

Fishman JA. Infection in solid-organ transplant recipients. N Engl J Med. 2007;357:2601-2614.

The risk of infection after transplantation changes over time, particularly with modifications in immunosuppression.

Donor-Derived Infections

Most often, these infections (e.g., CMV, TB, and *T. cruzi* infection) are latent in transplanted tissues. Transmission may also be due to active donor infection that was undiscovered at the time of organ procurement.

Clusters of infections derived from deceased donors have been described, including transplantation-associated West Nile virus infection, rabies, HIV infection, and Chagas' disease. In recent outbreaks of West Nile virus infection, lymphocytic choriomeningitis virus infection, and rabies, signs of infectious encephalitis in organs from deceased donors were masked by unrelated acute neurologic events and thus were not recognized.

The evaluation of donors relies on serologic testing for common infections. Since seroconversion may not occur during acute infections and the tests are not 100% sensitive, some active infections remain undetected.

Organs from donors with specified known infections may be considered for specific recipients based on the urgency of the need for transplantation and the availability of effective antimicrobial therapies.

- Some livers from donors who were seropositive for Chagas' disease have been used successfully with benznidazole prophylaxis
- Organs from donors infected with HBV are used for some recipients who have been vaccinated or who were previously infected, provided there is treatment with specific antiserum and anti-HBV antiviral agents.
- The use of organs infected with HCV is generally reserved for HCV-infected recipients.

Recipient-Derived Infections

Active infection in transplant recipients should be eradicated before transplantation, since immunosuppression will exacerbate the infectious process. Infections that can be treated or controlled do not preclude transplantation.

Common recipient-derived pathogens include *Mycobacterium tuberculosis*, parasites (e.g., *Strongyloides stercoralis* and *T. cruzi*), viruses (e.g., CMV, EBV, HSV, VZV, HBV, HCV, and HIV), and endemic fungi (e.g., *Histoplasma capsulatum*, *Coccidioides immitis*).

Activities such as travel, raising pigeons (associated with *Cryptococcus neoformans* infection), or marijuana use (associated with aspergillus infection) increase the risk of infection.

The importance of donor-derived or recipient-derived exposures to endemic fungi such as *H. capsulatum* or TB is reflected by the fact that the rate of activation of these infections is 50 times higher among transplant recipients than it is among the general population.

The course of HCV infection after liver transplantation remains discouraging. Since effective antiviral therapies are lacking, recipients are uniformly reinfected by HCV.

Successful transplantation has been achieved in HIV-infected patients with highly active antiretroviral therapy.

Prevention of Infection

3 preventive strategies are used: vaccination, universal prophylaxis, and preemptive therapy.

Vaccination is less effective during immunosuppression. Pneumococcal vaccine is recommended every 3 - 5 years, and influenza vaccine is recommended annually. Live vaccines are generally contraindicated after transplantation.

Lifestyle changes after transplantation may help limit exposures:

- Hand washing after food preparation, gardening, and contact with feces or secretions.
- Avoid close contact with people who have respiratory illnesses, and avoid environments such as construction sites, which have known pathogens.
- Avoidance of well water and lake water (which may contain cryptosporidium or giardia species), undercooked meats, unwashed fruits and vegetables, and unpasteurized dairy products.

The greatest risks associated with early fungal infections include aspergillus at the tracheal anastomosis after lung transplantation and candida species after pancreas or liver transplantation.

Invasive fungal infections are most common in liver recipients requiring ICU admission, surgical re-exploration or retransplantation, or transfusion of large amounts of blood products and in liver recipients with metabolic dysfunction (involving the liver allograft, kidney, or diabetes), respiratory failure, CMV infection, or HCV infection. The risk is increased after broad-spectrum antimicrobial therapy. Prophylaxis should be considered in such high-risk hosts.

Most transplantation centers use TMP-SMX prophylaxis for as little as 3 months or for as long as a lifetime to prevent pneumocystis pneumonia as well as infections with *Toxoplasma gondii*, and listeria species, and common urinary, respiratory, and GI pathogens.

The prevention of post-transplantation CMV and other herpesvirus infections and the availability of oral antiviral agents have revolutionized post-transplantation care. Two preventive strategies have emerged:

- Universal prophylaxis - antimicrobial therapy is provided to all at-risk patients for a defined period.
- Preemptive therapy - sensitive quantitative assays are used to monitor patients at predefined intervals in order to detect infection before symptoms arise. A positive assay triggers the initiation of antimicrobial therapy, a reduction in the intensity of immunosuppression, intensified monitoring, or all of these steps.

Changing the Pattern of Infection

Corticosteroid-sparing regimens and antipneumocystis prophylaxis have made pneumocystis pneumonia less common. Herpesvirus infections are rare while patients receive antiviral prophylaxis. Newer immunosuppressive approaches (e.g. the use of sirolimus) have largely replaced high-dose corticosteroids and azathioprine.

With changes in typical immunosuppression, new patterns of infection have emerged:

Sirolimus-based regimens have been associated with idiosyncratic noninfectious pneumonitis, which is easily confused with pneumocystis pneumonia or viral pneumonia.

T-lymphocyte-depleting antibodies commonly used for initial or induction therapy are associated with increased viral activation - notably, CMV, EBV, and HIV.

Cellular depletion after induction therapy often persists beyond the period of antimicrobial prophylaxis, resulting in late infections with viruses such as CMV and JC polyomavirus as well as fungal infections and malignant conditions after transplantation.

Infections that occur after the usual period or that are severe suggest excessive immunosuppression or exposure.

Early Post-Transplantation Period (1st month)

- Opportunistic infections are generally absent during the first month after transplantation, since the full effect of immunosuppression is not yet present.
- Infections with antimicrobial-resistant species (MRSA, VRE) are seen.
- Anastomotic leaks and ischemia occur.
- C. difficile colitis is common in this setting.
- Early graft injuries (e.g., ischemia of bile ducts or pulmonary reperfusion injury) may later become foci for liver or lung abscesses.
- Donor-derived infection is uncommon. Recipient-derived infection (colonization) – Aspergillus, pseudomonas – is seen.

Intermediate Post-Transplantation Period (1-6 months)

Viral pathogens & allograft rejection are responsible for the majority of febrile episodes that occur during this period.

TMP-SMX prevents most UTIs and opportunistic infections.

Herpesvirus infections are uncommon with antiviral prophylaxis. However, other viral pathogens, including polyomavirus BK, adenovirus, and recurrent HCV, have emerged.

Late Post-Transplantation Period (> 6 months)

The risk of infection diminishes 6 months after transplantation, since immunosuppressive therapy is usually tapered in recipients who have satisfactory allograft function. However, transplant recipients have a persistently increased risk of infection due to community-acquired pathogens.

Recurrent infection may develop in some patients despite minimization of their immunosuppression. These patients are at increased risk for opportunistic infection with listeria or nocardia species, invasive fungal pathogens, and unusual organisms. Minimal signs of infection merit careful evaluation in such high-risk patients.

Common Infections in Transplantation

CMV

Invasive disease:

- occurs during the 1st year after completion of prophylaxis
- manifested most often as fever and neutropenia
- some patients have lymphadenopathy, hepatitis, thrombocytopenia, pneumonitis, GI invasion, pancreatitis, chorioretinitis (which is often late), or meningoencephalitis (uncommon).
- Invasive disease generally warrants IV ganciclovir

“Indirect Effects”:

- an overall increase in the risk of additional infections, including other viruses and EBV-associated post-transplantation lymphoproliferative disorder.
- may contribute to vasculopathy in heart-allograft recipients and to the bronchiolitis obliterans syndrome in lung-allograft recipients.
- may contribute to allograft injury/rejection

Serologic assays are useful in determining a patient's risk of infection, but are of little use in the diagnosis of acute infections. Primary infection, the most severe form of disease, occurs when seronegative recipients who have not previously received immunologic therapy receive allografts from latently infected, seropositive donors.

Both universal antiviral prophylaxis and preemptive antiviral therapy reduce the risk of invasive CMV infection.

Most centers provide anti-CMV prophylaxis for 3 - 6 months after transplantation (e.g. valganciclovir or ganciclovir).

The use of induction therapy with depleting antilymphocyte antibodies for seropositive donors or seropositive recipients increases the risk of CMV reactivation and generally merits extended prophylaxis followed by monitoring for active infection.

Quantitative diagnostic assays for CMV (e.g. PCR) are essential for management of infection. In patients with neurologic manifestations of CMV and GI disease, blood-based cytomegalovirus assays may be negative. Thus, invasive procedures such as colonoscopy with biopsy or LP may be necessary.

Documentation of cure in patients with GI CMV infection includes negative results of microbiologic assays and healing of ulcers and colitis on endoscopic evaluation.

Epstein–Barr Virus and Post-Transplantation Lymphoproliferative Disorder

PTLD, a heterogeneous group of lymphoproliferative disorders, occurs in up to 10% of adults who are solid-organ transplant recipients; it carries a mortality of 40 - 60%. PTLD accounts for > 1/2 of post-transplantation malignant conditions in pediatric solid-organ–transplant recipients.

The clinical presentation of EBV-associated PTLD varies and can include a benign mononucleosis-like syndrome, abdominal mass lesions, infiltrative disease of the allograft, or malignant, monoclonal lymphoma.

Polyomaviruses BK and JC

Polyomaviruses have been identified in transplant recipients in association with nephropathy (e.g., polyomavirus BK–associated nephropathy) and ureteral obstruction, and the JC virus has been associated with progressive multifocal leukoencephalopathy.

No effective antiviral therapy exists for polyomaviruses; therapy requires a reduction in immunosuppression

Central Nervous System Infection

The broad spectrum of causative organisms includes listeria, herpes simplex virus, JC virus, and *C. neoformans*. Empirical therapy must be initiated while the results of imaging studies (preferably MRI), LP (including PCR for detection of herpes simplex virus and cryptococcal antigen), and cultures are pending.

Pneumonitis and Pneumocystis Infection

Pneumocystis pneumonia remains common in the absence of specific prophylaxis. No radiographic patterns are pathognomonic in the immunocompromised host.

Takhar SS, Hendey GW. Orthopedic illnesses in patients with HIV. Emerg Med Clin N Am. 2010;28:335-342.

DISSEMINATED DISEASES

Neoplastic

Immunosuppression predisposes patients to malignancy; Kaposi sarcoma (KS) and high-grade non-Hodgkin lymphoma (NHL) are prototypical AIDS-defining malignancies. AIDS increases the risk of KS by at least 310 times and NHL by more than 110-fold.

