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Most cases of thrombocytopenia seen in the emergency department (ED) are expected. Patients are known to have hematological disease or are receiving chemotherapy. At times, however, the ED physician is confronted with an unexpected laboratory finding in an assymptomatic patient, or with a patient who is bleeding. The challenge, as usual, is to determine the need for acute treatment and the appropriate disposition.

As this article discusses, one of the most important diagnostic procedures in patients with thrombocytopenia is the peripheral blood smear. The simple test will often determine the presence of pseudothrombocytopenia and more serious causes such as thrombotic thrombocytopenia and hemolytic uremic syndrome.

—Sandra M. Schneider, MD, FACEP, Editor

Thrombocytopenia

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Introduction

Case 1. A 45-year-old patient presents to the emergency department (ED). He has a long history of alcohol abuse, and is clearly intoxicated this evening. While you study his records and perform a medical screening examination, you learn that he has a diagnosis of cirrhosis. The only medication he is prescribed is folate, but he has been noncompliant with this for years. His examination is unremarkable except for splenomegaly. Specifically, he is alert without petechiae or ecchymoses. His urinalysis is negative for blood, and his stool is guaiac negative. His laboratory values are remarkable for a hemoglobin of 13.4 grams, a normal white blood count and differential, an INR of 1.0, normal electrolytes, and a platelet count of 8000/µL.

Case 2. A 3-year-old child presents with complaint of reddish spots on his legs of 3-4 days duration. He has been in good health, although his mother reports an upper respiratory infection one week ago, for which the child did not receive medication. On examination, his vital signs are normal, and he shows no evi-

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dence of recent epistaxis, and no blood in his urine or stool. The reddish spots do not blanch and are 2-3 mm in diameter. A complete blood count reveals a hemoglobin of 13.9, with a white blood count of 5,000 and a platelet count of 19,000/μL.

Case 3. A 56-year-old woman presents to a teaching hospital with shortness of breath of sudden onset. She has recently been hospitalized for a deep venous thrombosis in her left leg. Initially she had been fully heparinized with unfractionated heparin (UFH), then discharged from the hospital 4 days later with a therapeutic INR, on warfarin. She insists that she has been compliant with her warfarin therapy, and her measured INR is 2.7. Her hemoglobin is 14.3, but her platelet count is only 22,300/μL. Her story is typical for pulmonary embolism, and the primary physician wants to re-start heparin and admit her to the hospital for a filter placement. The intern is skeptical that she could have developed a pulmonary embolism given that her INR is therapeutic, her platelet count is very low, and therefore she should not be at risk to have a clot.

Thrombocytopenia

The normal platelet count in adults ranges from 150,000 to 450,000/microliter (μL). Thrombocytopenia is defined as a platelet count of less than 150,000/μL (150 x 10^9/L), with the implication that 2.5% of the normal population will have a platelet count lower than this. Clinically, thrombocytopenia may be asymptomatic or may present with bleeding, petechiae, or easy bruising. Regardless of cause, thrombocytopenia stimulates an increase in free thrombopoietin, which attempts to increase platelet production. Young platelets are larger than mature platelets and are often seen on the blood smear. Broadly, low platelet counts may be caused by decreased production, increased destruction, splenic sequestration, or a combination of the three. Approximately one-third of platelets are sequestered in the spleen, and the other two-thirds circulate for 7-10 days. The cause for a low platelet count may not be immediately apparent, especially in patients without evidence for systemic disease. A major goal in the ED is to control bleeding if present (often requiring platelet transfusion), and assess the risk of bleeding. The risk of spontaneous bleeding increases when the platelet level falls below 10,000 and 20,000/μL

The cause for the thrombocytopenia may not be immediately apparent, especially in patients without evidence of systemic disease. In many cases the exact cause can be determined later. However there are several disorders that should be determined in the ED such as thrombotic thrombocytopenia purpura, hemolytic uremic syndrome, and heparin-induced thrombocytopenia.

Pseudothrombocytopenia

The platelet count can be falsely low for a number of reasons. First, if the blood sample is inadequately anticoagulated, platelet clumps might be recognized as leukocytes by cell counters. A visual check of a blood smear generally will determine this diagnosis. The white blood cell count might be falsely elevated by up to 10% in this case.[1]

Some patients have intrinsic EDTA-dependent agglutinins, which lead to spurious leukocytosis and thrombocytopenia. Similar to inadequately anticoagulated blood, EDTA-induced platelet clumping can be diagnosed by examination of the peripheral smear. If the peripheral smear shows platelet clumping, the platelet count should be repeated using heparin or sodium citrate as the anticoagulant, correcting the platelet count for dilution if citrate solution is used.[2]

Dilutional thrombocytopenia occurs in patients who have sustained massive blood loss with subsequent transfusion of packed red blood cells (RBCs). In patients receiving 20 units of packed red blood cells over 24 hours, platelet counts have been reported to be 25,000 to 61,000/μL.[3] This may be prevented by giving platelet concentrate transfusions to patients receiving more than 20 units of packed RBCs over a 24 hour period.[2]

Dilutional thrombocytopenia also may be caused by splenomegaly. Normally, approximately one-third of circulating platelets are sequestered in the spleen, where they are in equilibrium with circulating platelets. Patients with cirrhosis, portal hypertension, and splenomegaly may have apparent thrombocytopenia, as splenic sequestration of platelets can be increased to as high as 90% with portal hypertension. However, since the total platelet mass and survival is relatively normal, clinical bleeding is rarely a problem from low platelets due to splenomegaly alone.[4]

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Table 1. Causes for Thrombocytopenia

DECREASED PLATELET PRODUCTION

- Viral infections: rubella, mumps, varicella, parvovirus, hepatitis C; Epstein-Barr virus, cytomegalovirus
- Live attenuated measles vaccination
- HIV
- Chemotherapy
- Radiation therapy
- Acquired or congenital bone marrow aplasia
  Fanconi anemia, pure megakaryocytic aplasia, thrombocytopenia with absent radius (TAR) syndrome
- Alcohol toxicity
- Vitamin B12 and folate deficiency
- Marrow infiltration: tumor, infection

INCREASED PLATELET DESTRUCTION

- Idiopathic thrombocytopenic purpura
- Systemic lupus erythematosus
- Disseminated intravascular coagulation
- Antiphospholipid syndrome
- Hemolytic anemia with elevated liver function tests and low platelet count (HELLP syndrome)
- Drugs, heparin, quinine, quinidine, valproate, protamine
- Thrombotic thrombocytopenic purpura/hemolytic uremic syndrome (TTP-HUS)
- Auto immune destruction: post transfusion, neonatal, post-transplant
- Viral: dengue hemorrhagic fever
- Malaria

Congenital

Kasabach-Merritt
Neonatal alloimmune thrombocytopenia
HPA-1a incompatibility

Other

Pregnancy
Rattlesnake envenomation
Wiskott-Aldrich

Categories and Causes for Thrombocytopenia

Platelet counts may be depressed because of decreased production or due to increased platelet destruction.

Decreased platelet production by the bone marrow may be related to viral infections: mumps, rubella, varicella, hepatitis C,[5] or Epstein-Barr virus. Neonatal infections such as cytomegalovirus (CMV) or rubella may present with other findings in addition to thrombocytopenia. The human immunodeficiency virus may damage megakaryocytes directly. Thrombocytopenia also may be related to measles vaccination.[6] A decreased platelet count due to viral infection may be more severe if present in a patient with bone marrow suppression, such as from chemotherapy. Chemotherapy or radiation therapy may decrease platelet production as well as other blood cells. Marrow infiltration from lymphoma or leukemia or myelofibrosis may cause deficits in multiple cell lines. Some congenital or acquired disorders are associated with bone marrow aplasia or hypoplasia. Alcohol may suppress platelet production, as may vitamin B12 or folate deficiency. Decreased platelet production may be drug-related, as with heparin, quinidine, valproic acid, or quinine. (*See Table 1.*)

Increased platelet destruction may be due to immune mechanisms, such as systemic lupus erythematosus (SLE), antiphospholipid syndrome, or idiopathic thrombocytopenic purpura (ITP). With ongoing platelet destruction, the circulating young platelets are usually large, indicating that the bone marrow is producing new/larger platelets to compensate for increased destruction. Thrombocytopenia may be related to consumption, as in disseminated intravascular coagulation (DIC) or to alloimmune destruction, as may occur in neonates, post-transplantation, or post-transfusion states. Some viral infections have been related to platelet destruction, notably infectious mononucleosis, cytomegalovirus, and HIV. Fever and thrombocytopenia in an adult or child with a history of recent travel should suggest malaria, and a blood smear examined for parasites.[7] Thrombotic thrombocytopenic purpura–hemolytic uremic syndrome (TTP–HUS), and the HELLP syndrome of hemolytic anemia, elevated liver function tests, and low platelet count are also associated with increased platelet destruction. (*See Table 1.*)

Incidental thrombocytopenia of pregnancy, or gestational thrombocytopenia, is generally mild, asymptomatic, and resolves spontaneously rapidly postpartum. It tends to occur in late gestation and is not associated with fetal thrombocytopenia. Platelet counts are generally greater than 70,000/μL.[2]

Splenic sequestration may be suspected in any patient with splenomegaly. An estimate of splenic size, therefore, should be made based upon physical examination supplemented if necessary by ultrasound or computed tomography. Portal hypertension secondary to liver disease, or splenic infiltration with myeloproliferative or lymphoproliferative disorders are common causes of splenomegaly.

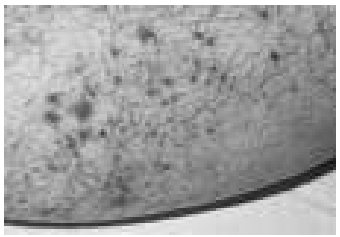
There are unusual causes of thrombocytopenia in children, some congenital. Thrombocytopenia associated with giant hemangioma of infancy is called the Kasabach-Merritt syndrome. Alloimmunization secondary to incompatibility of platelet antigens between mother and fetus is termed neonatal alloimmune thrombocytopenia (NAIT), due to platelet destruction by maternal IgG alloantibodies that have crossed the placenta. More common is incompatibility of the HPA-1a or PIA1 antigen, causing thrombocytopenia, and possibly hydrocephalus, seizures, hyperbilirubinemia, and fetal loss. Treatment is with PIA1-negative platelet transfusion.

Mild thrombocytopenia is suggestive of Bernard-Soulier syndrome, a congenital syndrome associated with platelet dysfunction and absence of glycoprotein 1b, V, and IX.[8] These proteins serve as receptors for von Willebrand factor and their absence results in decreased platelet adhesion.

Congenital idiopathic amegakaryocytic thrombocytopenia presents in infants as isolated thrombocytopenia, although this may progress later to pancytopenia.[9] Hereditary amegakaryocytopoiesis usually is associated with skeletal abnormalities.

Thrombocytopenia with absent radii (TAR) syndrome is one associated with radial agenesis and other upper limb defects.[10]

Figure 1. Petechiae



Wiskott-Aldrich syndrome is associated with small platelets, thrombocytopenia, eczema, and immunodeficiency. Hematopoietic cell transplant may be curative.[11]

The Clinical Presentation of Thrombocytopenia

Asymptomatic. Patients with thrombocytopenia may be asymptomatic, with detection only on a complete blood count. Mucosal bleeding may present as epistaxis or gingival bleeding. Cutaneous bleeding may manifest itself as petechiae, bullous hemorrhages, or ecchymoses. Petechiae are red, flat, non-palpable, discrete lesions that are pinhead sized and tend to cluster on the feet and ankles. (*See Figure 1.*) They are nontender and are due to the presence of extravasated red blood cells. Ecchymoses are also nontender areas of bleeding into the skin from extravasated blood, and usually develop without noticeable trauma. Hemoptysis, hematuria, and hematochezia may be presenting signs.

Prolonged bleeding during menstruation (menorrhagia) or bleeding between menses (metrorrhagia) are common presentations. Patients with platelet abnormalities tend to bleed immediately after vascular trauma, as opposed to delayed bleeding characteristic of coagulation disorders such as hemophilia. Bleeding into the central nervous system is uncommon without preceding trauma, but is the most common cause of death due to thrombocytopenia.[2] In patients with coagulation disorders such as hemophilia, bleeding tends to be deeper—in the tissues, muscles, and joints, as well as more delayed bleeding and more post-surgical bleeding.

