular ligands are termed the "second messengers."

E. Extracellular ligands are termed the "first messengers."

ANSWER: E

COMMENTS: Chemical messengers can influence intracellular physiology via several mechanisms. Some ligands, such as acetylcholine (binding to the nicotinic cholinergic receptor) or norepinephrine (binding to the potassium channel in cardiac muscle), directly bind to ion channels in the cell membrane to alter their conductance. Some lipid-soluble messengers, such as steroid and thyroid hormones, enter the cell and bind to nuclear or cytoplasmic receptors, which then bind to DNA to increase transcription of selected mRNA. Many other extracellular messengers bind to the extracellular portion of transmembrane receptor proteins to trigger the release of intracellular mediators. The extracellular ligands are termed as the "first messenger," whereas the intracellular mediators are "second messengers." Examples of second messengers include IP_3, DAG, calcium, and cAMP.

Ref.: 18, 20

24. A 67-year-old man undergoes revascularization of his right lower extremity after sustaining thrombosis secondary to a popliteal artery aneurysm. Shortly after surgery, a compartment syndrome of the affected limb develops and is attributed to reperfusion injury. Research suggests that ER stress may be responsible for apoptosis after ischemia. Which of the following statements regarding the ER is not true?

A. Rough ER is a primary site of lipid synthesis.

B. Smooth ER plays an important role in the metabolism of drugs.

C. Ribosomes attached to the rough ER manufacture proteins for use within the cell.

D. SR is found mainly in epithelial cells.

E. SR plays an important role in gluconeogenesis.

ANSWER: B

COMMENTS: The ER is part of a network that includes mitochondria, lysosomes, microbodies, the Golgi complex, and the nuclear envelope. This network forms an intracellular circulatory system that allows vital substrates to reach the interior of the cell for transportation and assembly. There are two types of ER. Rough ER is coated with ribosomes and functions as the site of synthesis of membrane and secreted proteins. Other ribosomes that circulate freely in the cytoplasm synthesize proteins destined to remain within the cell. Smooth ER plays a major role in metabolic processes, including the synthesis of lipids and steroids, metabolism of carbohydrates (especially gluconeogenesis), drug detoxification, and molecular conjugation. Smooth ER contains the enzyme glucose-6-phosphatase, which converts glucose-6-phosphate to glucose during gluconeogenesis. Cells that synthesize large amounts of protein for export have abundant rough ER, whereas cells that produce steroids (e.g., those in the adrenal cortex) generally have smoother ER. The smooth ER is continuous with the nuclear envelope. The SR is a distinct type of smooth ER found in striated and smooth muscles. The SR contains large stores of calcium, which it sequesters and then releases when the cell is stimulated. The release of calcium from the SR plays a major role in excitation–contraction coupling, which allows muscle cells to convert an electric stimulus to a mechanical response.

Ref.: 18, 20

25. Which of the following statements regarding lysosomes is true?

A. Primary lysosomes usually contain extracellular material targeted for digestion.

B. Lysosomal enzymes work effectively in the acidic pH of the cytoplasm.

C. Serum levels of lysosomal acid phosphatases may have prognostic value in diseases such as prostate cancer.

D. Lysosomal storage diseases such as Tay-Sachs result from unregulated activity of lysosomal enzymes.

E. To better isolate their hydrolytic enzymes, lysosomes are resistant to fusion with other cell membranes.

ANSWER: C

COMMENTS: Lysosomes are membrane-bound organelles that contain acid hydrolases. Heterolysosomes are involved in the endocytosis and digestion of extracellular material, whereas autolysosomes are involved in digestion of the cell's own intracellular material. Primary lysosomes are formed by the addition of hydrolytic enzymes (from the rough ER) to endosomes from the Golgi complex. Combining a primary lysosome with a phagosome creates a phagolysosome. Lysosomal enzymes are hydrolases that are resistant to autolysis. They function best in the acidic milieu of the lysosome; the slightly alkaline pH of the surrounding cytosol helps protect the cell from injury if the lysosome leaks. Acid phosphatase is a marker enzyme for lysosomes. Different forms of acid phosphatases are found in lysosomes from various organs, and serum levels may be indicative of specific diseases (for example, prostatic acid phosphatase may have prognostic significance in prostate cancer).

One of the distinguishing characteristics of lysosomal membranes is their ability to fuse with other cell membranes. Lysosomal membranes have a high proportion of lipids in a micellar configuration, primarily because of the presence of the phospholipid lysolecithin. This increased micellar configuration facilitates fusion of