KS:

- a vascular neoplastic disease primarily affecting the skin, causing violaceous nodules or plaques
- can involve a variety of sites including the lymph nodes, lungs, liver, and spleen.
- epidemic KS is the most common AIDS-associated cancer in the US.
- bone involvement is rare; osseous KS generally results from of contiguous invasion from nearby tissues.
- KS lesions are not well visualized on plain radiographs. CT, MRI, and nuclear studies are more helpful. The diagnosis should be confirmed by biopsy of the lesion.

NHL:

- in AIDS patients tends to be the aggressive B-cell type that is associated with marked immunosuppression.
- the bone marrow is involved in up 30% of cases.
- symptoms are variable and nonspecific; lymphoma presentation is often late.

Infectious

Mycobacteria

TB is the leading cause of death in persons infected with HIV worldwide. HIV infection is also the highest risk factor for progression from latent TB to active disease.

In patients with HIV extrapulmonary manifestations are common, and may be concurrent with pulmonary TB.

Extrapulmonary TB is believed to be the result of hematogenous dissemination and seeding of remote sites by the mycobacterium. A common site for musculoskeletal TB is the lower thoracic or the upper lumbar vertebral column (Pott disease).

Large paraspinal abscesses are also characteristic of TB. There can also be soft tissue extension leading to psoas muscle involvement.

TB can cause septic arthritis that preferentially affects the large weight-bearing joints such as the hip and knee; patients often have concurrent osteomyelitis and soft tissue involvement.

Atypical mycobacterial infections are a manifestation of advanced AIDS. They are not as pathogenic and the risk of systemic dissemination increases when the CD4 count decreases to < 100 cells/mm³.

Mycobacterium avium complex is the most common atypical mycobacterial infection in patients with HIV. Cutaneous lesions such as nodules and ulcers are often present and may be a clue to the diagnosis.

Bartonella

Bacillary angiomatosis (BA) is a disseminated rickettsia-like infection caused by *Bartonella henselae* and *Bartonella quintana*.

In the immunocompetent host, *Bartonella henselae* cause a local self-limited lymphadenitis.

The vascular proliferative lesions in the skin are difficult to distinguish clinically from KS. **Osteomyelitis may differentiate BA from KS as bony involvement is an unusual manifestation of KS.**

Antibiotic therapy can be curative; untreated disease can be fatal.

BONE DISORDERS

Osteopenia and Osteoporosis

Osteoporosis is defined by a BMD > 2.5 standard deviations from normal, which is based on a young control group. Osteopenia is defined as a BMD that is $1 - 2.5$ SD $<$ normal.

ART, especially protease inhibitors, have been linked to osteopenia and osteoporosis. In addition, HIV is believed to be an independent risk factor for reduced BMD.

Osteonecrosis

Osteonecrosis (AVN) = bone infarction at the epiphyseal regions of a bone near a joint. Traditional predisposing factors include **hypertriglyceridemia, corticosteroid use, and ethanol abuse**. ART, especially protease inhibitors, have also been implicated. Osteonecrosis occurs most often in the femoral head. The incidence of osteonecrosis is up to 45 times greater in HIV patients.

MRI of the hip is recommended in patients with persistent pain and in those with abnormal plain radiographs.

Osteomyelitis

Results from hematogenous spread of a remote infection, local spread of a contiguous infection, or direct inoculation.

TB osteomyelitis is extremely common in endemic areas, especially when the lesion involves the vertebral column. In most cases, patients are afebrile and present with back pain.

Normal plain films do not exclude the diagnosis of osteomyelitis. **A 30% - 50% reduction in bone density must occur and it can take 3 weeks for a lesion to become visible on plain films.** MRI and nuclear imaging are much more sensitive and specific.

MRI is the imaging modality of choice for osteomyelitis. Sensitivity is 82% - 100% with a specificity of 75% - 96%.

The diagnosis is made definitively by a bone biopsy and culture.

JOINT DISEASE

Septic Arthritis

Relatively uncommon in HIV patients; risk factors include IVDA or hemophilia.

The most common organism is *Staphylococcus aureus* regardless of HIV status. TB is a common cause of septic arthritis in developing countries.

Gram-negative bacilli such as *Pseudomonas aeruginosa* are found in increased incidence in IVDAs.

Polyarticular disease from gonococcus is more common in patients infected with HIV. The large weight-bearing joints are most often affected.

Patients with CD4 counts < 200 cells/mm³ may have a lower joint fluid WBC, making the diagnosis challenging.

Empiric therapy should be against MRSA which is emerging as the most common cause of bacterial septic arthritis.

Spondyloarthritis

Patients infected with HIV have a higher incidence of spondyloarthropathy; these include HLA-B27 associated reactive arthritis and psoriatic arthritis.

Reactive arthritis is 100 - 200 times more common in the HIV patient; some believe that the association of reactive arthritis with HIV is related to sexual activity and immune suppression rather than the virus itself.

Reactive arthritis is associated with GU and GI infections like *Chlamydia trachomatis*, *Campylobacter jejuni*, and *Shigella flexneri*.

Classically reactive arthritis presents with the triad of arthritis, urethritis, and conjunctivitis. Patients infected with HIV suffer a more severe and debilitating course of this disease and the classic triad is often absent.

Psoriatic arthritis is more common in those with advanced HIV disease and the skin findings are more extensive than in patients with no HIV infection. Psoriatic arthritis often involves the surrounding tendons and fascia (enthesopathy).

NSAIDs are first-line treatment but are often not effective. Sulfasalazine has been effective in some cases; occasionally immunosuppressive agents are indicated, which is problematic in this population. Effective ART is also helpful in treating these inflammatory conditions.

HIV-associated Arthritis

HIV infection is associated with an arthropathy similar to other viruses (eg, hepatitis B). It is a transient, nonerosive, oligoarthritis that affects the legs, lasting < 6 weeks. It can occur at any time during the course of HIV infection.

Synovial fluid analysis is noninflammatory. RF and ANA are negative. Treatment consists of NSAIDs, and the condition tends to be self-limited.

MYOPATHIES

Polymyositis - an idiopathic inflammation of the skeletal muscle which can occur at any stage of HIV infection. Patients present with a subacute, progressive, proximal muscle weakness with an increased CPK. It may be the first sign of HIV infection. Treatment is with corticosteroids.

Pyomyositis - a primary deep muscle abscess seen more often in patients infected with. *Staphylococcus aureus* is the culprit organism in > 90% of cases.

The inciting factor of the infection is unclear; it is postulated that a transient bacteremia seeds traumatized muscle. The most common sites of involvement include the quadriceps, the gluteal, and iliopsoas muscles. After 1 - 3 weeks, the pain becomes progressively worse and the fever more pronounced.

MRI more sensitive than CT or ultrasound early in the course before the fluid collection becomes prominent. Treatment is by drainage and systemic antimicrobial therapy directed at *S aureus*.

Butalia S, Palda VA, Sargeant RJ, Detsky AS, Mourad O. Does this patient with diabetes have osteomyelitis of the lower extremity? JAMA. 2008;299(7):806-813.

Introduction

Foot-related complications account for up to 20% of all diabetes-related admissions.

Diabetic foot problems are the most common cause of nontraumatic amputations, with infection responsible for a large proportion of these cases. The perioperative 30-day mortality of lower extremity amputation is 7.4%.

The diagnosis of lower limb osteomyelitis in patients with diabetes is a challenge. The classic signs and symptoms of infection may be absent or masked by the coexistence of vascular disease and neuropathy. **The gold standard for the diagnosis of osteomyelitis is a bone biopsy and culture, which is not always practical.**

It is sometimes difficult to distinguish between lower extremity ulcers due to diabetes and those caused primarily by venous or arterial insufficiency:

- Venous ulcers are typically found above the medial/lateral malleoli and frequently have irregular borders.
- Arterial ulcers often affect the toes or the shins, with the borders of the ulcer being pale and appearing as if they have been punched out. These ulcers may lack granulation tissue and are typically painful in the absence of coexisting neuropathy.
- Diabetic ulcers usually occur at areas of increased pressure, such as the sole of the foot, or areas where shoes have rubbed against the skin.

Quantifying ulcer size: multiply the longest and widest diameters of the lesion; this may not be completely accurate as some ulcers may be round or irregularly shaped.

Probe-to-bone test: performed at the bedside with a sterile, blunt, stainless steel probe. Gently probe the wound for the presence of a rock-hard, gritty structure at the wound base in the absence of any intervening soft tissue. The presence of such a finding indicates a positive result; the inability to probe the base of a wound to periosteum or bone is a negative result.

Wagner Grading Scale of Foot Ulcers

Grade 0: no open lesions; may have evidence of healed lesions or deformities

Grade 1: superficial ulcer

Grade 2: deeper ulcer to tendon, bone, or joint capsule

Grade 3: deeper tissues involved, with abscess, osteomyelitis, or tendinitis

Grade 4: localized gangrene of toe or forefoot

Grade 5: gangrene of foot (partial or total)

A limitation of this scale is that all deep tissue infections (e.g. abscess, tendinitis, and osteomyelitis) are accounted for in a single grade.

Characteristic signs of osteomyelitis on plain radiograph: focal loss of trabecular pattern, periosteal reaction, and frank bone destruction, often accompanied by soft tissue swelling.

Study Objective: To review the available literature to determine the accuracy of historical features, physical exam, and laboratory and basic radiographic testing for osteomyelitis of the lower extremity in the diabetic.

Data Synthesis

The two best clinical findings were:

- An ulcer area $>2\text{ cm}^2$ makes osteomyelitis more likely (LR, 7.2), while an ulcer area $<2\text{ cm}^2$ decreases the likelihood of osteomyelitis by about half (LR, 0.48).
- A positive probe-to-bone test result increases the likelihood of osteomyelitis (summary LR, 6.4).

An ESR of $>70\text{ mm/h}$ increases the probability of the diagnosis of osteomyelitis (summary positive LR, 11).

Radiographic results alone appear to be marginally useful if positive as an abnormal plain radiograph doubles the odds of osteomyelitis (summary LR, 2.3) and less useful when negative for osteomyelitis (summary LR, 0.63).

A positive MRI result increases the likelihood of osteomyelitis (summary LR, 3.8). However, a normal MRI result makes osteomyelitis much less likely (summary LR, 0.14).