Bleeding Risks. The risks of bleeding at any given platelet level may depend upon the underlying cause for the thrombocytopenia. Surgical bleeding due solely to a reduction in the number of platelets is unlikely unless the platelet count is less than 50,000/µL. Spontaneous bleeding does not occur until the platelet count is less than 10,000 to 20,000/µL. On the other hand, patients with idiopathic thrombocytopenic purpura (ITP) do not usually have serious bleeding, suggesting that the young platelets found in these patients are more hemostatically active than mixed age or older platelets in normal subjects. In patients with ITP, severe life-threatening bleeding may not occur until platelet counts are less than 6,000/µL, while self-limiting and spontaneous bleeding did not occur until platelet counts were less than 40,000/µL and 12,000/µL respectively, in one report.[12] (*See Table 2.*)

The risk of lumbar puncture in the thrombocytopenic patient is of importance in the ED. One study reported 29 lumbar punctures in children with platelet counts less than 10 x 10^9/L or less, and another 170 with platelet counts of 11-20 x 10^9/L, with no complications, among children with acute lymphoblastic leukemia. The authors felt that prophylactic platelet transfusions were not definitely indicated prior to lumbar puncture in thrombocytopenic children.[13]

Table 2. Platelet Counts in Relation to Bleeding Risk[14]

PLATELET COUNT	COMPLICATION
< 60,000/µL	Risk of bleeding after trauma
< 50,000/µL	Surgical bleeding may occur
< 40,000/µL	Self-limited bleeding
< 10,000 – 20,000/µL	Spontaneous bleeding may occur in ITP patients
< 12,000/µL	Spontaneous bleeding requiring special attention
< 6,000/µL	Severe life-threatening bleeding

The History in the Thrombocytopenic Patient

A history of recent viral or rickettsial infection, or of recent travel, should be sought even in a patient with known bone marrow suppression. A history of recent live virus vaccination and medication exposure or a positive family history of bleeding or thrombocytopenia should be sought. Poor nutritional status, including alcoholism or history of certain medications, may give a clue as to etiology. Dietary habits or antibiotic use that might predispose to deficiencies of vitamin K, vitamin B12, and folic acid should be queried in patients with suspected bleeding disorder. While a careful drug history is paramount, thrombocytopenia caused by undisclosed drug use has been described.[14] Non-hematologic disorders known to decrease platelet counts, such as eclampsia, sepsis, DIC, hypothermia, or massive transfusions, may be evident. Sepsis is the most common cause for thrombocytopenia developing for the first time in a patient in an intensive care unit setting (up to 50% of the cases).[15]

The Physical Examination of the Thrombocytopenic Patient

Examination for lymphadenopathy and splenomegaly may indicate the presence of a disseminated disorder—infectious or malignant. Funduscopic examination may reveal evidence for hemorrhage, as CNS bleeding is the most common cause for death in the thrombocytopenic patient. Examination of the stool may reveal occult blood. Skin evaluation and examination of catheter, drain, or surgical sites may reveal evidence for bleeding. The size of the spleen should be assessed as splenomegaly is suggestive of lymphoma, malaria, mononucleosis, or other disorder associated with splenic sequestration.

The Evaluation of the Patient with Thrombocytopenia. Laboratory evaluation of the thrombocytopenic patient begins with a

complete blood count and examination of the peripheral smear for estimation of the morphology and number of platelets, presence of platelet clumping, and morphology of platelets. Any associated white and red blood cell changes should be noted as well.

A peripheral smear of non-anticoagulated blood should be examined. As noted earlier, the presence of platelet clumps may result in a spuriously low platelet count due to inadequate sample anti-coagulation or to EDTA. Repeat blood sampling with an alternate anticoagulant such as heparin or sodium citrate helps to make the diagnosis. The blood smear is also important to examine to diagnose some of the more severe syndromes of TTP, HUS, and DIC.

A number of congenital thrombocytopenic disorders manifest on the peripheral smear as alterations in size, or with abnormal platelet granules, or with neutrophilic inclusions.[16] The May-Hegglin anomaly is an autosomal dominant trait characterized by giant platelets, leukocyte inclusion bodies, and mild to moderate thrombocytopenia. The laboratory particle counter may not recognize the platelets and give a falsely low reading; patients are generally asymptomatic, but may have a mild bleeding disorder. Alport's syndrome of congenital nephritis may present with hematuria and progressive renal failure. Some families have thrombocytopenia and deafness. Peripheral smear may show leukocyte inclusion bodies. Wiskott-Aldrich syndrome is an X-linked disorder characterized by immune deficiency, eczema, and thrombocytopenia with small platelets.

Inadequate sample anticoagulation may reveal EDTA-induced platelet clumping in the peripheral smear, as noted earlier. Repeat blood sampling with a different anticoagulant such as heparin or sodium citrate confirms the diagnosis.

The cause for decreased platelet production may be evident on smear. Circulating blast cells indicate the presence of acute leukemia. A leukoerythroblastic blood picture with nucleated red blood cells and early myeloid forms in the blood suggests bone marrow invasion with tumor, fibrosis, or granulomatous infection such as tuberculosis. Other cytopenias may be present in myelodysplastic states. Large oval red blood cells with hypersegmentation of neutrophils are present on vitamin B12 or folate deficiency.[2]

Increased platelet destruction may be suggested with a microangiopathic blood picture, with fragmented red blood cells, hemolytic anemia, and elevated lactate dehydrogenase. These findings occur in disseminated intravascular coagulation (DIC) or thrombotic thrombocytopenic purpura and hemolytic uremic syndrome (TTP-HUS).

Bone marrow aspiration and biopsy is indicated on nearly all patients with thrombocytopenia severe enough to constitute a risk for major bleeding. An exception is the patient younger than age 60 with isolated thrombocytopenia and no evidence for underlying disorder with a presumptive diagnosis of idiopathic thrombocytopenic purpura (ITP, see below).[17] Even if the diagnosis of ITP is contemplated, it has been proposed that bone marrow examination be accomplished prior to starting steroid therapy, as this may confound the diagnosis of acute leukemia in children.[18] The presence of normal to increased numbers of megakaryocytes indicates that the patient's thrombocytopenia is due, at least in part, to increased peripheral destruction, as in ITP. Decreased numbers of megakaryocytes along with overall decreased cellularity is consistent with decreased bone marrow production, as in aplastic anemia. Megaloblastic changes in the red blood cell and granulocytic series suggest vitamin B12 or folate deficiency. Dysplastic changes in the red cell, granulocytic, and megakaryocytic lineages suggest a myelodysplastic disorder.

Bone marrow invasion is suggested by the presence of malignant cells, granulomata, or collagen fibrosis. Rarely, there may be severe reduction or absence of megakaryocytes with no other abnormalities, suggesting the presence of an autoantibody against the thrombopoietin receptor, as in systemic lupus erythematosus.[2]

Drug-Induced Thrombocytopenia

The diagnosis of drug-induced thrombocytopenia can be made only by demonstrating resolution of thrombocytopenia once a suspected drug is discontinued.[19] It is important to note that many patients with drug-induced thrombocytopenia are initially diagnosed as having idiopathic thrombocytopenic purpura. A cause and

Table 3. Some Drugs Associated with Thrombocytopenia[17,19,22]

Acetaminophen	Interferons (alfa & beta)
Acetazolamide	Isoniazid
Amiodarone	Levetiracetam
Amrinone	Linezolid
Angiotensin converting enzyme inhibitors (ACEI)	Lopinavir
Aspirin	Measles-mumps-rubella vaccine
Bleomycin	Methicillin
Cephalosporins	Minoxidil
Chemotherapeutic agents: carboplatin, alkylating agents, anthracyclines, antimetabolites	Nitroglycerin
Chlorpromazine	Penicillin
Chlorothiazide	Phenytoin
Cimetidine	Platelet inhibitors: tirofiban, eptifibatide, abciximab, ticlopidine, clopidogrel
Dactinomycin	Procainamide
Diazoxide	Protamine sulfate
Digoxin	Quinidine, quinine
Eptifibatide	Ranitidine
Estrogens	Rifampin
Ethanol	Ristocetin
Furosemide	Tolbutamide
Glycoprotein II b/IIIa inhibitors	Trimethoprim- sulfamethoxazole and other sulfonamides
Gold salts	Valproic acid
Heparin	Vancomycin
Heroin	
Indinavir	
Indomethacin	

effect relationship depends upon establishment of the following:

• Therapy with the suspected drug preceded the thrombocytopenia;

• Recovery from the thrombocytopenia was complete and sustained after discontinuation of the drug;

• Other drugs were continued or re-introduced after discontinuation of therapy with the suspected drug, with a sustained normal platelet count—or the suspected drug was the only one used before the onset of thrombocytopenia;

• Other causes for thrombocytopenia were excluded;

• Re-exposure to the suspected drug resulted in recurrent thrombocytopenia.[20]

The number of medications associated with thrombocytopenia is quite long; one list from Denmark of thrombocytopenia-inducing agents included 110 different drugs.[21] Some drugs, such as aspirin or non-steroidal anti-inflammatory drugs (NSAIDs), can exacerbate an underlying platelet disorder. Commonly cited agents include gold salts, heparin, valproic acid, phenytoin, indomethacin, sulfonamides, glycoprotein IIb/IIIa inhibitors, quinidine, and quinine. (*See Table 3.*) Heparin-induced thrombocytopenia is the most common drug-related cause of a drop in platelet count and is addressed separately.

Some cytotoxic agents such as cisplatin and cyclophosphamide cause generalized bone marrow depression.[22] Other drugs induce selective suppression of megakaryocyte production (thiazides, ethanol, tolbutamide). Some accelerate platelet destruction by immunologic (acetaminophen, methicillin, rifampin, procainamide, interferons alfa and beta, others) or non-immunologic (ristocetin, protamine sulfate) mechanisms.

Current laboratory assays for drug-dependent antiplatelet antibodies are not useful for diagnosing drug-induced thrombocytopenia in the ED.[19] In some patients with a history that is typical for drug-induced thrombocytopenia, antibody tests may be negative.[22] One reason for this may be that a drug metabolite produced in vivo is the actual sensitizing agent.[23] Gold-induced immune thrombocytopenia may persist for months due to presence of the antigen in the reticuloendothelial system, but for the most part, thrombocytopenia should resolve within 2-4 weeks of discontinuation of an offending drug. Typically, a patient will have taken the sensitizing drug for approximately one week or intermittently over a longer period before presenting with petechiae or ecchymoses, but occasionally symptoms develop within 1 to 2 days of exposure to a drug. This is true particularly of the platelet inhibitor abciximab.[24] Abciximab-induced thrombocytopenia may occur within 30 minutes to several hours after initial administration. Other types of drug-induced thrombocytopenia require a much longer period of drug administration to induce sensitization.[25,26] Certain drugs that are cleared from body storage depots very slowly, such as phenytoin, may induce more prolonged thrombocytopenia.

Many patients with drug-induced thrombocytopenia have only petechial hemorrhages and occasional ecchymoses and require no treatment except to discontinue the sensitizing medication. More aggressive therapy including platelet transfusions may be necessary to prevent intrapulmonary or intracranial hemorrhage. Otherwise, treatment may include oral or intravenous steroids and intravenous immune globulin. The platelet count should be monitored frequently in patients receiving glycoprotein IIb/IIIa inhibitors, especially abciximab.[27] Three patients in one series underwent splenectomy before the drug-induced (quinidine) etiology was discovered.[28]

Medication exposure may not be obvious and, at times, some detective work is necessary. Heparin-induced thrombocytopenia is discussed separately, although it is worth noting that heparin flushes of vascular access lines may not be noted separately in the medical record. Vancomycin mixed into joint replacement cement may not be known to the patient. Drug-induced thrombocytopenia has occurred due to herbal remedies as well.[29]

Idiopathic Thrombocytopenic Purpura

Idiopathic thrombocytic purpura (ITP) is an acquired autoimmune disease that results in the destruction of platelets. There is no definitive test for ITP, making this a diagnosis of exclusion. It is characterized by thrombocytopenia, with petechiae or purpura, and a normal bone marrow. ITP may occur in all age groups, and may present acutely or chronically. Acute ITP is more common in younger children and typically resolves within 1-2 months.