MRI was shown to have a sensitivity of 90% (range, 77%-100%) and a specificity of 83% (range, 40%-100%) in all patients and a summary positive LR of 3.8 and a summary negative LR of 0.14 in patients with diabetes. MRI was also shown to be more accurate than technetium bone scan, plain radiography, and WBC scan. The overall accuracy (ie, the weighted average of the sensitivity and specificity) of MRI is 89%.

A recent meta-analysis reported that nuclear imaging lacks specificity in the diagnosis of osteomyelitis.

The presence or absence of ulcer inflammation (erythema, swelling, purulence) does not modify the probability of disease (positive LR, 1.5; negative LR, 0.84).

The clinical impression of osteomyelitis, without formal rules or weighting of the findings, increases the likelihood of osteomyelitis about 5-fold (summary LR, 5.5). When a clinician judges that osteomyelitis is absent, the likelihood decreases (summary LR, 0.54). These data suggest that clinicians might be more proficient at detecting the presence of osteomyelitis than detecting its absence.

The value of an elevated WBC count was examined in a single study and demonstrated poor sensitivity regardless of the cutoff studied.

In patients with suspected osteomyelitis, a positive swab was equally common in patients with and without biopsy proven osteomyelitis. Superficial swab cultures do not reliably predict bone microorganisms.

Conclusions

An ulcer $>2\text{ cm}^2$ or a positive probe-to-bone finding may be helpful to establish the diagnosis. An ESR $>70\text{ mm/h}$ or positive plain radiograph findings are helpful in increasing the likelihood of osteomyelitis. MRI results should be interpreted in the context of the pretest probability. A negative MRI result makes the diagnosis much less likely when all of these findings are absent. Temperature, ulcer inflammation, WBC count, and swab culture are not helpful in establishing the diagnosis or directing therapy in patients with diabetes and a lower extremity ulcer. No single feature on history or physical examination reliably excludes osteomyelitis. The diagnostic utility of a combination of findings is unknown.

BFraze BW, Fee C, Lambert L. How common is MRSA in adult septic arthritis? Ann Emerg Med. 2009;54(5):695-700.

Introduction

Because the clinical examination is unreliable to rule out septic arthritis, emergency physicians must maintain a very low threshold for performing diagnostic arthrocentesis. The level of synovial fluid leukocytosis generally correlates with likelihood of bacterial infection; however, a low cell count does not rule out the diagnosis. Synovial fluid culture is considered the criterion standard test to establish the diagnosis.

Community-associated MRSA is now the predominant cause of skin and soft tissue infections in US EDs, and MRSA is an increasingly common cause of invasive infections of all types, both community and hospital acquired. At the public hospital in this study, 41% of all clinical *S aureus* isolates in 2007 were MRSA.

The objective of this study was to determine the proportion of ED patients with septic arthritis caused by MRSA. The study was a retrospective review in 2 urban academic EDs in California, one tertiary care and one public. Subjects included patients who underwent arthrocentesis in the ED.

Results

109 synovial fluid cultures were sent from the EDs. Of 12 septic arthritis cases, 6 grew MRSA, 4 MSSA, and 1 each *Streptococcus pneumoniae*, *Enterococcus faecalis*, and *Pseudomonas aeruginosa*.

Only 2 patients, both with MRSA, were febrile at triage. The median synovial fluid leukocyte count in MRSA cases was 15,184 cells/ μ L compared with 84,700 cells/ μ L in non-MRSA cases.

Of the 6 MRSA cases, 5 were administered appropriate antibiotics in the ED. All 6 MRSA isolates from septic arthritis were susceptible to vancomycin, TMP-SMX, and doxycycline; 5 were susceptible to clindamycin; and 4 were susceptible to levofloxacin.

Discussion

S aureus is the most common causal organism in adult septic arthritis, accounting for approximately 50% of cases in large case series. Gonococcal arthritis has become uncommon since the 1980s. Most cases of septic arthritis are caused by hematogenous spread, although the source of *S aureus* bacteremia is often occult.

Evidence is mounting that MRSA should be considered a likely pathogen in any patient presenting to the ED with septic arthritis. Studies specifically showing a high prevalence of MRSA in community-onset septic arthritis are limited to recent pediatric case series, in which MRSA accounted for 47% - 70% of *S aureus* infections.

Taken together with other studies involving children and older adults elsewhere in the US, the results of this study strongly suggest that antibiotics with activity against MRSA should be included in the empirical treatment of suspected septic arthritis encountered in the ED.

3 of 6 patients with MRSA septic arthritis had significant recent contact with the health care system in the form of hospitalization within the previous 12 months. These cases are therefore considered health care-associated MRSA infections by widely accepted clinical criteria. Two of the remaining 3 patients injected drugs, which is a recognized risk factor for MRSA infection.

This study found a relatively low synovial fluid leukocyte count in the MRSA cases; It was $< 25,000$ cells/ μL in 4 of 5 cases in which it was measured and generally much lower than in the non-MRSA cases. In large studies before 1998, only 12% - 37% of all septic arthritis patients had a synovial fluid leukocyte count $< 25,000$ cells/ μL .

None of the MRSA patients in this study reported receiving antibiotics at admission, nor were they known to be immunosuppressed. The low synovial fluid leukocyte count may be related to toxins produced by community-associated MRSA, such as Panton Valentine leukocidin.

Conclusion

MRSA was the most common cause of community-onset adult septic arthritis. Synovial fluid cell counts were unexpectedly low in MRSA septic arthritis cases.

Cornia PB, Hersh AL, Lipsky BA, Newman TB, Gonzales R. Does this coughing adolescent or adult patient have pertussis? JAMA. 2010;304(8):890-896.

Childhood vaccination for *Bordetella pertussis* (the cause of whooping cough) confers limited immunity that wanes after 5 - 10 years and rarely lasts > 12 years. Physicians often forget that a prolonged cough in an adult or adolescent may be due to pertussis.

The severe cough of pertussis can cause subconjunctival hemorrhage, rib fractures, urinary incontinence, hernias, posttussive syncope, or even ICH and stroke from vertebral artery dissection.

Approach to Patients With Cough

Acute (<3 weeks) cough

- May be caused by a serious condition (eg, pneumonia, CHF, lung CA, or PE), but the most common cause is a self-limited, viral URI.

Subacute (3-8 weeks) cough

- Often represents persistence of an acute respiratory infection
- If a respiratory infection did not precede the cough, proceed with an evaluation for chronic cough

Chronic (>8 weeks) cough

- For persons who smoke or take ACEIs, the first step is to stop them.
- If the cough persists, it is most commonly caused by GERD, asthma, or postnasal drip/chronic sinusitis (also known as upper airway cough syndrome).
- Another common cause = **nonasthmatic eosinophilic bronchitis** - cough accompanied by sputum showing eosinophils and without dyspnea, wheezing, airflow obstruction by spirometry, or airway hyperreactivity by methacholine provocation testing.

Physicians should be aware that **pertussis also causes subacute and chronic cough.**

Classic Stages of Pertussis Infection

Infection with B pertussis in a person without immunity is characterized by 3 phases:

Catarrhal Phase

- Usually lasts 1 - 2 weeks, but diagnosis during this stage is difficult as symptoms are nonspecific and overlap with more common viral URIs (malaise, rhinorrhea, and mild cough).
- Patients may have low-grade fever, but significant fever is atypical.
- **2 early findings that may be clinically useful: excessive lacrimation and conjunctival injection.**

The incubation period for B pertussis is 7-10 days; for most viral URIs it is 1-3 days. Thus, exposure to a person with a cough illness 1 - 2 weeks prior to symptoms is more suggestive of pertussis, particularly if that contact belongs to a high-risk group for pertussis (eg, works with young children or lives in a community with low vaccination rates).

Paroxysmal Phase

- Begins during the 2nd week of illness.
- Paroxysm = a series of coughs during a single expiration; often occur in groups throughout the day and night, with patients experiencing few symptoms between paroxysms.
- A cough paroxysm causes low lung volumes, leading to a vigorous inspiration that may result in a whoop, particularly in infants and children, in whom the caliber of the trachea is smaller.
- Other classic symptoms described at this stage are posttussive emesis or syncope.

Convalescent Phase

- Occurs after 2 – 3 months
- Characterized by a gradual transition to persistent but decreased frequency and severity of cough.

Symptoms of pertussis infection in previously immunized or infected adolescents and adults, in contrast with the classic symptoms observed in unimmunized infants and children, are variable and often atypical. The predominant symptom may simply be a persistent cough.

Several studies have shown that pertussis is the cause 12% - 32% of prolonged cough illnesses in adolescents and adults; *for most patients, the duration of the cough illness is > 3 weeks.*

Epidemiology of Pertussis Infection

Pertussis was associated with high mortality in infants until a vaccine was introduced in the US in the late 1940s.

Widespread vaccination of children led to a dramatic decline in disease incidence, from a peak of > 250,000 cases in 1934 to a nadir of 1010 cases in 1976. The incidence of the disease began to steadily increase in the early 1980s, with 11,647 cases reported in 2003.

The incidence of pertussis cases decreased in 2006, suggesting that the cyclic epidemic peaks and valleys that occurred every 2 - 5 years in the prevaccine era are now recurring.

The recent decreased incidence is unlikely to be due to use of the newly available acellular booster pertussis vaccine (Tdap) because the recommendations for booster vaccinations of adolescents and adults were not issued until 2006.

Currently, about 1/2 of reported cases occur in adolescents and adults - persons aged 10 - 19 years account for 33% of infections; persons aged \geq 20 years or older account for 23%.

Adolescents and adults with unrecognized pertussis are a reservoir of infection for infants and children. Infants, especially those < 6 months, and young children who have not been fully immunized are at the highest risk of hospitalization and pertussis- related morbidity and mortality.

Most infants acquire the infection from adolescents and adults in the household.

Laboratory Diagnosis of Pertussis

Bordetella pertussis is a gram-negative coccobacillus readily transmitted via respiratory secretions.

The CDC endorses only culture and PCR methods for diagnosis in community practice.

Specimens must be collected from the ciliated respiratory epithelium of the posterior nasopharynx where *B pertussis* preferentially resides, not the anterior nares or throat. It is best to obtain the specimen using a Dacron rather than a cotton swab, as the latter is toxic to *B pertussis* organisms.

The sensitivities of PCR, serologic testing, and, particularly, culture decrease with the duration of illness. Thus, in adolescents and adults, who generally present to medical care only after several weeks of coughing, the sensitivity of the available diagnostic tests is likely to be reduced.

Culture from nasopharyngeal secretions is the criterion standard for diagnosis. However, sensitivity of culture in clinical practice is only 30% - 60%. Growth of *B pertussis* requires special culture media and takes 7 - 10 days.