Immune thrombocytopenic purpura is classified as either primary or as secondary to an underlying disorder. Primary immune thrombocytopenia is the classic ITP that is not secondary to any systemic illness.[30] Secondary immune thrombocytopenic purpura is associated with SLE, chronic lymphocytic leukemia, HIV infection, hepatitis C infection, and a variety of other disorders including therapy with drugs such as heparin or quinidine.[31]

ITP in children usually occurs between the ages of 2 and 4 years. There may be a history of antecedent viral illness, such as an upper respiratory infection or exanthem, but the child with ITP is otherwise in excellent health.[32] The onset of petechiae, bruising, epistaxis, hematuria, or gastrointestinal hemorrhage is what brings the patient to medical attention. In approximately 90% of children with ITP, the disease is acute and self-limited, resolving within six months. Chronic ITP is more common in children older than age 10 years or younger than 1 year of age.[33] Mortality is almost always associated with intracranial hemorrhage.[34]

With immune thrombocytopenias, platelet destruction is mediated by the production of autoantibodies that attach to circulating platelets. The initial inciting event in ITP is unknown, but mechanisms that lead to platelet destruction involve the activation of helper T cells and cytotoxic T cells, and antibodies against glycoproteins in the platelet membrane.[31] Platelets coated with IgG antibodies undergo accelerated clearance through Fcγ receptors that are expressed through tissue macrophages. The antibody-coated platelets are removed by the reticuloendothelial system. The platelets that are not destroyed do function normally, and frequently bleeding is not a significant problem despite low platelet counts. The methods that are currently used to treat immune thrombocytopenic purpura are directed at different aspects of the cycle of antibody production and platelet sensitization, clearance, and production.

Acute ITP is unusual in adults. Most adults present with an indolent form of thrombocytopenia that may persist for many

years, and is referred to as chronic ITP. Chronic ITP is more insidious, and approximately twice as many women as men are affected, most commonly between the ages of 18 and 40 years. It is more likely to occur in patients with underlying disease or immune disorder including systemic lupus erythematosus, Graves' disease, Hashimoto's thyroiditis, HIV, or antiphospholipid syndrome.

The CBC should demonstrate normal cell lines except for platelets. The peripheral smear is expected to show large platelets, but fewer platelets than normal. Platelet-associated IgG can be measured, but the specificity of the test is not high enough to make it clinically useful in making the diagnosis. The direct assay for the measurement of platelet-bound antibodies has an estimated sensitivity of 49-66% and an estimated specificity of 78-92%.[35,36]

Treatment of ITP includes avoidance of antiplatelet medications such as aspirin or non-steroidal anti-inflammatory drugs (NSAIDs). Fall risks should be addressed. If platelet counts are greater than 50,000/µL, no treatment is recommended. Otherwise, treatment should be initiated with steroids: 1-1.5 mg/kg or 60 mg of prednisone/day typically. A response rate of 50-80% can be expected, although when treatment is stopped, remission is sustained in only 10-30% of cases.[31] If this does not elicit a response within 6-8 weeks, splenectomy may produce long-standing remission. Splenectomy may impair the clearance of antibody-coated platelets by the Fcγ receptors and may also impair the T cell/B cell interactions involved in antibody synthesis in some patients.[30] The risks associated with splenectomy are small, but patients postoperatively have a lifelong risk of bacterial sepsis. For this reason, the American Society of Hematology recommends that splenectomy be considered in children who have had ITP for at least one year with symptomatic severe thrombocytopenia.[17] Prior to splenectomy, patients should be immunized with pneumococcal and *Hemophilus influenzae* type B vaccines. Occasionally, patients may fail to respond to therapy because of the presence of an accessory spleen, which may be detectable on nuclear scanning.

For patients who decline splenectomy, a variety of third-line therapies are available. Plasmapheresis transiently removes autoantibody from the plasma. Rituximab, a monoclonal antibody against CD20+ B cells, has an overall response rate of 25-50%. It may be preferable to long-term steroid therapy. Rituximab eliminates normal B cells, including those that produce the antiplatelet antibody. The B cell depletion lasts for 12-18 months, and there have been few side effects or toxicities demonstrated.

Other agents that have induced responses include Rh_0 (D) immune globulin, intravenous immune globulin, azathioprine, cyclophosphamide, danazol, vinca alkaloids (vincristine, vinblastine), dapsone, cyclosporine, and mycophenolate mofetil.[37]

For acute bleeding episodes, bleeding should be controlled with high-dose steroid therapy (methylprednisolone 1-2 grams IV/day) and with immune globulin at a dose of 1 gram per kilogram per day for two or three consecutive days.[30] Phagocytic blockage may be accomplished with either intravenous immune globulin (IVIG) or anti-Rh_0D immune globulin (25-75 µg/kg for two consecutive days). IVIG may contain anti-idiotypic antibodies that impede antibody production. It should be noted that IVIG can cause meningismus and headache, prompting consideration of lumbar puncture. Platelet transfusion should be withheld until the first dose of steroids has been given but may be used in emergencies to treat bleeding. An infusion of platelets should be two to three times the usual dose infused.[30] The platelets associated with ITP are young and metabolically active as detected by flow cytometry, offering an explanation for the fact that bleeding is typically less pronounced with ITP than in states of bone marrow failure at similar platelet counts.[38] Antifibrinolytic therapy with aminocaproic acid may reduce mucosal bleeding, and recombinant factor VII may be considered.[39]

The decision to treat a child with ITP is based upon the unproven assumption that shortening the duration of severe thrombocytopenia (platelet counts below 10,000-20,000/µL) affords protection from intracranial hemorrhage. The case for observation is that most children with typical ITP recover completely within a few weeks.[30]

Small pilot studies have investigated the use of thrombopoietic agents. A non-immunogenic thrombopoietic agent, AMG 531, administered subcutaneously for 3 to 6 weeks showed an overall response rate of 68%—a rise in platelet count to greater than 50,000/µL, or at least twice the baseline count—in a pilot study.[40]

TTP-HUS-DIC

Three related syndromes are important to diagnose in a patient with thrombocytopenia.

Thrombotic thrombocytopenic purpura (TTP) is a life-threatening disease that typically presents with fever, neurologic abnormalities, and renal dysfunction in addition to thrombocytopenia. It occurs primarily in adults. Platelet microthrombi form throughout the body leading to clogging of the vasculature. Most vulnerable are the kidney, brain, heart, and adrenal glands. However other organ systems are affected. Untreated, the mortality rate is as high as 90%, although with aggressive treatment 80-90% survive.

A related syndrome, hemolytic uremic syndrome (HUS), occurs primarily in children with hemolytic anemia, thrombocytopenia, and acute renal failure. This disease often occurs after a viral illness or infectious diarrhea. Despite thrombocytopenia, bleeding is rare.

Finally, disseminated intravascular coagulation (DIC) presents as a systemic disease usually associated with sepsis or severe illness. Platelets are low and bleeding is common.

Common to all of these diseases is the finding of schistocytes on the peripheral blood smear along with decreased and large (young) platelets.

Heparin-Induced Thrombocytopenia

First described in 1958, heparin-induced thrombocytopenia (HIT) is a life-threatening disorder that follows exposure to unfractionated heparin (UFH) or, less commonly, low-molecular weight heparin (LMWH). Classically, patients present either with a low platelet count (less than 150,000/µL) or a relative decrease of 50% or more from baseline.[41] Deep venous thrombosis and pulmonary embolism are its most frequent sequelae, although arterial events—loss of limb, stroke, and myocardial infarction—can also

occur.[42] Differences in the absolute platelet count greater than 70,000 to 90,000/µL infrequently occur within the same patient. Therefore, if a patient's platelet count has recently fallen 50% or more from a prior value, this should raise the strong possibility of HIT in any patient begun on heparin therapy within the preceding five to 10 days, especially with clinical evidence for new thrombosis. Resistance to UFH, defined as an inability to maintain a therapeutic activated PTT despite increasing dosage, may herald HIT.[43]

Heparin-induced thrombocytopenia is caused by antibodies against complexes of platelet factor 4 (PF4) and heparin. These antibodies also may be present in patients exposed to heparin but in whom no clinical manifestations develop. The time of onset of thrombocytopenia after initiation of heparin is typically 5-10 days in patients who have had no exposure to heparin or have had remote (over 100 days) exposure. Precipitous declines in platelet counts may occur if patients have had a recent exposure to heparin and have detectable levels of PF4-platelet antibodies.[44] Platelet levels seldom drop below 10,000/µL, and typically recover within 4-10 days. It is not uncommon; the incidence of HIT may be as high as 5% in patients receiving UFH, and approximately 1% in patients receiving LMWH.[41] It is important to note that heparin flushes, prophylactic doses of heparin subcutaneously, or small amounts of heparin on coated catheters, all can cause HIT.

Type I HIT is non-immune mediated and entails a small transient drop in platelet count between days 1 and 4 of treatment. Type II HIT is an immune-mediated process that can result in thromboembolic complications and death.[42]

HIT is seldom associated with bleeding. However, the thrombotic risk is more than 30 times that of control populations.[45] The risk of thrombosis remains high for days to weeks after discontinuation of heparin, even after the platelet count normalizes.[46] HIT may manifest as skin necrosis, venous gangrene of the limbs, and anaphylactic-type reactions after intravenous heparin. Thrombosis may develop one to seven days before an apparent fall in the platelet count. Thromboses may occur in either venous or arterial beds, with venous thromboembolism occurring four times as often as arterial events. Limb ischemia has resulted in amputation in 5-10% of patients with HIT. Venous thromboses predominate in medical and orthopedic patients, while arterial thromboses occur frequently in patients who have undergone cardiac or vascular surgery, including multiple saphenous grafts causing myocardial infarction.[47] Thromboses may occur at unusual sites, such as in adrenal veins causing hemorrhagic necrosis of the adrenal gland, or in cerebral venous sinuses.[48] Thrombotic risk appears to be greater among patients with higher levels of PF4-heparin antibody, or with a drop in platelet levels of more than 70%.[49]

The incidence of HIT appears to be approximately 10 times higher in patients receiving UFH, as opposed to LMWH. However, patients receiving LMWH have a more frequent incidence of HIT if they have had a recent exposure to UFH (within 100 days).[50]

The clinical diagnosis of HIT depends upon ruling out other causes for thrombocytopenia, such as infection, bone marrow disease, DIC, post-transfusion purpura, and drugs other than heparin. DIC may occur along with HIT, characterized by hypofibrinogenemia, prolonged INR and PTT, low levels of antithrombin and protein C, renal failure, and schistocytes on the peripheral smear. Platelet counts should recover after the discontinuation of heparin. Laboratory diagnosis includes testing for heparin-dependent antibodies with the use of serologic or functional assays.[42]

Serologic assays are available at most clinical laboratories; they detect circulating IgG, IgA, and IgM antibodies. Immunoassays have high sensitivity (more than 97%), but their specificity (74-86%) is limited by the fact that they also detect PF4-heparin antibodies in patients who do not have HIT. The negative predictive value of serologic assays is high.[48,51]

To confirm HIT in patients with positive serologic assays, functional assays measuring platelet activation to detect heparin-dependent antibodies capable of binding to and activating the Fc receptors on platelets may be performed. The serotonin release assay is considered the gold standard among the washed-platelet tests, but may not be readily available in all laboratories.[52] The positive predictive value of functional assays tends to be high (89-100%).[53] A rapid (within 30 minutes) and reliable HIT antigen assay may be available soon.[42]

Management of HIT centers on reduction of the thrombotic risk by reducing platelet activation and thrombin generation. All sources of heparin, including intravenous heparin used to keep lines open and LMWH, should be discontinued. Alternative anticoagulant therapy should be initiated and tailored to the patient's condition. Warfarin monotherapy is contra-indicated, due to reports of venous gangrene in the limbs, and warfarin-induced skin necrosis.[54]

The mainstay of treatment for HIT centers on anticoagulation with one of two classes of anticoagulants: direct thrombin inhibitors (DTI) or heparinoids.[48] Direct thrombin inhibitors bind and inactivate thrombin. Three are currently available: lepirudin, argatroban, and bivalirudin. Lepirudin is a recombinant analogue of hirudin, a leech protein. It is metabolized by the kidney; the dose must be adjusted if the patient has renal insufficiency. Fatal anaphylaxis has been reported after sensitization to lepirudin, and patients should not be treated with this agent more than once. Argatroban is a small synthetic molecule that binds reversibly to the catalytic site of thrombin. As with lepirudin, the benefit to treatment appears to be mainly in the reduction of new thromboembolic complications, as opposed to reduction in death or amputation.[55] Both lepirudin and argatroban can be monitored by the aPTT, which should be 1.5-3 times the baseline level for argatroban, and 1.5 to 2.5 times the baseline level for lepirudin. Argatroban is metabolized in the liver; dose adjustments are recommended in patients with moderate liver disease. It has been demonstrated to decrease the likelihood of new stroke and stroke-associated mortality in HIT.[56] Only argatroban and lepirudin are FDA approved for the management of HIT.[42]

Bivalirudin is another synthetic thrombin inhibitor approved by the Food and Drug Administration for percutaneous coronary intervention in patients who have or are at risk for HIT. Its action is monitored by measuring the PTT or by following the activated clotting time (ACT). Danaparoid, a mixture of heparin sulfate and dermatan sulfate, another inhibitor of activated factor X, is available in Canada and Europe, but not in the United States.[48]

Therapy with an alternative anticoagulant agent should be fol-

lowed by a transition to warfarin, but only after platelet counts have recovered to more than 150,000/µL. Oral anticoagulants should be overlapped with a direct thrombin inhibitor until the international normalized ratio (INR) is therapeutic for at least 48 hours.[57] PF4-heparin antibodies disappear from the circulation within a median of 85 days.[44] Documentation of heparin-induced thrombocytopenia should be included in the patient's medical record, and future exposure to heparin generally should be avoided. For certain procedures, such as cardiac bypass surgery, the use of direct thrombin inhibitors poses a considerable bleeding risk. Patients with a remote history of HIT with negative tests for PF4-heparin antibodies may therefore receive heparin during the procedure.[48]

Re-exposure to UFH may be safe after 100 days from the last heparin dose, by which time the UFH-dependent antibody will have disappeared—provided that exposure to UFH is brief, and that it can be demonstrated that no antibody is present.[42]

Platelet Transfusions

In the early 1980s and 1990s, use of platelet transfusion increased rapidly in the United States, doubling in the decade of the 1980s alone.[58] This increased use of platelets correlates with increasingly aggressive myelosuppressive therapy for malignancies and increased availability of platelets because of cost-effective methods for storage of platelet concentrates. During the past 2 decades, technical improvements have doubled the number of platelets in each unit. The range around this average is high: 0.4-1.8 x 10^{11} related to the variability in donor platelet level.[59,60] For this reason, at least 5 units must be pooled to ensure that the pool contains at least 3 x 10^{11} platelets. Platelet recovery and survival is satisfactory after 7 days of storage[61]; however, because of bacterial contamination, it has been recommended that the storage period be only 5 days.

It has been estimated that the average patient has an increase in platelet concentration of 10,000/µL per square meter of body surface area (BSA) per whole-blood-derived unit of platelets. Therefore, an adult with a BSA of 2 m^2 should have a rise in platelet count of 5000/µL for each unit transfused. One unit is adequate only for transfusion of a small child weighing less than 14 kg. For transfusion of adults, 4 to 8 units must be pooled to provide a therapeutic dose. No standard dose fits all patients, regardless of size and clinical situation. For example, 4 units might be enough for prophylaxis in a patient with a BSA of 2 m^2 who is not bleeding, to raise the platelet concentration from 5000/µL to the range of 20,000-30,000/µL.[62] On the other hand, a person undergoing an invasive procedure or who is actively bleeding might be better served with a 10 unit transfusion to attain a platelet concentration of more than 50,000/µL.[63]

The traditional platelet concentration that should trigger a platelet transfusion has been 20,000/µL, but studies have shown that this level may be lowered to 10,000/µL in patients with production levels that are stable.[64] Crossmatching is unnecessary for platelet transfusions. However, Rh negative patients should receive Rh negative platelets due to the potential for Rh sensitization. Each bag contains at least 5.5 x 10 platelets in 50-70 mL of plasma. The usual transfusion dose in adults is 6 to 10 units. In children it is 1 unit per 10 kg body weight. If human leukocyte antigen (HLA) matching of platelets is required, leukocyte-reduced apheresis platelets may be administered to prevent HLA antibody formation.[62]

Table 4. Complications of Platelet Transfusion[62]

Resulting from contaminating leukocytes
- Alloimmunization to class I HLA antigens
  - Refractoriness to platelet transfusion
  - Febrile nonhemolytic transfusion reactions (FNHTR)
- Transmission of cytomegalovirus
- Graft-versus-host disease

Resulting from contaminating red cells
- Rh alloimmunization
- Parasites: malaria, babesiosis

Resulting from plasma and its contents
- Contaminating microorganisms
  - Bacteria
  - Viruses: HBV, HCV, HIV, HTLV
  - Parasites: Chagas disease
- Plasma proteins
  - Minor and major allergic reactions
  - ABO antibody-mediated hemolysis
  - Transfusion-related acute lung injury

Resulting from platelets themselves
- Febrile non-hemolytic transfusion reaction
- Refractoriness to platelet transfusion
- Posttransfusion purpura

Complications from platelet transfusion most frequently result from contaminating leukocytes, red cells, plasma proteins, and micro-organisms. (*See Table 4.*) The frequency of complications resulting from contaminating leukocytes can be reduced by prestorage leukoreduction of the platelet products. HLA alloimmunization can be reduced by consistent use of leukoreduced blood products.[65,66]

Two specific situations are of particular relevance to the emergency physician. Massive trauma may necessitate large amounts of blood transfusions, causing dilutional thrombocytopenia. Even after one to two blood volumes are replaced, however, the platelet count is likely to be not less than 50,000/µL. Therefore, unless abnormal bleeding is noted, transfusion of platelets is generally unnecessary.[67] Secondly, the patient with ITP generally does not require platelet transfusion because the bleeding tendency tends not to be severe relative to thrombocytopenic disorders resulting from decreased production. Furthermore, there is generally a satisfactory and rapid response to medical therapy. If critical bleeding occurs or surgery is required, 3 to 6 units of platelet concentrates per square meter of BSA generally raises the platelet count for 12 to 48 hours, recognizing that the survival of these transfused platelets is relatively brief.[68]

Resolution of Cases

Case 1. It is clear that this patient has isolated thrombocytopenia, without other evidence for bone marrow depression. Because the hospital had no in-patient beds, the patient stayed overnight in the Clinical Decision Unit (CDU) pending placement in a detoxification center. He is transfused with 10 units of platelets overnight. His repeat platelet count the next day is 55,000/µL. You are satisfied that his platelets are not undergoing immune destruction and that his thrombocytopenia is secondary to a combination of marrow suppression of platelet production by alcohol, congestive splenomegaly, and folate deficiency. After one week without alcohol intake in a detoxification unit, his platelet count is 113,000/µL. He never requires any further work-up.

Case 2. Although you are fairly certain this child has idiopathic thrombocytopenia due to the lack of any symptoms except for petechiae, he is admitted to the pediatric service for a diagnostic work-up. The child undergoes a bone marrow biopsy, as the consulting hematology service is worried about the possibility of leukemia. After the biopsy, he is started on high-dose steroids. The biopsy demonstrates no evidence for leukemia, and his platelet count improves after 4 weeks to 95,000/µL.

Case 3. Heparin-induced thrombocytopenia is not uncommon shortly after discharge from the hospital for a thrombotic event treated with UFH. You know not to simply increase the patient's warfarin, and start her instead on argatroban. While in the hospital, she does indeed have a Greenfield filter placed in her inferior vena cava, and is kept on warfarin for an additional 6 months. She recovers uneventfully from the pulmonary embolus.

Summary

When thrombocytopenia is discovered, the physician should attempt to determine the cause and assess the risk of bleeding. The most important laboratory test is the peripheral smear. Platelet counts of less than 100,000/µL are considered thrombocytopenic, and the bleeding time increases proportionately with a decrease in count below this level. Patients with platelet counts below 5000-10,000/µL are at risk for spontaneous bleeding, and should be admitted. Platelet counts above 50,000/µL are usually sufficient to control bleeding caused by local pathology or by trauma, provided that platelet function is normal.

Platelet transfusions should be initiated if there is active bleeding unresponsive to local measures and the platelet count is less than 50,000/µL. Prophylactic transfusion should be considered to prevent intracranial hemorrhage if the platelet count is below 10,000/µL. There are several reasons not to transfuse platelets unnecessarily: cost, disease transmission, and avoidance of alloimmunization, most prominently—especially if bone marrow transplantation in the future is a possibility. Immune destruction of platelets may occur in patients with certain disorders, but transfusion may be lifesaving in the actively bleeding patient. The mainstay of diagnosis in thrombocytopenia for the emergency physician is the history, exam, CBC, and peripheral smear.

Conclusions

Thrombocytopenia is a common hematologic disorder that may herald systemic disease, and may be caused by a variety of toxic, immunologic, infectious, and neoplastic disorders. Therapy depends upon the presentation and the underlying disorder. The emergency physician should recognize initial treatment and, with the growth of observation medicine, be prepared to manage bleeding complications, prescribe medications for stabilization of the underlying process, and be familiar with transfusion issues.

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Physician CME Questions

11. The risk of spontaneous bleeding becomes especially concerning with platelet counts below which level?
    A. 150,000/µL
    B. 100,000/µL
    C. 50,000/µL
    D. 10,000-20,000/µL
    E. 1000/µL

12. Under normal circumstances, approximately what fraction of platelets are sequestered in the spleen?
    A. 10%
    B. One-third
    C. 50%
    D. 70%
    E. 90%

13. Which virus has *not* been implicated as a potential cause for thrombocytopenia?
    A. Mumps
    B. Rubella
    C. Adenovirus
    D. Hepatitis C
    E. HIV

14. Bleeding into the central nervous system is the most common cause of death in thrombocytopenia.
    A. True
    B. False

15. What is the most common cause for thrombocytopenia developing for the first time in a patient in the intensive care unit?
    A. Deficiency of vitamin K
    B. Disseminated intravascular coagulation
    C. Sepsis
    D. Alcoholism
    E. Massive transfusion

16. If a peripheral smear is performed in a thrombocytopenic adult patient, and a leukoerythroblastic blood picture with nucleated red blood cells and early myeloid forms are found, what is the suggested diagnosis?
    A. Vitamin B12 deficiency
    B. Bone marrow infiltration with tumor, fibrosis, or tuberculosis
    C. ITP
    D. Wiskott-Aldrich syndrome
    E. Alcohol-induced thrombocytopenia

17. The most common drug-related cause of a drop in platelets is due to:
    A. gold salts.
    B. non-steroidal anti-inflammatory drugs.
    C. sulfonamides.
    D. heparin.
    E. phenytoin.

18. Which platelet inhibitor has been associated with very rapid (less than 24 hours, as low as 30 minutes) onset of thrombocytopenia?
    A. Ticlopidine
    B. Clopidogrel
    C. Dipyridamole
    D. Eptifibatide
    E. Abciximab

19. Treatment of ITP may include which of the following?
    A. Intravenous immune globulin
    B. Dapsone
    C. Splenectomy
    D. Prednisone
    E. All of the above

20. What risk following splenectomy makes the American Society of Hematology particularly reluctant to recommend this surgery in children with ITP?
    A. Lifelong risk of sepsis
    B. Lymphoma
    C. Leukemia
    D. Growth retardation
    E. Thrombocytosis

CME Answer Key: 11. D; 12. B; 13. C; 14. A; 15. C; 16. B; 17. D; 18. E; 19. E; 20. A

Emergency Medicine Reports®
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Thrombocytopenia

Causes for Thrombocytopenia

DECREASED PLATELET PRODUCTION

- Viral infections: rubella, mumps, varicella, parvovirus, hepatitis C; Epstein-Barr virus, cytomegalovirus
- Live attenuated measles vaccination
- HIV
- Chemotherapy
- Radiation therapy
- Acquired or congenital bone marrow aplasia
  Fanconi anemia, pure megakaryocytic aplasia, thrombocytopenia with absent radius (TAR) syndrome
- Alcohol toxicity
- Vitamin B12 and folate deficiency
- Marrow infiltration: tumor, infection

INCREASED PLATELET DESTRUCTION

- Idiopathic thrombocytopenic purpura
- Systemic lupus erythematosus
- Disseminated intravascular coagulation
- Antiphospholipid syndrome
- Hemolytic anemia with elevated liver function tests and low platelet count (HELLP syndrome)
- Drugs, heparin, quinine, quinidine, valproate, protamine
- Thrombotic thrombocytopenic purpura/hemolytic uremic syndrome (TTP-HUS)
- Auto immune destruction: post transfusion, neonatal, post-transplant
- Viral: dengue hemorrhagic fever
- Malaria

Congenital

Kasabach-Merritt
Neonatal alloimmune thrombocytopenia
HPA-1a incompatibility

Other

Pregnancy
Rattlesnake envenomation
Wiskott-Aldrich

Complications of Platelet Transfusion

Resulting from contaminating leukocytes

- Alloimmunization to class I HLA antigens
  - Refractoriness to platelet transfusion
  - Febrile nonhemolytic transfusion reactions (FNHTR)
- Transmission of cytomegalovirus
- Graft-versus-host disease