Tests for rapidly detecting pertussis antigens:

- DFA – inexpensive, but is no longer recommended because of poor sensitivity and specificity.
- PCR – offers increased sensitivity and specificity, detects even small numbers of organisms, is unaffected by recent use of antibiotics, and typically provides results in 1 - 2 days. But, it is costly, is not available in many settings, and can produce false-positive results. There is no FDA-approved PCR kit for pertussis.

Serologic testing compares the levels of pertussis antibodies in acute and convalescent (>4 weeks after the acute sample is obtained) serum samples; a 2- or 4-fold increase in titers suggests infection. Alternatively, a single sample with a level above a designated threshold or a substantial decrease in titer is sometimes considered diagnostic.

Serologic testing is neither widely available nor standardized and no FDA-approved test exists.

Treatment of Pertussis

Thresholds for initiating testing and treatment are the same because of the contagiousness and public health implications of pertussis.

Antibiotic treatment during the catarrhal phase may decrease the duration and severity of cough, but the diagnosis is rarely considered during this early phase in adolescents and adults. Administering antibiotics later in the course of disease does not affect the course of symptoms but reduces spread of the infection.

Persons with pertussis may remain contagious for \geq a month; most will eventually recover without antibiotic therapy. The recommended antibiotic regimens are identical for treatment and postexposure prophylaxis (for close contacts of persons diagnosed as having pertussis).

Macrolides typically eradicate *B pertussis* within 5 days. Erythromycin has been the antibiotic of choice for decades; azithromycin and clarithromycin have comparable efficacy and are better tolerated. TMP-SMX is an alternative treatment for persons who are unable to tolerate macrolides.

CDC Case Definition of Pertussis Infection - a cough illness lasting \geq 2 weeks without other apparent cause with 1 or more of the following: paroxysms of coughing, inspiratory whoop, or posttussive vomiting.

Study Objective: Review the literature regarding the diagnostic value of 3 classically described symptoms of pertussis: paroxysmal cough, posttussive emesis, and inspiratory whoop.

Results: 3 studies were used in this analysis. Among adolescents and adults with pertussis, paroxysmal cough is common, but its specificity is low. Posttussive emesis and whoop are less common, but both show greater specificity: Presence of posttussive emesis (LR, 1.8) or inspiratory whoop (LR, 1.9) increases the likelihood of pertussis. Absence of paroxysmal cough (0.52) or posttussive emesis (LR, 0.58) reduced the likelihood. Absence of inspiratory whoop was less useful (LR, 0.78). No studies evaluated combinations of findings.

Conclusions: In a nonoutbreak setting, data to determine the diagnostic usefulness of symptoms classically associated with pertussis are limited and of weak quality. The presence or absence of posttussive emesis or inspiratory whoop modestly change the likelihood of pertussis; therefore, clinicians must use their overall clinical impression to decide about additional testing or empirical treatment.

CLINICAL BOTTOM LINE

Paroxysmal cough is a very common symptom in pertussis infection, but it appears to be nonspecific (ie, paroxysmal cough may also commonly occur in other respiratory illnesses). The presence of posttussive emesis and inspiratory whoop modestly increase the likelihood of pertussis infection. The absence of classic symptoms of pertussis may not have sufficiently low LRs to exclude the diagnosis of pertussis.

Given this, additional information should influence the decision to test and empirically treat for pertussis. This should include recent exposure to known or suspected cases of pertussis and subsequent exposure to vulnerable populations (eg, infants). Additional testing and treatment decisions in a patient with prolonged cough should be based on the overall clinical impression, independent of the classic clinical features of pertussis.

Most experts consider the combination of a whooping cough and posttussive emesis more suggestive of the diagnosis than either finding alone.

These data do not apply to an outbreak setting in which the pretest probability of pertussis for a patient with a cough illness may be substantially higher.

Fesmire FM, Brown MD, Espinosa JA, et al; for American College of Emergency Physicians Clinical Policies Subcommittee on Critical Issues in the Evaluation and Management of Adult Patients Presenting to the Emergency Department With Suspected Pulmonary Embolism; and American College of Emergency Physicians Clinical Policies Committee. Critical issues in the evaluation and management of adult patients presenting to the emergency department with suspected pulmonary embolism. Ann Emerg Med. 2011;57(6):628-652.

Approximately 50% of patients with documented DVT have perfusion defects on lung scanning; asymptomatic venous thrombosis is found in approximately 40% of patients with confirmed PE.

1. Do objective criteria provide improved risk stratification over gestalt clinical assessment in the evaluation of patients with possible PE?

Level B recommendations: Either objective criteria or gestalt clinical assessment can be used to risk stratify patients with suspected PE. There is insufficient evidence to support the use of one method over another.

Geneva Score – Uses 8 parameters relating to risk factors, signs & symptoms to define probability of PE and also to split patients into PE likely/PE unlikely to select patients safe for use of D-dimer testing for exclusion of PE.

Wells Score

- Uses 7 clinical criteria to stratify patients into low/moderate/high risk of PE; also used to classify patients into PE unlikely/PE likely to identify those for whom a negative D-dimer test results in a PE rate of 2%.
- A criticism is that it is not truly objective because it contains the subjective variable “an alternative diagnosis is less likely than PE.” This variable represents physician judgment override of the objective components because it alone places the patient in the intermediate-risk group.

Kline Rule

- A decision rule based upon 6 clinical variables to identify ED patients with suspected PE for whom a negative D-dimer result reliably excludes the presence of PE.
- There are no prospective outcome studies validating the use of the Kline rule in conjunction with D-dimer.

Pisa Model – A mathematical model for predicting probability of PE based upon 15 clinical characteristics.

In comparing the Geneva score to the Wells score, 3 studies found no significant differences in performance.

Gestalt Clinical Assessment

- Based on the clinician's training, clinical experience, and judgment.
- In the PIOPED study, low risk gestalt was considered pretest probability of < 20%, intermediate risk 20%-79%, and high risk 80%-100%. PE was diagnosed in 9.2%, 29.9%, and 67.8% of patients in the low-, intermediate-, and high-risk groups, respectively.
- Both objective criteria and gestalt assessment appear to perform equally well; one study notes that both perform disappointingly in categorizing the pretest probability in patients with suspected PE.

Several issues concerning performance of clinical decision rules and gestalt assessment have been raised:

- There is only moderate interrater agreement for gestalt of low probability and for Wells score < 2.
- Accurate determination of the pretest probability of PE trends with clinical experience.
- Gestalt assessment is inversely proportional to clinical experience, suggesting with experience, physicians recognize the difficulties in ruling out PE and are reluctant to exclude it on clinical grounds.
- In one survey, only half of all clinicians reporting familiarity with the rules use them in more than 50% of applicable cases. Spontaneous recall of the rules was low to moderate.

2. What is the utility of the PERC in the evaluation of patients with suspected PE?

Level B recommendations: In patients with a low pretest probability for suspected PE, consider using the PERC to exclude the diagnosis based on historical and physical examination data alone.

The PERC employs 8 variables: age < 50 years, pulse rate < 100 beats/min, SaO₂ > 94% (at sea level), no unilateral leg swelling, no hemoptysis, no recent trauma or surgery, no previous PE or DVT, and no hormone use. When all criteria are met, a patient is considered to be PERC negative.

A validation study concluded that the PERC could be used in combination with a low pretest probability to identify very low-risk patients for whom the diagnosis of PE can be excluded based on history and physical exam alone. If a patient is low risk by gestalt impression and PERC, the posttest probability of VTE is <2%.

In a validation study, 3.5% of enrolled patients were PERC negative but not considered to be low risk by clinical gestalt. This subgroup had a 3.1% prevalence of VTE.

In studies, the use of the PERC rule was performed retrospectively; there is no prospective outcome study of the PERC rule for clinical decisionmaking which limits the strength of recommendations supporting the use of PERC.

3. What is the role of quantitative D-dimer testing in the exclusion of PE?

Level A recommendations: In patients with a low pretest probability for PE, a negative quantitative high-sensitivity D-dimer assay (eg, turbidimetric, ELISA).result can be used to exclude PE.

Level C recommendations: In patients with an intermediate pretest probability for PE, a negative quantitative D-dimer assay result may be used to exclude PE.

D-dimer has excellent sensitivity (pooled sensitivity = 0.93 - 0.96) but only moderate specificity (pooled specificity = 0.39 - 0.51).

In patients with a low pretest probability (10%), a negative D-dimer test result would be expected to decrease the probability of PE to approximately 1%.

D-dimer has very low specificity among cancer patients suspected of having PE. Pregnancy is also associated with increasing concentrations of D-dimer, particularly in women beyond the first trimester.

4. What is the role of the CT pulmonary angiogram (CTPA) of the chest as the sole diagnostic test in the exclusion of PE?

Level B recommendations: For patients with a low or PE unlikely (Wells score ≤ 4) pretest probability for PE who require additional diagnostic testing (eg, positive D-dimer result, or highly sensitive D-dimer test not available), a negative, multidetector CTPA alone can be used to exclude PE.

Level C recommendations:

(1) For patients with an intermediate pretest probability for PE and a negative CTPA result in whom a clinical concern for PE still exists and CT venogram has not already been performed, consider additional diagnostic testing (eg, D-dimer, lower extremity imaging, VQ scanning, traditional pulmonary arteriography) prior to exclusion of VTE disease.

(2) For patients with a high pretest probability for PE and a negative CT angiogram result, and CT venogram has not already been performed, perform additional diagnostic testing (eg, D-dimer, lower extremity imaging, VQ scanning, traditional pulmonary arteriography) prior to exclusion of VTE disease.

A negative, highly sensitive, quantitative D-dimer result in combination with a negative multidetector CTPA theoretically provides a posttest probability of VTE < 1%.

Studies on multidetector CT published since 2001 indicate sensitivities of 83% - 100% and specificities 89% - 98%. Data are lacking about the performance of the most current CTPA technology (eg, 128-channel multidetector CTs).

It appears that CTPA may be falsely negative in approximately 15% of PE cases. It is hypothesized that the PE currently missed by CT may be small and clinically insignificant.

The false-negative rate of CTPA alone in patients clinically deemed high risk for PE ranges in studies from 5% - 40%. Outcome studies support the use of additional testing (eg, D-dimer, leg venous imaging, VQ scanning, traditional arteriography) after a negative CTPA alone result before definitively ruling out VTE in these patients.