Resulting from contaminating red cells

- Rh alloimmunization
- Parasites: malaria, babesiosis

Resulting from plasma and its contents

- Contaminating microorganisms
  - Bacteria
  - Viruses: HBV, HCV, HIV, HTLV
  - Parasites: Chagas disease
- Plasma proteins
  - Minor and major allergic reactions
  - ABO antibody-mediated hemolysis
  - Transfusion-related acute lung injury

Resulting from platelets themselves

- Febrile non-hemolytic transfusion reaction
- Refractoriness to platelet transfusion
- Posttransfusion purpura

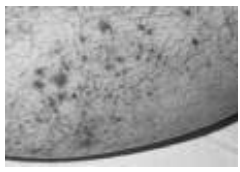
Platelet Counts in Relation to Bleeding Risk

PLATELET COUNT	COMPLICATION
< 60,000/μL	Risk of bleeding after trauma
< 50,000/μL	Surgical bleeding may occur
< 40,000/μL	Self-limited bleeding
< 10,000 – 20,000/μL	Spontaneous bleeding may occur in ITP patients:
< 12,000/μL	Spontaneous bleeding requiring special attention
< 6,000/μL	Severe life-threatening bleeding

Some Drugs Associated with Thrombocytopenia

Acetaminophen
Acetazolamide
Amiodarone
Amrinone
Angiotensin converting enzyme inhibitors (ACEI)
Aspirin
Bleomycin
Cephalosporins
Chemotherapeutic agents: carboplatin, alkylating agents, anthracyclines, antimetabolites
Chlorpromazine
Chlorothiazide
Cimetidine
Dactinomycin
Diazoxide
Digoxin
Eptifibatide
Estrogens
Ethanol
Furosemide
Glycoprotein II b/IIIa inhibitors
Gold salts
Heparin
Heroin
Indinavir
Indomethacin
Interferons (alfa & beta)
Isoniazid
Levetiracetam
Linezolid
Lopinavir
Measles-mumps-rubella vaccine
Methicillin
Minoxidil
Nitroglycerin
Penicillin
Phenytoin
Platelet inhibitors: tirofiban, eptifibatide, abciximab, ticlopidine, clopidogrel
Procainamide
Protamine sulfate
Quinidine, quinine
Ranitidine
Rifampin
Ristocetin
Tolbutamide
Trimethoprim-sulfamethoxazole and other sulfonamides
Valproic acid
Vancomycin

Petechiae



Supplement to *Emergency Medicine Reports*, January 7, 2008: "Thrombocytopenia." *Author:* **Jonathan Glauser, MD, FACEP**, Department of Emergency Medicine, Cleveland Clinic, Cleveland, OH.

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Trauma Reports

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Current Status and Controversy Surrounding Trauma Care in the Elderly: A Collective Review

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Geriatric common is increasingly encountered in the emergency department, and based on current statistics will continue to increase as a percentage of trauma care rendered. Geriatric trauma patients have unique physiologic features and require careful assessment to identify subtle signs of injury. Standard trauma triage guidelines need to include patient's age as a risk factor for more severe injury. Early identification and transfer of an elderly patient may significantly improve both morbidity, including functional outcome and mortality. This articles provides an overview of geriatric trauma, with an emphasis on the unique features of the elderly trauma patient.

— The Editor

Introduction

The elderly represent a unique group of patients requiring care after an injury. Elderly trauma patients experience higher overall mortality rates, longer hospital stays, and greater morbidity than younger patients who are injured, even with lower overall injury severity. There also is a significant negative impact from associated co-morbid medical conditions, as well as a greater risk of care-related complications.

Studies show that the fastest growing subset of the elderly trauma population is octogenarians; defined as those age 80 and older. One review of geriatric trauma demonstrated that octogenarians had higher mortality than other elderly trauma patients, despite lower overall injury severity scores.[1] Cardiovascular disease was the most frequently encountered pre-existing medical condition in both groups, although octogenarians had higher incidences of congestive heart failure, as well as hematologic disorders, neurologic disorders, and dementia. Diabetes, obesity, and pulmonary com-

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plications were more commonly seen in the non-octogenarian patients. The rate of complications found during hospital stays was comparable for both groups of elderly trauma patients. Pulmonary and infectious complications were the most common complications encountered in both groups.

Elderly trauma patients spend more time in the hospital and ICU (intensive care unit) than non-elderly trauma patients, but octogenarians have shorter LOS (length of stay) and ICU stays. This is thought to be due to the higher mortality rate in this subset of patients. Octogenarians more commonly were discharged to skilled nursing facilities than their younger counterparts in the elderly trauma population, and also had worse functional outcomes. Functional independence in feeding and social interactions appears to be preserved in octogenarians even after moderate injury severity.

Elderly patients may have subtle, unappreciated, pre-existing volume deficits due to medications they may be taking, such as those for chronic diuretic therapy or malnutrition. Medications may prevent an increase in the heart rate in response to blood loss. Pacemaker devices also may obscure rate and rhythm changes. The therapeutic range for volume resuscitation is extremely narrow for the elderly patient; therefore, aggressive hemodynamic monitoring may play an important role in successful resuscitation.

Injury research has generally concentrated on the population of patients in which that research is considered to have the most potential impact. Injury is known to be the leading cause of death in the first four decades of life. As a result, less research attention has been paid to the study of the impact of injury on elderly (> 65 years of age) individuals. However, injury is the ninth leading cause of death in elderly patients and the elderly population continues to increase dramatically in the United States. This has resulted in more elderly trauma patients being treated by trauma centers across the country.

Census data have documented this increase in the elderly population in the United States. Between 1980 and 1990, the elderly population increased to 12% of the population. This number is expected to rise to 20% by the year 2050. Similarly, injury admissions among the elderly have increased noticeably over the same time period, representing 23% of all admissions to trauma services; this number is projected to increase to 40% by the year 2050. Falls represent the most common mechanism of injury seen in elderly patients presenting to trauma centers; however, motor vehicle crashes are increasingly representing the next most frequent category. *(See Figure 1.)* In contrast to the younger population of trauma patients, elderly women are injured more frequently than men.

Lack of research most likely has negatively impacted the experience of the elder patient who has been injured. There are specific areas of care for the elder injured patient that remain undefined. There is a lack of accurate guidelines for trauma center transfer for the injured elderly, beyond a general recommendation that is based on age greater than 65 years. Beginning resuscitation treatment upon presentation to the emergency department is standardized and not age specific.

There is a lack of recognition of the unique resources geriatric specialists can provide in the early care of the injured elderly, and of the impact this may have on subsequent care or outcomes. Two particular problems that occur in injured elder patients as a result of admission to the intensive care unit (ICU) or floor, new-onset disorientation and multisystem organ dysfunction, have not been adequately addressed by health care providers. There is a critical need for the health care team to collaborate to optimize elder trauma care throughout a patient's hospitalization, with the goal of returning patients to independent function in as short a time as possible, to preserve quality of life, and to respect and honor end-of-life decisions in this group of patients.

Therefore, the objectives of this article are to: describe age-specific aspects of injury management, including triage decisions and ED resuscitation specifics; characterize the outcomes risk profile for the injured elderly; and identify the specific risks that may be encountered with the elderly patient who has been injured and requires ICU or in-patient care.

Overview

In 1793, Edward Wigglesworth published the first life table for the young United States. At that time, he calculated the life expectancy from birth in New England to be a mere 35 years.[2] Since that time, the life expectancy has steadily increased due to multiple improvements within the health and social sectors. *(See Figure 2.)*[2,3] Older adults have successfully taken advantage of the additional years of their lives by maintaining active lifestyles. However, increased life expectancy may be viewed as a double-

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Figure 1. Ten Leading Causes of Injury Death by Age Group

Highlighting Unintentional Injury Deaths, United States – 2004

	Age Groups										
Rank	<1	1-4	5-9	10-14	15-24	25-34	35-44	45-54	55-64	65+	Total
1	Unintentional Suffocation 725	Unintentional MV Traffic 520	Unintentional MV Traffic 584	Unintentional MV Traffic 922	Unintentional MV Traffic 10,757	Unintentional MV Traffic 6,834	Unintentional MV Traffic 6,451	Unintentional MV Traffic 6,088	Unintentional MV Traffic 3,936	Unintentional Fall 14,899	Unintentional MV Traffic 43,432
2	Unintentional MV Traffic 139	Unintentional Drowning 430	Unintentional Fire/burn 169	Suicide Suffocation 204	Homicide Firearm 4,127	Unintentional Poisoning 3,641	Unintentional Poisoning 6,444	Unintentional Poisoning 6,033	Suicide Firearm 2,328	Unintentional MV Traffic 7,175	Unintentional Poisoning 20,950
3	Homicide Unspecified 133	Unintentional Fire/burn 228	Unintentional Drowning 131	Homicide Firearm 139	Unintentional Poisoning 2,259	Homicide Firearm 3,503	Suicide Firearm 2,868	Suicide Firearm 3,349	Unintentional Poisoning 1,577	Unintentional Unspecified 4,868	Unintentional Fall 18,807
4	Homicide Other Spec., Classifiable 101	Homicide Unspecified 164	Homicide Firearm 45	Unintentional Drowning 138	Suicide Firearm 2,104	Suicide Firearm 2,283	Homicide Firearm 1,895	Suicide Poisoning 1,737	Unintentional Fall 1,393	Suicide Firearm 3,756	Suicide Firearm 16,750
5	Unintentional Drowning 62	Unintentional Suffocation 125	Unintentional Suffocation 45	Unintentional Fire/burn 87	Suicide Suffocation 1,516	Suicide Suffocation 1,592	Suicide Suffocation 1,667	Suicide Suffocation 1,231	Suicide Poisoning 801	Unintentional Suffocation 3,369	Homicide Firearm 11,624
6	Undetermined Suffocation 56	Unintentional Pedestrian, Other 113	Unintentional Other Land Transport 37	Unintentional Other Land Transport 87	Unintentional Drowning 574	Suicide Poisoning 817	Suicide Poisoning 1,546	Unintentional Fall 1,184	Suicide Suffocation 575	Adverse Effects 1,857	Suicide Suffocation 7,336
7	Homicide Suffocation 42	Homicide Other Spec., Classifiable 69	Unintentional Pedestrian, Other 36	Unintentional Suffocation 68	Homicide Cut/pierce 484	Undetermined Poisoning 602	Undetermined Poisoning 1,116	Homicide Firearm 1,062	Homicide Firearm 468	Unintentional Fire/burn 1,125	Unintentional Unspecified 6,173
8	Unintentional Fire/burn 28	Unintentional Fall 47	Unintentional Struck by or Against 21	Suicide Firearm 59	Suicide Poisoning 363	Homicide Cut/pierce 479	Unintentional Fall 659	Undetermined Poisoning 1,019	Unintentional Suffocation 443	Unintentional Poisoning 901	Unintentional Suffocation 5,891
9	Undetermined Unspecified 24	Unintentional Natural/ Environment 39	Homicide Unspecified 20	Unintentional Poisoning 47	Undetermined Poisoning 329	Unintentional Drowning 385	Homicide Cut/pierce 450	Unintentional Fire/burn 504	Unintentional Fire/burn 427	Suicide Suffocation 544	Suicide Poisoning 5,800
10	Unintentional Fall 23	Homicide Firearm 36	Four* Tied 13	Unintentional Firearm 35	Unintentional Other Land Transport 284	Unintentional Fall 320	Unintentional Drowning 435	Unintentional Suffocation 468	Adverse Effects 403	Suicide Poisoning 521	Undetermined Poisoning 3,455

*Four causes are: Unintentional Firearm, Unintentional Natural/Environmental, Unintentional Other Transport, and Unintentional Unspecified.

Source: National Vital Statistics System, National Center for Health Statistics, CDC.

Produced by: Office of Statistics and Programming, National Center for Injury Prevention and Control, CDC.

edged sword, composed not only of increased activity, but also of the risk for increased trauma.