5. What is the role of venous imaging in the evaluation of patients with suspected PE?

Level B recommendation: When venous ultrasound is performed as the initial imaging modality, a positive finding in a patient with symptoms consistent with PE may preclude the need for additional diagnostic imaging in the ED.

Examples of situations in which a venous ultrasound may be considered as initial imaging may include patients with obvious signs of DVT for whom venous ultrasound is readily available, patients with relative contraindications for CT scan (eg, borderline renal insufficiency, CT contrast agent allergy), and pregnant patients.

Level C recommendations

(1) For patients with an intermediate pretest probability for PE and a negative CT angiogram, for whom a clinical concern for PE still exists and CT venogram has not already been performed, consider lower extremity venous ultrasound as an additional test to exclude VTE disease.

(2) In patients with a high pretest probability for PE and a negative CT angiogram, and CT venogram has not already been performed, perform additional testing to exclude VTE disease. As one of these additional tests, consider lower extremity venous ultrasound to exclude VTE disease.

CT venous imaging is performed directly after CT angiogram. This technique uses the opacification of the venous system that follows rapid infusion of contrast medium that is involved with the performance of CT angiogram but also results in additional radiation exposure. Images are obtained of the veins of the legs, pelvis, and abdomen.

Studies indicate that venous ultrasound and CT venous imaging after negative CTPA result are equally useful.

The use of venous ultrasound as the initial diagnostic test for suspected PE may establish the diagnosis of VTE in approximately 10% of patients and preclude the need for CT angiogram.

The use of venous imaging (venous ultrasound or CT venous imaging) identifies DVT in approximately 0% - 6% of patients with a negative CT angiogram.

6. What are the indications for thrombolytic therapy in patients with PE?

Level B recommendations:

Administer thrombolytic therapy in hemodynamically unstable patients with confirmed PE for whom the benefits of treatment outweigh the risks of life-threatening bleeding complications (In centers with the capability for surgical or mechanical thrombectomy, procedural intervention may be used as an alternative therapy).

Level C recommendations:

(1) Consider thrombolytic therapy in hemodynamically unstable patients with a high clinical suspicion for PE for whom the diagnosis of PE cannot be confirmed in a timely manner.

(2) At this time, there is insufficient evidence to make any recommendations regarding use of thrombolytics in any subgroup of hemodynamically stable patients. Thrombolytics have been demonstrated to result in faster improvements in RV function and pulmonary perfusion, but this has not translated to improvements in mortality.

Treatment of PE with thrombolysis results in more rapid resolution of arterial emboli, decreased PA pressure, and improvements in cardiac output and pulmonary circulation. However, none of these benefits have been demonstrated to result in improvement in mortality or recurrent PE in unselected PE patients.

No randomized trial has investigated potential time-dependent benefits during the initial hours of symptom onset.

2 thrombolytic drugs are FDA approved for PE: streptokinase (250,000-unit bolus, followed by 100,000 units/hour for 24 hours) and recombinant tissue plasminogen activator (100 mg infused over 2 hours).

In the appropriate clinical setting, the finding of RV dysfunction on echocardiography is indirect evidence for presence of PE. Although patients with RV dysfunction on echocardiography have more rapid return of RV function and restoration of pulmonary perfusion when treated with thrombolytics, these improvements have not translated to decreases in mortality.

A large registry (ICOPER) found overall 3-month mortality from PE to be 17%. Factors associated with higher mortality from PE: age > 70 years, CHF, COPD, presence of one lung, cancer, hypotension, tachypnea, hypoxia, tachycardia, altered mental status, RV hypokinesis, syncope, chronic renal failure, previous CVA, elevated troponin, elevated BNP, and right heart thrombus.

The Pulmonary Embolism Severity Index (PESI) may assist the physician in determining the risk of mortality in a patient with PE. This prediction rule is based on 11 patient characteristics and stratifies patients into 5 severity classes. It appears to reliably predict mortality and thus has the potential to assist physicians in making risk-benefit decisions when considering administration of thrombolytics.

A meta-analysis of studies on thrombolytic therapy in PE found an ICH rate of 2%, with a mortality rate of 0.5%. Diastolic hypertension was the principal risk factor in predicting development of ICH.

Data from the ICOPER registry found that intracranial bleeding in thrombolytic-treated patients occurred in 3.0% and major bleeding occurred in 21.7% versus 0.3% and 8.8%, respectively, in patients not receiving thrombolytics. Factors associated with increased bleeding complications are increasing age, uncontrolled hypertension, recent stroke or surgery, and bleeding diathesis.

There is little evidence to guide the emergency physician in the administration of thrombolytic therapy. Overwhelming consensus opinion is to treat hemodynamically unstable patients with confirmed PE when the benefits of treatment outweigh the risks. Also, based on available evidence, thrombolytic therapy does not reduce mortality in the majority of hemodynamically stable patients.

Samaras N, Chevalley T, Samaras D, Gold G. Older patients in the emergency department: a review. Ann Emerg Med. 2010;56(3):261-269.

Epidemiology

Older people account for 12% - 24% of all ED visits. They visit the ED more frequently (during 2006, the annual ED visit rate was 49/100 persons > 65 years and 60/100 persons > 75 compared with an overall rate of 41/100). ED visits of patients aged 65 - 74 years increased by 34% between 1993 and 2003.

Older patients have a 2.5 - 4.6 times higher risk for hospitalization and a 5-fold higher ICU admission rate. They are also more likely to be misdiagnosed.

Conditions Frequently Encountered

Neuropsychiatric Disorders

Delirium is by definition a result of an underlying condition; it occurs in 7-10% of this population. 50% of patients with delirium in the ED also have an underlying dementia.

Delirium in the ED is recognized with a high specificity (98% to 100%) but a fairly low sensitivity (16% to 35%).

Confusion Assessment Method - has a high specificity (100%) and sensitivity (86%) for the diagnosis of delirium.

The diagnosis of delirium requires the presence of features 1 and 2 and either 3 or 4:

1. Is there evidence of an acute change in mental status from the patient's baseline?
- 2a. Did the patient have difficulty focusing attention, for example being easily distractible or having difficulty keeping track of what was being said?
- 2b. Did the behavior fluctuate during the interview, i.e., come and go, or increase and decrease in severity?
3. Was the patient's thinking disorganized or incoherent, such as rambling or irrelevant conversation, unclear or illogical flow of ideas or unpredictable switching from subject to subject?
4. Overall, what was the patient's level of consciousness? Alert/vigilant (hyperalert)/lethargic/stupor/coma

Differential diagnosis between dementia and delirium

	Dementia	Delerium
Onset	Progressive	Acute (associated with acute disease, drug modifications, environment changes, etc)
Moment of Onset	Uncertain, hard to identify	Usually precise, easy to identify
Progression	Slow chronic decline (years)	Condition fluctuates and is reversible
Duration	Long (years)	Short (hours to weeks)
Vigilance	Normal	Altered, varies between states of hyper- and hypovigilance
Orientation	Space and time orientation disorders present in late stages of the disease	Disorders present early and may fluctuate

Once delirium has been excluded, patients can be screened for the presence of the chronic cognitive deficits observed in dementia, a condition that affects medication compliance and adherence to discharge instructions and increases the risk of repeated ED visits.

Depression may be present in up to 1/3 of older ED patients. The ED depression screening instrument has a sensitivity of 79% and a specificity of 66%; At least one positive response corresponds to a positive screening result for depression:

1. Do you often feel sad or depressed?
2. Do you often feel helpless?
3. Do you often feel downhearted and blue?

Falls

Falls are the main cause of ED admissions for elderly patients (15% - 30%).

20% of elderly patients with cardiovascular syncope present with a complaint of unexplained falls.

Inability to recollect the falls' circumstances, fall recurrence, impossibility to get up after a fall and inability to arise from the hospital bed and walk should incite emergency physicians to admit the older patient for further assessment.

Hip fractures are more frequently missed on radiographs in this population; the premature mortality after hip (25% at 1 year) and vertebral fractures is now well recognized. Pelvic fractures in elderly patients carry a higher risk of bleeding and need for angiography, as well as high inhospital mortality (12% vs 2% for younger patients).

Age-related changes such as lower elasticity and higher fragility of vessels, modified mechanical properties of bridging veins, and stress on venous structures as a result of cerebral atrophy increase the brain's vulnerability to injury. The increased space between brain and skull permits expansion of intracranial content with fewer symptoms.

Even trivial injury mechanisms such as falls from standing could result in serious intracranial injury with an atypical presentation. Thus, chronic subdural hematoma may be present for months before symptoms appear and motivate an ED visit, whereas the initial head trauma may be so trivial that it is not recalled in 30% - 50% of cases.

Acute subdural hematoma, on the other hand, is mostly encountered in younger patients after severe trauma and presents with initial coma in 40% - 80% of cases.

Coronary Disease

Acute MI presentation in older patients is frequently atypical:

- In the ED, approximately 20% of older patients have dyspnea or chest pain as principal complaints.
- Only 40% of patients > 85 years with NSTEMI and 57% with STEMI have chest pain as their main complaint compared with 77% of NSTEMI and 90% of STEMI patients < 65 years.
- ECG is nondiagnostic in 43% of patients > 85 years with NSTEMI compared with only 23% of patients < 65.
- LBBB is seen in 34% of patients > 85 with STEMI compared with 5% of those < 65, making diagnosis harder.

The likelihood for treatment with aspirin and β -blockers decreases by 15% and 21%, respectively, for every 10 years of increasing age after 65. Patients > 80 years are also less likely to receive thrombolytics than younger patients. The main factor related to a lower use of recommended therapies in older patients is age itself.

Polypharmacy and Adverse Drug Effects

Older patients admitted to the ED receive an average of 4.2 medications per day, with 13% receiving ≥ 8 . On presentation, 11% of these patients receive at least 1 inappropriate medication.

3 medication classes caused 48% of all ED visits for adverse drug effects in patients > 65 years: oral anticoagulant or antiplatelet agents (warfarin, aspirin, and clopidogrel), antidiabetic agents (insulin, metformin, glyburide, and glipizide), and agents with a narrow therapeutic index (digoxin and phenytoin). *Most frequently implicated medications from these classes, accounting for 1/3 of adverse-effect-induced ED visits, were warfarin, insulin, and digoxin.*

Alcohol and Substance Abuse

Alcohol disorders are present in 5% - 14% of older patients in the ED.

One study found that undeclared substance abuse was strongly related to an age > 65 years and mainly involved opioids, benzodiazepines, and stimulants.