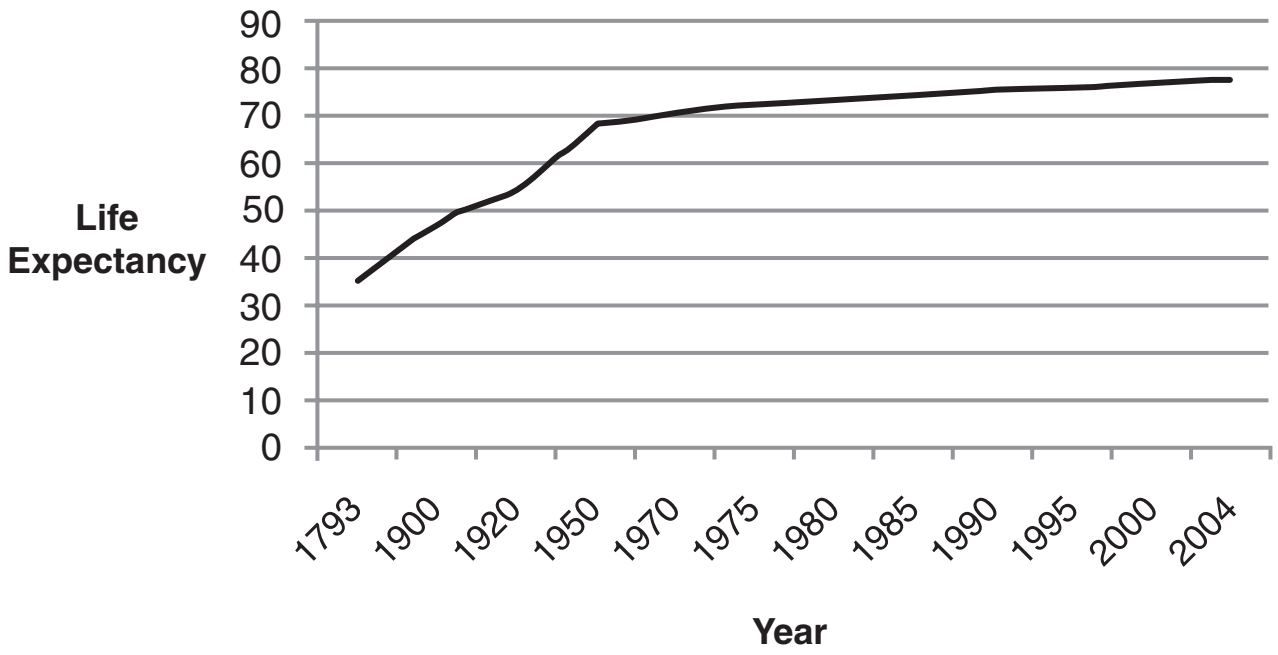
According to the 2006 National Vital Statistics Report, unintentional injuries are the ninth leading cause of death in adults over 65 years of age.[4] Falls are the leading cause of fatal and nonfatal trauma. *(See Figure 3.)* For the 1.8 million older adults who survived fall-related injuries in 2003, many were left with a fear of recurrent falls.[5] Recently, motor vehicle accidents were noted as the second leading cause of fatal traumatic events for the elderly.[6] *(See Table 1.)* Pedestrian-automobile accidents are the seventh most frequent cause of geriatric trauma mortality and are especially lethal, with a greater than 50% fatality rate.[7]

Despite the recognition of the scope of geriatric trauma, little is known regarding effective treatment. Organizations such as the Eastern Association for the Surgery of Trauma[8] have attempted to fill this gap. Yet lack of definitive, age specific protocols remains and may be responsible for the continuing under-triage of elderly trauma patients.[9] Much work remains to be done to ensure that these vulnerable members of our society are provided with optimal specialized care.

The concept that the elderly are not simply older adults is paramount when first discussing their treatment following a traumatic injury. The aging process alters the physiology of multiple organ systems. For example, cardiac output and the ability of the heart rate to increase in response to stress diminishes. Pulmonary, neurologic, and renal functions also decrease. Loss of structural components of bone is seen with aging.[10] These modifications that are caused by age may contribute not only to the mechanism of injury, but also to the presentation of the patient, as well as their subsequent care, and outcome.

The body's capability to mount an immune response to injury and heal traumatic wounds is hampered with increasing age, although many now believe the quality of the end result of healing is unchanged.[11] Recent studies have indicated that age alone is a predictor of delayed wound repair, even when comorbid conditions and medications that could further exacerbate the problem are

Figure 2. Life Expectancy at Birth in the U.S.



Sources: "Life Expectancy." U.S. History Encyclopedia. http://www.answers.com/topic/life-expectancy. Accessed on December 3, 2007; Centers for Disease Control and Prevention. Life Expectancy at Birth, 65 and 85 Years of Age, by Sex and Race: United States Selected Years 1900-2003. http://www.cdc.gov/nchs/data/hus/ hus06.pdf#027. Accessed on December 3, 2007.

excluded.[12] Factors that contribute to this slow down include delayed infiltration of inflammatory mediators, such as lymphocytes, and delayed production and deposition of collagen. A decrease in the overall strength of the healing wound, as well as the increased risk of infection seen with the decreased healing rates, complicates an already difficult recovery period for the elderly patient.[11] To date, many therapeutic interventions, such as hormonal and growth factor treatments and exercise, have been investigated through animal and human studies in order to discover avenues that may enhance would healing in the elderly.[13,14] However, lack of a universally accepted treatment for improving wound repair in the elderly continues. The impaired healing response that is attributable to aging presents a complex picture to those who care for the injured elder following a hospital admission.

In addition to advancing age, co-morbid medical conditions play a role in the outcome of geriatric trauma. Common chronic diseases seen in these patients include congestive heart failure, chronic obstructive pulmonary disease (COPD), and diabetes.[7] Richmond and colleagues reported that risks for experiencing complications following injury are increased three-fold due to the presence of co-morbid disease.[15] These factors lead to what has been termed the grim triad: advanced age + co-morbid disease + moderate injury, which may lead to loss of function and death for the injured elderly.[16] The importance of recognizing and addressing these components in the management of geriatric patients cannot be overstated.

Caring for victims of trauma is typically divided into three components: triage, transport, and treatment. Special considerations, including those previously mentioned, must be incorporated into this decision-making process by health care personnel caring for elderly patients. Each step in geriatric trauma care will be discussed with the aid of previously performed research and clinical experience. By outlining a more concise protocol for managing these special patients, it is hoped that more timely and age-specific care will be delivered to the injured elderly that may aid their faster return to active lifestyles.

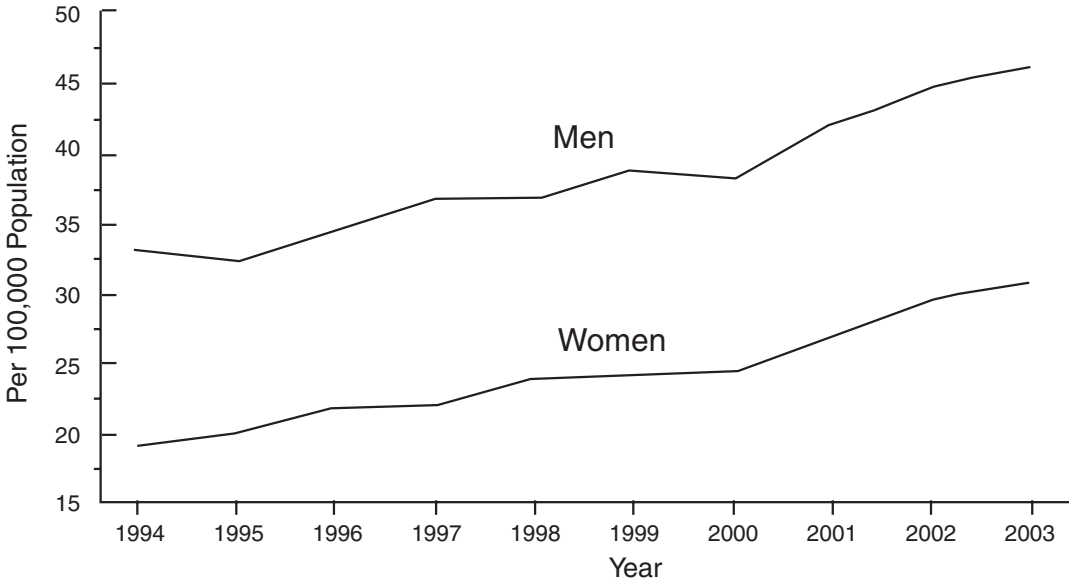
Triage

Under-triage. The first element of elder trauma care, triage, has historically been the first pitfall to obtaining a positive outcome. Despite disproportionately higher levels of mortality when compared with their younger counterparts,[17] geriatric trauma patients are under-triaged 80% of the time.[18] It is suspected that this is partially a result of the discrepancy that can exist between triage classifications and the actual severity of the injury. Physiologic parameters and injury mechanisms typically are utilized in the triage setting. However, the physiologic alterations that accompany aging, coupled with apparently minor causes of injury, may lead to lower estimations of the seriousness of the elderly patient's condition. Lack of early identification of a potentially serious injury can lead to a tragic outcome.

Under-triage also may result from lack of compliance when

Figure 3. Falls Among Older Adults

Age Adjusted Fatal Fall Injury Rates Among Men and Women Aged 65 Years and Older, United States, 1994-2003



Source: Centers for Disease Control and Prevention. Injury Center. Falls among older adults: Figures and Maps. http://www.cdc.gov/ncipc/duip/adultfallsfig-maps.htm. Accessed on November 30, 2007..

applying triage protocols to geriatric patients.[19] It is unclear whether this is attributable to a bias that exists to consideration of aggressive management. Studies have shown that more than 50% of trauma patients ages 65-79 are discharged home, and that 20% are discharged to rehabilitation facilities. Even patients older than age 80 largely maintain their ability to independently feed themselves and interact with others following a traumatic event.[1] Thus, old age should not be used as an independent factor for deciding against trauma center treatment.

Age as Guideline for Triage. Conversely, age has been adopted as a guideline for triage to a high-level trauma center. Demetriades and researchers found that 75% of patients older than age 70 did not meet trauma team activation criteria upon presentation. Due to the high mortality in this age group, it was suggested that age older than 70 years be added to the existing trauma triage protocol.[20] Other centers have adopted an age older than 55 to be a consideration for transport to a trauma center.[19] When determining whether or not age should be a predominant factor in triage decisions, overtriage may be an economic and resource concern. Nevertheless, it is clear that the potential hazards of under-triage in the elderly mandate age to be included in the criteria for triage to a trauma center.

Identify Need and Correctly Triage. Identifying the level of need and correctly triaging elderly trauma patients is the crucial first component of providing appropriate care. Due to the multiple unique characteristics presented by these patients, triage personnel should adopt the following considerations when making decisions regarding subsequent treatment.

First, physiologic parameters, such as heart rate, may appear "normal" despite significant injury as a result of the lack of physiologic reserve that accompanies aging. Similarly, a normal blood pressure may portend hemodynamic instability for a population that frequently struggles with hypertension. In addition, the potential for complications substantially increases with the presence of co-morbidities. Thus, every effort should be made to obtain as thorough a preliminary medical history as possible. Finally, advanced age increases mortality risk but does not independently predict whether aggressive treatment will be futile. Age has not been shown to have an association with inhospital mortality. Of patients older than age 55 who are eventually found to require a trauma center, only 29% initially met criteria for the trauma center care they need;[18] it is, therefore, recommended that age greater than 55 be included in the decision to triage patients to trauma centers. Physiologic age, co-morbid conditions, and chronologic age should be constituents of the decision to triage these patients to levels I or II trauma centers.[21] Milzman and colleagues, in a study of nearly 8000 trauma patients, noted a threefold increase in trauma mortality in patients with pre-existing conditions.[21]

Transport

Method of Transport and Location Decisions. The complexities which have confounded the issue of adequately triaging geriatric trauma patients continue into the sphere of patient transport. Ensuring that these patients arrive at centers that are equipped to handle their distinctive needs begins with their method of transfer. Typically, patients utilize either EMS or personal modes of transportation. Upon arrival to the emergency department, a trauma team may or may not be alerted based upon EMS or emergency physician evaluation. While a patient's self-transport is obviously not a decision with which medical personnel are involved, those who first examine such a patient must be cognizant of the fact that their treatment has already been delayed. Such a delay may place additional strain on an already frail condition.

The decision to transport an elderly trauma patient to a trauma center versus an acute care hospital may mean the difference between life and death in certain situations. Meldon and col-

Table 1. Older Adult Drivers

- In the United States, 3,355 occupants ages 65 and older died in motor vehicle crashes during 2004 (CDC 2006).
- In the United States, more than 177,000 adults ages 65 and older suffered nonfatal injuries as occupants in motor vehicle crashes during 2005 (CDC 2006).
- In 2004, there were more than 28 million licensed drivers age 65 years and older— a 17% increase from the number in 1994. During this same time period, the total number of licensed drivers increased by only 13% (NHTSA 2006).

Source: Department of Health and Human Services. Centers for Disease Control and Prevention. Older adult drivers: Fact sheet. http://www.cdc.gov/ncipc/factsheets/older.htm. Accessed November 30, 2007

Table 2. Signs of Possible Elder Abuse

SIGNS OF POTENTIAL ABUSE

- ❑ Multiple bruises
- ❑ Burns
- ❑ Fractures
- ❑ Abrasions in various stages of healing
- ❑ Pressure sores
- ❑ Extreme withdrawal
- ❑ Injury to breasts or genitalia.

SIGNS OF POSSIBLE NEGLECT, WHETHER SELF-IMPOSED OR AT THE HANDS OF OTHERS

- ❑ Poor hygiene
- ❑ Refusal to accept medical attention
- ❑ Poor living conditions
- ❑ Dehydration
- ❑ Malnutrition

Source: National Center on Elder Abuse: The Basics. http://www.elderabusecenter.org/default.cfm?p=basics.cfm. Accessed on December 3, 2007.

leagues found that for trauma victims older than age 80, transfer to a nontrauma center resulted in higher-than-predicted levels of mortality.[19] Scalea has reported that early aggressive cardiovascular monitoring can reduce mortality by 50%.[22] Aggressive treatment at a trauma center has been found to be an independent variable determining a patient's chance of survival.

Initial Response. Initial responders to elderly trauma patients must take into account physiologic and chronologic age when aiding in transport, which is reminiscent of the factors which play a role in triage. Vital signs within accepted limits actually may mask hemodynamic instability due to altered physiology. Treatment at acute care hospitals and delays in trauma team activation and assessment increase the risk for mortality in the elderly. Age greater than 55 years old and physiologic considerations should alert emergency responders to the potential need for timely transport to a high-level trauma center.

Amid triage and transport decisions, first-responders also commence the third step in the management of geriatric trauma victims: treatment. Currently, there is little information available which specifically addresses the treatment of geriatric trauma patients. With elderly patients comprising up to 39% of EMS runs,[23] it is essential to recognize the need for an age-appropriate resuscitation and treatment protocol that would aid emergency responders with their initiation of treatment. This paper will examine the standard trauma care protocols that have been utilized, along with special considerations of presentation and response to treatment in elderly patients.

Gaining Details of Trauma. Pre-hospital providers have the unique advantage of assessing patients at the scene of the injury event. Witnesses to the trauma and the trauma environment itself can both provide valuable information to emergency responders who are trying to piece together details regarding the mechanism of injury. Every opportunity must be taken to gather as much data as possible regarding the trauma itself so that the patient's injuries can be better understood and treated.[24] This also would include collecting information on the patient's past medical history and medication usage, which will better aid in the triage and transport decisions previously discussed.

Possible Elder Abuse. In addition to gathering information regarding the trauma incident itself, first-responders must be vigilant for signs of elder abuse. According to the 2004 Survey of State Adult Protective Services, 253,426 incidents of elder abuse were reported in 32 responding states.[25] However, it is feared that many instances go unrecognized, leading the Senate Special Committee on Aging to estimate that there are a staggering 5 million victims of elder abuse every year.[26] Signs that should alert emergency responders to potential abuse include multiple bruises, burns, fractures, abrasions in various stages of healing, pressure sores, extreme withdrawal, and injury to breasts or genitalia. Neglect, whether self-imposed or at the hands of others, could present with poor hygiene, refusal to accept medical attention, poor living conditions, dehydration, or malnutrition.[27] *(See Table 2.)* In these cases, treatment may consist not only of physically addressing wounds, but also of making the appropriate agencies aware of the situation. Attention to patterns of injury and seemingly trivial details could rescue an older adult from the nightmare of abuse.

Beginning Trauma Care. The ABCs of trauma care should be provided to geriatric patients starting in the field and be continuously monitored. Confirming or securing an adequate airway and maintaining breathing are the first concerns. Ill-fitting dentures or macroglossia are just two of the conditions seen in the elderly that may precipitate airway obstruction.[28] Intubation also may be more challenging due to cervical arthritis and friable nasopharyngeal tissues. Patients with multiple traumatic injuries, decreased neurologic function (Glasgow Coma Scale [GCS] score < 8), cardiac arrest, hypoxemia, or airway obstruction should be immediately intubated.[29] Supplemental oxygen should be administered to elderly trauma patients due to their poor tolerance of hypoxia, with special care not to cause respiratory depression in patients with COPD.[7]

We have already noted how circulatory status may be difficult to determine in geriatric patients due to their altered physiology.

Medication regimens, such as those including beta-blockers, may add to the uncertainty of the degree of hypovolemia. Intravenous access and fluid replacement should begin during the initial pre-hospital assessment. Due to their inability to tolerate hypovolemia or fluid overload, it has been determined that boluses of 250 cc of crystalloid solution should be administered at a time, followed by examination for rales and other signs of fluid overload.[22]

Neurologic status and injuries also are surveyed in the pre-hospital phase of care. Pupillary size, response to pain and commands, and mental status should be determined. Admittedly, this component of the evaluation may be hindered by the presence of a concomitant disease, such as Alzheimer's. The high incidence of cervical spine injury in the elderly following blunt trauma necessitates cervical immobilization prior to arrival at the hospital.

During transport to the trauma center, emergency personnel should continue to evaluate airway, breathing, circulation, and neurologic status. Vital signs and ECG findings should be recorded in preparation for presentation in the emergency department. The patient also should be exposed for a thorough examination, with special care to prevent hypothermia.[24] The care that is initiated by pre-hospital providers is the geriatric trauma patient's first chance for a positive outcome.

Initial Care in the Emergency Department (ED)

The age appropriate resuscitation protocol initiated by emergency personnel in the field is continued and expanded in the emergency department. The goals of this stage of care include stabilizing the patient and expediting their stay in the ED. Scalea has reported that an ED admission to monitoring time of 5.5 hours is associated with nearly 100% mortality figures for hemodynamically unstable patients.[22] Consequently, Biffl and colleagues implemented a system at their level I trauma center that stressed the importance of quickly moving elderly patients through the emergency room to the ICU.[30] The fragile nature of the geriatric trauma patient demands that definitive care be provided as soon as possible to limit deterioration.

Airway and Breathing. Airway management and breathing are the first steps in immediate resuscitation efforts following presentation of an elderly trauma patient to the ED. The potentially disastrous outcomes of hypoxemia on the cardiovascular and neurologic systems, which are only heightened with increasing age, mandate an aggressive approach. Orotracheal intubation is the preferred method for obtaining a definitive airway in all trauma patients, including elderly trauma patients; however, elderly patients may present unique challenges. Dentures, bleeding associated with anti-coagulation therapy, and the inability to adequately visualize the airway may make these individuals a "difficult airway" from the onset. Medications typically used in rapid sequence intubation protocols may have a disastrous post-procedure impact on blood pressure. Underlying cervical spinal column age-related changes may hamper the clinician's ability to even achieve a neutral position for inline immobilization.

No one should ever take the performance of orotracheal intubation lightly in the frail elderly. The most experienced physician with airway expertise should perform the intubation. Cricothyrotomy may be necessary in patients with difficult airways. This, too, may be a difficult procedure for similar reasons.

A pulse oximeter should be utilized to continually assess oxygen saturation, and supplemental oxygen must be used in elderly patients, with careful monitoring of those with COPD.[31] Arterial blood gases should be drawn to further assess oxygenation status. Aggressive pulmonary resuscitation has been linked with decreased complications and mortality and is encouraged in the treatment of the injured elderly.[32]

Circulation. Circulatory status must be re-evaluated upon hospital admission. Pre-existing cardiac disease, poor fluid intake, and medications may complicate the presentation and response to treatment. Discrete fluid boluses should be administered intravenously, with care being given to prevent fluid overload in these patients, whose cardiac contractility has diminished with age.

Blood products may be necessary in severely hemodynamically unstable patients. A multistate study published in 2004 recognized that patients greater than 65 years of age receive the majority of blood transfusions, and that they also suffer higher mortality rates post-transfusion.[33] Much work remains regarding understanding the relationship between blood products and outcomes in the elderly, yet the aggressive approach to providing volume stability in these patients is still emphasized.

Mental Status. Geriatric patients must be screened for neurologic disability during the initial hospital assessment. The key aspects of this evaluation remain as in the nonelder injured patient: the GSC score, assessment of pupils, and the specific aspects of a detailed sensory and motor examination. Underlying chronic mental status changes can have an impact on the "baseline neurological examination" and it is important to reconcile the findings of the current examination with what is known of the patient's mental status prior to injury. When in doubt, the default position is that the current findings are acute and should be aggressively researched with imaging studies, particularly in the face of anti-platelet, anticoagulant therapy. Ocular changes may occur as a consequence of aging or surgery to treat an age-related disability.

Cervical Spine Precautions. The high prevalence of cervical spine injuries in elderly patients, even following seemingly minor trauma, mandates a thorough examination and spinal precautions. Studies have shown that patients with no posterior midline cervical tenderness on palpation, no focal neurological abnormalities, no potentially distracting painful injury, no intoxication, and who are fully awake, alert, and oriented may have their cervical spine cleared clinically.[34] It is incredibly difficult to apply this algorithm to the elderly, however.

Imaging Modalities. Age-related changes noted on routine imaging studies essentially mandate a more definitive evaluation. Plain radiographs, computerized tomography (CT) scans, or magnetic resonance imaging (MRI) should be used to further investigate positive or questionable clinical characteristics, with MRIs being the most sensitive for detection of a ligamentous injury.[29] The remainder of the spine may be cleared with CT scanning; this should be completed as soon as possible after stabilizing the patient to avoid unnecessary prolonged immobilization.

Secondary Survey. As we have seen, the ABCs of initial

resuscitation, while similar for all victims of trauma, must be implemented with unique considerations for elderly patients. Attention to age-related conditions and complications continues with the secondary survey. Certain labs and tests to be ordered are protocol-driven, regardless of the age of the patient. On the other hand, advanced age is an indication for increased vigilance regarding specific social and medical disabilities.

Standard Laboratory Tests. The secondary examination is performed while continually assessing ABC status and immediately addressing instabilities as they arise. Standard labs to be ordered at this time include a complete blood count, complete metabolic panel, urinalysis, prothrombin time (PT), partial thromboplastin time (PTT), and type and screen. Elderly patients with specific co-morbidities may require additional labwork.

Plain radiography of the C-spine, chest, and pelvis should be completed. An ECG typically is performed, and some believe that a pulmonary artery catheter should be placed in severely injured patients when they are in an appropriately monitored setting.[35] A FAST (focused assessment by sonography for trauma) ultrasound examination should be considered in the hemodynamically unstable patient with suspected blunt abdominal trauma. Stable patients may be taken for CT scanning of the head, abdomen, and pelvis.

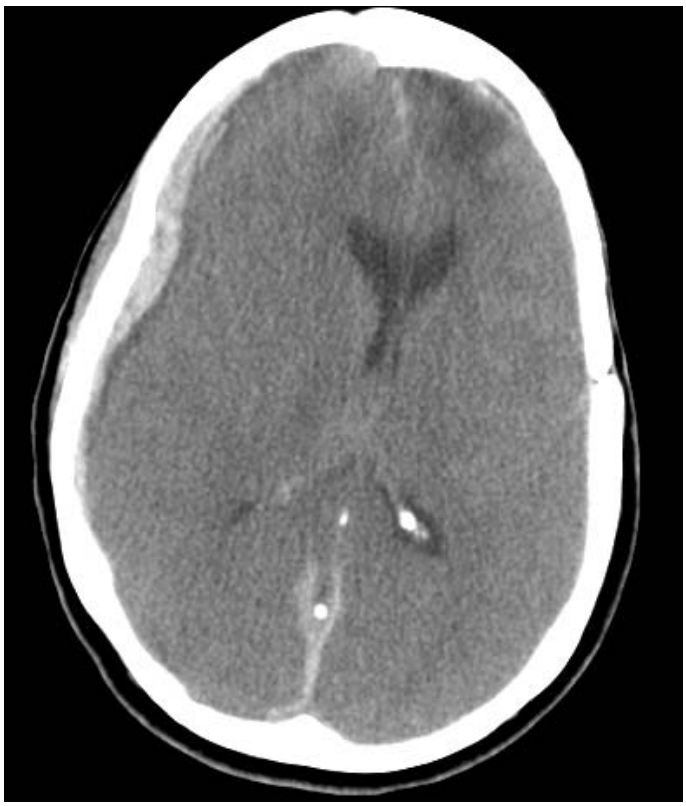
Along with standard evaluation protocols, social situations frequently seen in the geriatric population can drive laboratory work-up following trauma. Despite a common public misconception, the elderly population is not immune from suffering with alcoholism. Zautcke and researchers found that nearly 50% of elderly trauma patients who were evaluated for the presence of alcohol tested positive.[36] Benzodiazepines and opiates were the most common drugs detected in their patients. Thus, old age should certainly not preclude the need to assess coexistent substance use in the presence of trauma.