Only 21% of elderly current alcohol abusers are detected in the ED.

Abdominal Pain

Mortality rates in older patients are 6 - 8 times higher and surgery rates are increased 2-fold.

Abdominal CT is performed for 37% - 59% of older patients and leads to a diagnosis in 57% to 67% of cases. In one study, it modified the admission decision for 26% of cases, the need for surgery for 12%, antibiotics prescription for 21%, and the suspected diagnosis in almost half.

Best imaging examination, depending on pain location according to the ACR

Pain Location	Radiologic Examination
RUQ	Ultrasonography
RLQ	CT with IV contrast
LLQ	CT with PO and IV contrast
LUQ	CT
Suprapubic	Ultrasonography

Infections

The most frequent conditions are pneumonia (25%), UTI (22%), and sepsis and bacteremia (18%).

Falls or delirium may be the only clinical manifestations of otherwise serious infections, whereas more classic symptoms such as tachycardia and fever may be absent.

Acute cholecystitis may present without pain (5%), fever (56%), or CBC abnormality (41%).

Appendicitis presents with classic symptoms in only 20% of geriatric cases, and fever occurs in < half of cases.

Old (between 65 - 84 years) and oldest old (> 85 years) patients with community-acquired bacteremia have a higher risk of developing organ failure and higher 90-day mortality rates (15% for young patients versus 20% and 26%, respectively, for old and oldest old).

Social Cases, the Search for Hidden Illness

Subacute or acute illness can present as functional decline, motivating the social ED visit.

A study reported that although 9% of older patients were admitted to the ED ostensibly for social reasons (inability to take care of self), 51% had an underlying acute medical problem such as infectious (24%), cardiovascular (14%), neurologic (9%); Another study found the 1-year mortality of such patients was as high as 34%.

Elder Abuse and Neglect

Definition: “actions/omission of actions that result in harm or threatened harm to the health or welfare of the elderly.”

Among a multitude of risk factors, the most important are a relationship of dependency, social isolation, and psychopathology of the abuser. Elder abuse prevalence in the US is approximately 10%.

In a state elderly protective program, 66% of older patients who visited the ED in a 5-year period had an injury-related discharge diagnosis. Only 9% of these ED visits resulted in referral to appropriate services.

Targeting “High-Risk” Elderly

The Identification of Seniors at Risk tool

- It performs as well as other screening tools and was developed for the ED.
- Known to have an excellent concurrent validity for detecting impaired functional status and depression.
- It has both immediate clinical relevance and good predictive validity as it predicts ED revisits and hospitalization after the index ED visit, mortality, admission to a nursing home, use of community services, and decrease in functional status in a 4-month or 6-month follow-up.

Each high-risk response counts as 1 point. A patient is considered high risk when the score is 2 or more:

1. Before the illness or injury that brought you to the ED, did you need someone to help you on a regular basis?
2. Since the illness/injury that brought you to the ED have you needed more help to take care of yourself?
3. Have you been hospitalized for one or more nights during the past 6 months?
4. In general, do you see well?
5. In general, do you have serious problems with your memory?
6. Do you take more than 3 different medications every day?

Rokos IC, French WJ, Mattu A, et al. Appropriate Cardiac Cath Lab Activation: Optimizing electrocardiogram interpretation and clinical decision-making for acute ST-elevation myocardial infarction. Am Heart J. 2010;160:995-1003.

Classic STEMI = acute ≥ 1 mm ST-elevation in 2 adjacent ECG leads

Approximately 5% of cath lab activations by Emergency Physicians are “unnecessary” (ie, cardiologist did not perform emergency coronary angiography).

Evaluations of prehospital-ECG interpretation by paramedics found an approximate 20% rate of inappropriate cath lab activation (ie, cardiologist did not perform emergency coronary angiography).

In recognition of benign ST-elevation that is frequently observed in healthy adults, the NCDR data dictionaries currently set the STEMI threshold in leads V2-V3 at 2 mm for men and 1.5 mm for women. A recent AHA/ACC statement listed the same criteria (except for men age <40 , the threshold is >2.5 mm ST-elevation in leads V2-V3).

<u>Common STE-mimics</u>	
<u>Narrow QRS Complex STE-mimics</u> Benign early repolarization Pericarditis Left ventricular aneurysm Normal variant “male pattern” Preexcitation	<u>Tall/Wide QRS Complex STE-mimics</u> Left ventricular hypertrophy (LVH) LBBB Paced rhythm Hyperkalemia Brugada syndrome

Reciprocal changes (ie, ST-depression ≥ 0.5 mm in leads 180° opposite those with ST-elevation) should exist for all ECGs with acute STEMI, but they might be of lesser magnitude or undetectable due to technical limitations of the standard 12-lead ECG.

By definition, reciprocal ST-depression should never occur in ECGs considered normal or those with narrow-complex STE-mimics (except lead aVR with pericarditis). In one study, the presence of any reciprocal ST-depression in ≥ 2 leads was associated with $>95\%$ diagnostic specificity and positive predictive value for acute MI.

Left bundle-branch block

Traditional criteria using new (or presumed new) LBBB as a STEMI-equivalent results in low diagnostic specificity and high rates of inappropriate cath lab activation. Studies indicate $>90\%$ of LBBB patients evaluated in the ED do not have an acute coronary occlusion nor require PPCI. In one PCI study, 44% of patients with “presumed new LBBB” did not have a culprit artery on emergency angiography and 36% had no elevation of serial biomarkers.

The latest ESC guidelines acknowledge these findings by stating that biomarker results “may sometimes be helpful” in evaluating LBBB patients, thus implying treatment of stable patients with an urgent rather than emergent PCI strategy.

Importantly, clinically unstable LBBB patients or those with acutely abnormal anterior wall motion by echocardiography should still receive emergency angiography.

A chronic LBBB normally has discordance (the direction of the major component of the QRS complex is opposite that of ST segment/T wave in any lead), whereas QRS/ST concordance (with ST elevation ≥ 1 mm in ≥ 1 lead) appears to be the most robust predictor of acute ischemia.

Posterior myocardial infarction

True posterior MI should be treated as a STEMI-equivalent, in which case isolated ST-depression ≥ 0.5 mm in leads V1 - V3 represents the dominant finding on a standard ECG. Associated T waves are either upright or inverted. Appearance of tall R-waves in V1-V2 may be delayed. The use of posterior chest wall leads (V7-V9) to detect ST elevation consistent with posterior MI is often recommended, but their use remains uncommon.

Despite guideline recommendations, the vast majority of study patients with isolated ST-depression in leads V1 - V3 are treated with non-emergent PCI (>6 hours after index ECG). However, the cohort of "slowly treated" posterior MIs had an acutely occluded coronary (most commonly the left circumflex) and had a significantly higher rate of 30-day death or MI as compared with those classified as non-STEMI.

Left main coronary occlusion

LMCO generally causes massive ischemia and is rapidly lethal, but a small proportion of patients have enough perfusion from right-sided collaterals to arrive alive at the hospital.

A registry analysis of patients with acute STEMI from a left main culprit that was "unprotected" (ie, no prior coronary artery bypass grafting to distal vessels) revealed that 1/3 did not present in cardiogenic shock, even though angiography demonstrated that 85% of these patients had >90% stenosis and 55% had complete LMCO. Importantly, survival to hospital discharge was 42% in this series.

One series reported that ≥ 0.5 -mm ST-elevation in lead aVR is consistent with acute LMCO, especially when the degree of ST-elevation in aVR is > lead V1 and inferior ST-depression is present.

A 2009 AHA statement recommended "when the resting ECG reveals ST-depression >1 mm in 8 or more surface leads coupled with ST-elevation in aVR and/or VI but is otherwise unremarkable, the computerized interpretation should suggest ischemia due to multi-vessel or left main coronary artery obstruction."

A 2010 international consensus provided STEMI-equivalent criteria for acute LMCO (or severe angiographic disease): ST-depression in ≥ 6 leads (maximal in V4-V6) and associated ST-elevation limited to lead aVR and V1.

de Winter ST/T-wave complex

- signifies acute occlusion of the proximal LAD.

ECG criteria: 1 - 3 mm of ST-depression that is up-sloping at the J-point in leads V1 - V6 and associated with persistently tall, upright, and symmetric precordial T-waves.

The complex is distinct from transient hyper-acute T-waves that may occur within minutes of an acute coronary occlusion but generally morph quickly into a classic STEMI pattern. In addition, the complex should not be confused with Wellens syndrome (biphasic or inverted T waves in leads V2 - V3). Wellens syndrome typically involves a chronic high-grade LAD stenosis that can usually be evaluated by non-emergent angiography.

Resuscitated cardiac arrest

Approximately 50% of patients with out-of-hospital cardiac arrest (OHCA) and ROSC have an acute coronary artery occlusion when evaluated by immediate diagnostic angiography.

PROCAT registry - OHCA patients with no obvious extracardiac cause of arrest received emergency coronary angiography. 96% with a post-ROSC ECG demonstrating classic STEMI had at least one significant lesion (>50% reduction in luminal diameter) and 74% underwent successful PCI. In the remaining patients without classic STEMI on post-ROSC ECG, 58% had a significant lesion and 26% received PCI.

Analysis demonstrated successful PCI to be an independent predictor of survival irrespective of postresuscitation ECG pattern. As compared to a historically low rate of survival (<10%), overall survival to hospital discharge was 40%. Moreover, there was a 94% rate of favorable neurologic outcomes in a cohort with a 68% rate of shockable first rhythm and 85% rate of in-hospital therapeutic hypothermia.

Baseline neurologic status immediately after ROSC should not preclude early Cath Lab activation because current AHA expert statements emphasize deferral of cerebral recovery prognostication for at least 72 hours after collapse in patients treated with therapeutic hypothermia. Furthermore, although the “best” hypothermia protocol has yet to be defined, current consensus suggests initiating cooling as early as possible (ie, pre-arrival to the Cath Lab).

Bobrow BJ, Spaite DW, Berg RA, et al. Chest compression-only CPR by lay rescuers and survival from out-of-hospital cardiac arrest. JAMA. 2010;304(13):1447-1454.

Overall survival from out-of-hospital cardiac arrest is < 10% among those in whom resuscitation is attempted.

Bystander CPR significantly improves outcome but is generally performed in < 30% of cases.

Preclinical reports have raised the possibility that it is not necessary to perform active ventilation during CPR soon after sudden collapse from out-of-hospital cardiac arrest. Animal studies have shown COCPR to be at least as effective as conventional CPR.