Mechanism of Injury. Likewise, clinical suspicion should be elevated for certain mechanisms of injury in the elderly. We have already discussed the need for awareness and subsequent intervention in cases of elder abuse. Similarly, the prevalence of depression in the elderly population can be associated with trauma and must be addressed. Nearly 10% of hospitalizations involving patients older than age 65 are the result of suicide attempts.[37] These patients are most likely to be Caucasian males injured with a firearm. A patient who survives such an injury, or who is suspected of having attempted suicide, should be psychiatrically evaluated following stabilization. Recognition of such a sequence of events begins during ED evaluation.

Chest Wall Injuries. Certain injuries, while potentially severe in any trauma patient, require extra surveillance to prevent consequent decline and disastrous complications in the elderly. One such injury involves the chest wall.

Patients older than age 65 who have rib fractures following trauma were found to be five times more likely to die than patients younger than age 65 who have rib fractures.[38] Rib fractures also significantly increase the risk for pneumonia, which is the leading cause of hospital mortality in elderly patients.[22,39] Fractured ribs may alert the physician to other accompanying underlying injuries, such as those involving the spleen, lungs, or heart. Admission to a trauma center for ventilatory support, sufficient pain control, and early mobilization are steps that should be taken in the management of geriatric patients with confirmed or suspected rib fractures.[29]

Figure 4. Subdural Hematoma



Head Injuries. Head injury in the elderly trauma patient may have a dramatic or an occult presentation, requiring increased suspicion by the clinician. The cerebral atrophy and decreased blood supply to the brain that typically accompany aging place the injured elder in a neurologically precarious situation. Cerebral contusions and subdural hematomas *(see Figure 4)* are the most frequently diagnosed head injuries resulting from falls.[40] Traumatic brain injury has been associated with twice the rates of mortality for elderly patients when compared with younger patients.[41] Thus, all elderly patients with suspected head trauma, regardless of severity, should undergo a head CT scan.

Substance abuse, suicide attempts, chest wall injuries, and head trauma are just a few of the conditions that should be screened for during the emergency department comprehensive survey. Again, the goal is to complete a thorough evaluation and expeditiously move the patient to an area of definitive care. The optimal location of that definitive care has been debated, but studies have shown that ICU admission is the preferred destination for elderly trauma patients.[42,43]

Subsequent Care, Transition of Care, or Critical Care

There is some debate as to whether or not aggressive care is warranted in a population with a higher propensity toward mor-

tality following injury. Demetriades and colleagues found that aggressive management concomitant with ICU admission resulted in decreased mortality and permanent disability.[42] We have already seen how decisions aimed at avoiding under-triage and inadequate initial evaluation and treatment can improve outcomes in this susceptible population. Accordingly, routine admission to an ICU for continued strict monitoring is recommended for elderly trauma victims with at least a moderate injury.[43]

Confusion is one important complication that may arise following transfer to the ICU. Geriatric patients already suffering from the presence of dementia are at increased risk for confusion during hospitalization.[44] Polypharmacy, which is highly prevalent in the elderly, can add to this condition, along with initiation of a different routine and lack of familiar surroundings.

The first step in evaluation should be to rule out potentially life-threatening causes of delirium, such as alcohol withdrawal or electrolyte abnormalities.[45] Medications that are not necessary should be discontinued, and every effort should be made to control pain. Patients should be frequently re-oriented and mobilization should be encouraged as soon as possible. Restraints should be used sparingly as they may exacerbate confusion and enable skin breakdown.

The ICU stay is perhaps the most important part of geriatric trauma management in terms of achieving a positive outcome. Caring for these patients may easily appear daunting as their pre-existing comorbidities and their traumatic injuries coalesce into a complicated presentation. Very little has been written regarding this phase of treatment, but recent studies that have implemented geriatrician consultations have shown their effectiveness by improving outcomes. A team approach that utilizes experts in the fields of trauma and geriatric medicine provides the elderly patient with the best opportunity for survival and a return to their baseline function.

In 2002, Richmond and coworkers suggested that the comprehensive care offered by a geriatric consultation service could be an invaluable addition to a trauma team caring for geriatric patients.[46] Fallon and colleagues instituted the concept of a Geriatric Trauma Team (GTT), which included geriatricians and advanced practice nurses who collaborated with the trauma surgical team, physical therapists, and social workers in the management of trauma patients older than age 65.[16] The geriatricians were able to advise in areas related to pain control, delirium, rehabilitation, and hypertension. Those patients who were seen by the GTT had a lower incidence of mortality compared with those who were not seen (5% versus 31%), as well as an increased ability to return to independent living. It was felt that patients who were not seen, yet returned to independent functioning, represented patients with higher physiologic reserve and less comorbidities than their age would suggest. Patients evaluated by the GTT had physiologic characteristics that mirrored chronologic age. Those who were not seen and succumbed to their injuries represented patients with severe physiologic decline or excessive comorbid disease. It was determined that the GTT was successfully able to address age-specific physical conditions in the elderly, while also providing advice concerning emotional and social factors. The value of this service was evident by the fact that GTT recommendations were followed 91% of the time.

The goal of the GTT is to appropriately manage pre-existing disease in the wake of traumatic injury. Suggestions were also made that would limit the impact of the ICU environment on the patient's mental status, as well as propose treatments to maximize the potential for a return to previous functioning. In light of the promise evidenced by the GTT study, it is recommended that consulting a geriatrician be a mandatory part of the comprehensive hospital care of elderly trauma patients.

Summary

The triage, transport, and treatment of the older adult suffering from a traumatic injury should be driven by age appropriate assessment protocols that have been developed to attend to the unique considerations found in the elderly. The recommendations made in this review reflect these efforts. However, the need for further research in the field of geriatric trauma is evidenced by the relatively sparse information that is currently available. The need is amplified with the realization that, according to the United States Census Bureau, those who are 65 years of age and older will account for roughly 20% of the total population in 2050.[47] Therefore, management of these patients should be taught in residency in order for the increased incidence of elderly trauma victims to be met with an increased number of prepared medical personnel.

The "grim triad" of chronological age, co-morbid disease, and moderate injury cannot be altered by trauma responders. Nevertheless, timely and aggressive decisions starting in the field can decrease mortality and improve overall function following discharge.

Proper care of the injured elder is a team effort and should include everyone from emergency providers to trauma surgeons to geriatricians. As work continues to better outline geriatric trauma management strategies, the goal is to maximize the quality of life for these active yet vulnerable members of society. The anticipated future of trauma demands these efforts, and these valuable patients deserve no less.

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CME Questions

1. A 79-year-old woman is transported to the trauma room of the emergency department after having been involved in a van crash as an unrestrained rear seat passenger. She states that she was "tossed around like a package" as the van rolled several times before coming to a stop. She is complaining of right-side abdominal pain, has a closed deformity of her right calf, and diffuse neck and back pain. She has a history of HTN and CHF. Her initial trauma room vital signs are: pulse 110, BP 180/100, O_2 SAT 99%, and temp 36.5°C. Which of the following statements regarding the presence of shock in the elderly is correct?
   A. Elderly patients have an unaltered ability to increase heart rate in response to blood loss.
   B. Blood pressure accurately correlates with cardiac output in this patient population.
   C. The therapeutic range for volume resuscitation in the elderly patient is often narrow and may require invasive hemodynamic monitoring to accomplish successfully.
   D. Pre-existing medical conditions do not affect outcomes from injury in the elderly.

2. Which of the following statements is correct regarding the management of shock in the elderly trauma patient?
   A. Blood pressure correlates well with cardiac output in the elderly patient with blood loss.
   B. Elderly patients often have the same pre-injury intravascular volume status as younger patients who are injured.
   C. Therapeutic resuscitation ranges are identical in the elderly patient and the younger patient.
   D. Age is an important independent predictor of outcome following injury, regardless of the mechanism.

3. An 82-year-old female is transported to the trauma center from a community hospital after having fallen at home several hours previously. She has a type II odontoid fracture and a closed fracture of her humerus. Which statement regarding the potential outcome following injury in the elderly is most correct?
   A. Octogenarians have no difference in outcome when compared to the general elder trauma patient population.
   B. Length of hospital stay and ICU stay are similar regardless of the age of the patient.
   C. The dismal prognosis associated with this patient's injury should prompt more conservative management.
   D. Pulmonary and infectious complications are likely to occur with equal frequency in octogenarian and non-octogenarian elderly trauma patients.

4. Which of the following statements is correct regarding the potential outcome from injury in the elderly trauma patient?
   A. Octogenarians have a lower average injury severity score and lower mortality rates than non-octogenarian elderly trauma patients.
   B. Length of hospital stay and ICU stay are comparable for both groups of elderly trauma patients.
   C. Octogenarians are discharged to skilled nursing facilities more frequently than non-octogenarian elderly trauma patients.
   D. Pulmonary and infectious complications are encountered with higher frequency in octogenarian trauma patients.

5. A 72-year-old male is transported to the emergency department of a level I trauma center after a fall from standing. He reportedly struck is head and sustained a brief loss of consciousness. His Glasgow Coma Scale (GCS) score is currently 13. He has a past medical history of insulin-dependent diabetes. The trauma team was not activated prior to his arrival. Which statement is correct regarding the potential outcome following injury in the elderly?
   A. Elderly trauma patients may be severely injured despite not meeting standard criteria for trauma team activation.
   B. Only major injury can lead to sudden, unanticipated deterioration in the elderly trauma patient.
   C. The patient encountered in the emergency department rarely requires ICU admission or operative intervention if there has not been a trauma team activation for the patient.
   D. Vital signs are good indicators of the elderly trauma patient's need for trauma team activation.

6. Which of the following statements is correct regarding the potential outcome from injury in the elderly trauma patient?

CNE/CME Objectives

Upon completing this program, the participants will be able to:

a.) discuss conditions that should increase suspicion for traumatic injuries;
b.) describe the various modalities used to identify different traumatic conditions;
c.) cite methods of quickly stabilizing and managing patients; and
d.) identify possible complications that may occur with traumatic injuries.

CNE/CME Instructions

Physicians and nurses participate in this continuing medical education/continuing education program by reading the article, using the provided references for further research, and studying the questions at the end of the article. Participants should select what they believe to be the correct answers, then refer to the list of correct answers to test their knowledge. To clarify confusion surrounding any questions answered incorrectly, please consult the source material. **After completing this activity, you must complete the evaluation form provided and return it in the reply envelope provided in order to receive a letter of credit.** When your evaluation is received, a letter of credit will be mailed to you.

A. Vital signs are often misleadingly normal in the elderly trauma patient.
B. Common medications frequently taken by the elderly have no effect on the diagnosis and prompt management of significant injury.
C. Rarely is a normal blood pressure indicative of hypotension in the elderly trauma patient.
D. Stable elderly trauma patients never require ICU admission and operative intervention.

7. Evaluation of the cervical spine in older patients is common. Which of the following statements regarding it is most true?
A. Acceptable criteria for clinical clearance of CSI should not be done in older patients.
B. Radiographic clearance can be accomplished with a negative lateral c-spine film.
C. Appropriate radiographic clearances may require a CT scan to evaluate the upper C-spine
D. The rate of CSI is significantly lower in older patients compared with younger patients.

8. Which of the statements is correct regarding airway issues?
A. Although hypoxia may be present, use of supplemental oxygen should be limited in older patients.
B. Dentures and cervical degenerative spine disease have important implications in airway management in this population.
C. Airway reflexes tend to be increased in older persons.
D. Orotracheal intubation is no more difficult in elderly patients when compared to their younger counterparts.

9. Resuscitation following traumatic injury in older persons:
A. Should not be initiated until all injuries have been assessed.
B. Should consist of blood products and pressor agents initially.
C. Should begin with discrete boluses of crystalloids followed by warmed blood products if hemodynamic compromise persists.
D. Should be limited because of the significant risk of volume overload and heart failure.

10. Following traumatic injury, shock is:
A. best defined as the presence of hypotension and tachycardia.
B. less commonly recognized in the geriatric trauma patient.
C. equally important in contributing to outcomes in all age groups.
D. portends a poor prognosis in older patients and its presence should limit further futile efforts.

Answers: 1. C; 2. D; 3. D; 4. C; 5. A; 6. A; 7. C; 8. B; 9. C; 10. B

In Future Issues:

Pediatric Concussions