There are multiple reasons COCPR might have advantages over conventional CPR:

- the rapid deterioration of forward blood flow that occurs during even brief disruptions of chest compressions
- the long ramp-up time to return to adequate blood flow after resuming chest compressions
- the reduction of cardiac venous return with the use of positive pressure ventilation
- the complexity of conventional CPR
- the significant time required to perform breaths
- the critical importance of cerebral and coronary circulation during arrest
- the reduced time required for dispatchers to instruct a bystander over the phone how to perform COCPR
- the reluctance to perform mouth-to-mouth ventilation on strangers

In 2005 Arizona established a statewide effort to encourage bystanders to use compression-only CPR. This 5-year prospective observational study of survival in patients > 18 years old evaluated whether widespread public endorsement of COCPR for adult sudden cardiac arrest would be associated with an increased likelihood that lay rescuers would perform CPR and an increased likelihood of survival to hospital discharge compared with no bystander CPR and conventional CPR.

Results

4415 met inclusion criteria: 2900 received no bystander CPR, 666 received conventional CPR, and 849 received COCPR.

The cardiac arrest was witnessed in 45% of cases and a lay bystander performed CPR in 34.3%. Overall, 15% of patients received conventional bystander CPR and 19.2% received COCPR. Overall survival was 7.1%.

Rates of survival to hospital discharge were 5.2% for the no bystander CPR group, 7.8% for conventional CPR, and 13.3% for COCPR. The adjusted odds ratio for survival for conventional CPR vs no CPR was 0.99, for COCPR vs no CPR, 1.59, and for COCPR vs conventional CPR, 1.60 (i.e., a significant independent association between COCPR and survival when compared with conventional CPR).

From 2005 - 2009, lay rescuer CPR increased from 28.2% to 39.9%; the proportion of CPR that was COCPR increased from 19.6% to 75.9%. Overall survival increased from 3.7% to 9.8%.

Survival increased significantly over time for the subgroup of witnessed arrests with a shockable rhythm, from 10.8% in 2005 to 30.4% in 2009.

4.2% of the cases of out-of-hospital cardiac arrest had a good neurologic status. The proportion of individuals with good neurologic status differed significantly based on the type of CPR provided: no CPR, 3.0%; conventional CPR, 5.2%; COCPR, 7.6%.

Although the Arizona statewide program advocated for conventional CPR for suspected noncardiac etiology arrests and children, it was suspected that lay rescuers might perform COCPR on these individuals. The study examined the incidence and survival of presumed noncardiac etiology arrests by the type of bystander CPR and found a similar and low survival rate regardless of the type of CPR. Also, the total number of pediatric cases of out-of-hospital cardiac arrest was relatively small (5.6%), and importantly, in the group in which rescue breathing would provide the most benefit (children aged < 12 years), the proportion who received COCPR was only 7.9%.

Conclusion Among patients with out-of-hospital cardiac arrest, layperson compression-only CPR was associated with increased survival compared with conventional CPR and no bystander CPR in this setting with public endorsement of chest compression-only CPR.

Morgenstern LB, Hemphill JC III, Anderson C, et al. Guidelines for the management of spontaneous intracerebral hemorrhage: a statement for healthcare professionals from the American Heart Association/American Stroke Association. Stroke. 2010;41:2108-2129.

Early deterioration is common in the first hours after ICH onset. > 20% of patients will experience a decrease in the GCS of ≥ 2 points between prehospital EMS assessment and initial ED evaluation.

Among those patients with prehospital neurological decline, the GCS score decreases by an average of 6 points and the mortality rate is >75%. Further, within the 1st hour of hospital presentation, 15% of patients demonstrate a decrease in the GCS score of ≥ 2 points.

Neuroimaging

CT is very sensitive for identifying acute hemorrhage and is considered the gold standard; gradient echo and T2-susceptibility-weighted MRI are as sensitive as CT for detection of acute blood and are more sensitive for identification of prior hemorrhage.

Among patients undergoing head CT within 3 hours of ICH onset, 28% - 38% have hematoma expansion of > 1/3 on follow-up CT. Hematoma expansion is predictive of clinical deterioration and increased morbidity and mortality.

CTA and contrast-enhanced CT may identify patients at high risk of ICH expansion based on the presence of contrast extravasation within the hematoma.

Medical Treatment for ICH

Reversing Oral Anticoagulants (OACs)

Vitamin K - remains only an adjunct because even when given IV, it requires hours to correct the INR.

FFP - efficacy is limited by risk of allergic and infectious transfusion reactions, processing time, and the volume required for correction. In one study, 17% of patients still did not have an INR ≤ 1.4 at 24 hours.

PCCs – are increasingly recommended for warfarin reversal

- contain factors II, VII, IX and X
- have the advantages of rapid reconstitution and administration, having high concentrations of coagulation factors in small volumes, and processing to inactivate infectious agents.
- several studies have shown that PCCs can normalize the INR within minutes.
- may theoretically increase the risk of thrombotic complications, but this risk appears relatively low
- **Recommendation:** PCCs have not shown improved outcome compared with FFP but may have fewer complications compared with FFP and are reasonable to consider as an alternative to FFP

rFVIIa -

- although it rapidly normalizes the INR in the setting of OAC use, it does not replenish all of the vitamin K-dependent factors and thus may not restore thrombin generation as well as PCCs.
- American Society of Hematology - recommends against routine use for warfarin reversal.
- Although rFVIIa can limit the extent of hematoma expansion in noncoagulopathic ICH patients, there is an increase in thromboembolic risk and no clear clinical benefit in unselected patients. Thus rFVIIa is not recommended in unselected patients.

Studies of the effect of prior antiplatelet agent use or platelet dysfunction on ICH hematoma growth and outcome have found conflicting results. The usefulness of platelet transfusions in ICH patients with a normal platelet count but with a history of antiplatelet use is unclear and is considered investigational.

Patients with ICH have a high risk of thromboembolic disease; they should have intermittent pneumatic compression in addition to elastic stockings. After cessation of bleeding, low-dose subcutaneous LMWH or unfractionated heparin may be considered for prevention of VTE in patients with lack of mobility after 1 - 4 days from onset.

Blood Pressure Management

BP is frequently, and often markedly, elevated in patients with acute ICH; these BP elevations are greater than that seen in patients with ischemic stroke.

A systolic BP > 140 - 150 mm Hg within 12 hours of ICH is associated with more than double the risk of subsequent death or dependency.

Recent studies show a trend toward lower hematoma growth with intensive BP treatment without an excess of neurological deterioration or other adverse events related to intensive BP lowering.

In patients presenting with SBP 150 - 220 mm Hg, acute lowering to 140 mm Hg is probably safe.

Recommended Guidelines for Treating Elevated BP in Spontaneous ICH

1. If SBP is >200 mm Hg or MAP is >150 mm Hg, then consider aggressive reduction of BP with continuous IV infusion, with BP monitoring every 5 min.
2. If SBP is >180 mm Hg or MAP is >130 mm Hg and there is the possibility of elevated ICP, then consider monitoring ICP and reducing BP using intermittent or continuous IV medications while maintaining a cerebral perfusion pressure \geq 60 mm Hg.
3. If SBP is >180 mm Hg or MAP is >130 mm Hg and there is no evidence of elevated ICP, then consider a modest reduction of BP (eg, MAP of 110 mm Hg or target BP of 160/90 mm Hg) using intermittent or continuous IV medications to control BP and clinically reexamine the patient every 15 min.

Prevention of Secondary Brain Injury

Care of ICH patients in a dedicated neuroscience ICU is associated with a lower mortality rate.

Nursing care required for ICH patients in ICUs include (1) surveillance and monitoring of ICP, CPP and hemodynamic function; (2) implementation of protocols for management of ICP, BP, mechanical ventilation, fever, and serum glucose; and (3) prevention of complications of immobility through positioning, airway maintenance, and mobilization within physiological tolerance.

Glucose Management - High blood glucose on admission predicts an increased risk of mortality and poor outcome in patients with and without diabetes and ICH. Tight glucose control using insulin infusions is associated with hypoglycemic events and possibly, an increased mortality. Recommendation: Glucose should be monitored and normoglycemia is recommended.

Temperature Management: There are no data linking fever treatment with outcome. The incidence of fever after basal ganglionic and lobar ICH is high, especially in patients with IVH. Therapeutic cooling has not been systematically investigated in ICH patients.

Seizures and Antiepileptic Drugs

In ICH patients, clinical seizures have not been associated with worsened neurological outcome or mortality and the clinical impact of subclinical seizures detected on EEG is also not clear.

A recent analysis found that patients who received antiepileptic drugs (primarily phenytoin) without a documented seizure were significantly more likely to be dead or disabled at 90 days, after adjusting for other established predictors of ICH outcome.

Recommendation: Seizures should be treated with antiepileptics. Continuous EEG monitoring is probably indicated in ICH patients with depressed mental status out of proportion to the degree of brain injury. Patients with a change in mental status who are found to have electrographic seizures on EEG should be treated with antiepileptic drugs. Prophylactic anticonvulsant medication should not be used.

Procedures/Surgery

ICP Monitoring and Treatment

Because the usual causes of elevated ICP are hydrocephalus from IVH or mass effect from the hematoma (or surrounding edema), patients with small hematomas and limited IVH usually will not require treatment to lower ICP.

ICP is measured using devices inserted into the brain parenchyma, typically at the bedside. A ventricular catheter (VC) inserted into the lateral ventricle allows for drainage of CSF, which can help reduce ICP in patients with hydrocephalus. A parenchymal catheter ICP device is inserted into the brain parenchyma and allows for monitoring of ICP, but not CSF drainage.

Upon insertion of an ICP monitor, the ICP treatment algorithm calls for interventions in a step wise fashion if the ICP is > 20-25 mm Hg. Such interventions include CSF drainage, mannitol bolus, sedation & neuromuscular blockade, mild hyperventilation (PaCO₂ 30-35 mm Hg) and, ultimately, second tier therapies such as hypothermia, hemicraniotomy, and a barbiturate coma. A repeat CT scan should be considered as the clinician progresses down the algorithm.

Recommendations:

Patients with GCS ≤8, those with clinical evidence of transtentorial herniation, or those with significant IVH or hydrocephalus might be considered for ICP monitoring and treatment. A CPP of 50 - 70 mm Hg may be reasonable to maintain depending on the status of cerebral autoregulation.

Ventricular drainage as treatment for hydrocephalus is reasonable in patients with decreased LOC.

Intraventricular Hemorrhage

- occurs in 45% of patients with spontaneous ICH.
- can be primary (confined to the ventricles) or secondary (originating as an extension of an ICH).
- most IVHs are secondary and related to hypertensive hemorrhages in the basal ganglia and the thalamus.
- Although a VC should aid in drainage of blood and CSF from the ventricles, VC use alone may be ineffective because of difficulty maintaining catheter patency and the slow removal of intraventricular blood.

Intraventricular administration of fibrinolytic agents may reduce morbidity and mortality by accelerating blood clearance and clot lysis. This treatment is considered investigational

Surgery

Indications are controversial. For most patients with ICH, the usefulness of surgery is uncertain. Specific exceptions:

1. Patients with cerebellar hemorrhage who are deteriorating neurologically or who have brainstem compression and/or hydrocephalus from ventricular obstruction should undergo surgical removal of the hemorrhage as soon as possible. Treatment of these patients with ventricular drainage alone rather than surgical evacuation is not recommended.
2. For patients presenting with lobar clots >30 mL and within 1 cm of the surface, evacuation of supratentorial ICH by standard craniotomy might be considered

The effectiveness of minimally invasive clot evacuation is considered investigational.

No clear evidence indicates that ultra-early removal of supratentorial ICH improves functional outcome or mortality rate. Very early craniotomy may be harmful due to increased risk of recurrent bleeding.

Most patients that die from ICH do so during the initial acute hospitalization. Aggressive full care early after ICH onset and postponement of new DNR orders until at least the second full day of hospitalization is probably recommended. Patients with preexisting DNR orders are not included in this recommendation.

Prevention of Recurrent ICH

The rate of recurrent ICH after a first hemorrhagic stroke = 2.1% - 3.7% per patient-year, substantially higher than these individuals' rate of subsequent ischemic stroke.

The most consistently identified risk factor for recurrent ICH is lobar location of the initial ICH. This finding likely represents the association of cerebral amyloid angiopathy with lobar location and increased recurrence. Other risk factors include older age, ongoing anticoagulation, presence of the apolipoprotein E ϵ 2 or ϵ 4 alleles, and greater number of microbleeds on MRI.

Hemorrhage in locations characteristic of hypertensive vasculopathy, such as basal ganglia, thalamus, or brainstem, also recur, but less frequently.

After the acute ICH period, absent contraindications, BP should be controlled, particularly for patients with ICH location typical of hypertensive vasculopathy. A target BP <140/90 (<130/80 if diabetes or chronic kidney disease) is reasonable.

The effects of antiplatelet agents on ICH recurrence/severity are smaller than for anticoagulation, suggesting that antiplatelet treatment may be a safer alternative to anticoagulation after ICH.

Avoidance of long-term anticoagulation as treatment for nonvalvular atrial fibrillation is probably recommended after spontaneous lobar ICH because of the relatively high risk of recurrence.

Anticoagulation after nonlobar ICH and antiplatelet therapy after all ICH might be considered, particularly when there are definite indications for these agents.

Avoidance of heavy alcohol use can be beneficial. There is insufficient data to recommend restrictions on use of statin agents or physical or sexual activity.

In general, recovery is more rapid in the first few weeks but may continue for many months after ICH, with approximately half of all survivors remaining dependent on others for activities of daily living. However, patients vary in their speed and degree of recovery, and there is no rule regarding when recovery is over.

Wolf SJ, Bebarta VS, Bonnett CJ, Pons PT, Cantrill SV. Blast injuries. Lancet. 2009;374:405-415.

Several factors affect the magnitude of the maximum pressure (peak or blast overpressure) of an explosion:

- the medium in which the explosion takes place; e.g. water is non-compressible - a blast wave in water propagates rapidly with slow dissipation and has a greater potential for injury than an explosion in air.
- distance - the energy of the blast rapidly decreases in a manner inversely proportional to the cube of the distance from the explosion. Thus, if the distance from an explosion is doubled, the peak overpressure will decrease to 1/8th of the original value.
- amplification - pressure waves reflect back from solid surfaces and increase its force: people in close proximity to a wall will be subject to enhanced blast overpressure and be at a raised risk of blast injury.
- explosion site - in an open space, a blast wave spreads circumferentially from its origin and quickly dissipates. However, in a confined space (eg, a bus, room, or building) the maximum pressure is markedly amplified in magnitude because the explosive forces are contained.

Types of explosives

Low-order Explosives

- burn rapidly, produce large volumes of gas that only explode if confined (eg, a pipe bomb).
- examples; black powder and smokeless powder, which are used as propellants for bullets & artillery shells.

High-order Explosives

- do not burn, but instead detonate when a shock wave passes through the material generating a substantial blast overpressure, even if unconfined.
- examples: chemically pure compounds (eg, nitroglycerin, trinitrotoluene), and compositions (dynamite, ammonium nitrate-fuel oil, and plastic explosives)

Plastic explosives are made by combining a high-order explosive such as nitroglycerine or cyclonite with plasticisers, which make explosives easily mouldable with a clay-like quality; they are difficult to detect by security authorities.

High-order explosives are further subdivided into primary explosives (those that can be detonated by mechanical shock, friction, or heat) and secondary explosives (those that need an initiating explosion to detonate). Primary explosives (e.g. lead azide, mercury fulminate) are often used to initiate the detonation of secondary explosives, such as dynamite, ammonium nitrate-fuel oil, and cyclonite.

Improvised explosive device = any makeshift incendiary device constructed to injure, incapacitate, harass, or distract. IEDs caused 2/3 of the military deaths and 40% of all injuries sustained during the Iraq conflict.

Primary blast injuries

Primary blast injuries occur when the blast overpressure reaches the person and causes direct tissue damage.

- Spallation - a pressure wave passes from a dense medium to a less dense medium, resulting in displacement and fragmentation of the dense medium into the less dense medium. Example: an explosive detonated under water will cause the dense water to spall into the less dense air, causing fragmentation (the upward splash).
- Implosion - gaseous contents within tissues are suddenly compressed by the blast overpressure.
- Inertial, or shearing, forces - deceleration forces

Secondary blast injuries

Result from debris that is physically displaced by the blast winds. Commonly, small puncture wounds that represent secondary-blast injuries hide penetrating fragments and severe underlying injuries.

The distance over which fragments travel is much greater than the distance over which a blast overpressure travels. Hence, secondary blast injuries are more common than are primary blast injuries.

Tertiary blast injuries - Caused when a person is physically displaced by the force of the peak overpressure and blast winds and sustains blunt trauma injury.

Quaternary blast injuries - (miscellaneous blast injuries) include but are not limited to burns, toxic substance exposures (eg, radiation, CO poisoning, cyanide poisoning), asphyxia, and psychological trauma.

Quinary blast injuries - A hyperinflammatory state in which patients manifest hyperpyrexia, diaphoresis, low CVP, and a positive fluid balance.

Primary blast injury patterns and management

Primary blast injuries happen with greatest frequency at air–tissue interfaces. Thus, organ systems with high air content, such as the pulmonary, GI, and auditory systems, are most susceptible.

Pulmonary system

Explosive forces can cause pulmonary hemorrhage and contusions, direct barotrauma, and arterial air embolism.

17-47% of people who die from explosions have evidence of pulmonary primary blast injury, and up to 44% of people hospitalized and 71% of those who are critically ill and hospitalized have pulmonary injury.

With early diagnosis and aggressive treatment, in-hospital mortality rates range from 3 - 25%. Furthermore, people who are discharged have a very good prognosis at 1-year follow-up.

Progressive vascular leak and inflammatory changes from lung injury develop over 12–24 hrs, possibly contributing to some delayed presentations, although most blast lung injuries develop immediately.

The ribs protect the lung parenchyma from the full force of the blast overpressure, which results in stripes of hemorrhagic congestion that correspond to the intercostal spaces.

Blast lung syndrome = the combination of dyspnea, cough, and hypoxia that accompanies these injuries.

Arterial air emboli can subsequently develop immediately after the explosion or can arise later, especially if the patient needs positive-pressure ventilation. When massive, these emboli can cause stroke, myocardial infarction, spinal cord infarction, intestinal ischemia, or death.

Fluid resuscitation needs to be carefully monitored in moderate to severe blast lung injuries as excessive crystalloid can lead to pulmonary edema in patients with pulmonary contusions.

Respiratory status should be optimized with non-invasive ventilation and adequate pain management, because positive-pressure ventilation can worsen pulmonary barotrauma and increase the risk of arterial air embolism.

Prophylactic chest tube use should be considered in severe blast lung injuries that need positive-pressure ventilation or for patients who need air transportation.

Blast lung injury induces poor compliance. When positive-pressure ventilation is needed, use lung protective techniques: acceptably low O₂ saturations (90%) and low tidal volumes (5–7 mL/kg), pressure-controlled ventilation, PEEP, and permissive hypercapnia. By contrast, strategies to minimize the sequelae from arterial air emboli include maximizing spontaneous ventilation, low PEEP, and using 100% FiO₂ to encourage quick absorption of emboli.

Management of an arterial air embolism: most researchers support placing the patient in a recumbent, left-lateral decubitus position to decrease the risk of systemic embolization. However, some postulate that by placing the most likely affected lung in the dependent position, alveolar pressures become lower than vascular pressures, which makes further entrainment of air into the vascular system less probable. Many experts endorse hyperbaric oxygen therapy as the preferred treatment for arterial air embolism despite little clinical data.

Gastrointestinal system

Abdominal injury occurs more commonly after underwater or closed-space explosions; the colon and ileocaecal region are the visceral structures at greatest risk of intestinal perforation.

Intramural edema and hemorrhage results from contusion of the intestinal wall, which puts the intestine at risk of delayed perforation. Also, interruption of the mesenteric blood supply by shearing forces or arterial air embolism leads to intestinal ischemia.

Although abdominal solid organ injury can arise as a primary blast injury, it is more likely to be a result of a secondary or tertiary blast injury.

Abdominal CT, although specific for solid organ injury and perforation, lacks sensitivity to exclude intestinal contusions and mesenteric injury definitively. Hence, symptomatic patients must be observed for 6–8 hours.

Auditory system

The auditory system is the system most commonly affected by blast overpressure. Up to 94% of those with primary blast injuries will have a ruptured TM.

Asymptomatic patients with intact TMs have a very low likelihood of occult pulmonary or intestinal primary blast injury. Some experts postulate that an intact TM suggests little exposure to blast overpressure, alleviating the need for further assessment for primary blast injuries. However, results of studies have shown that a substantial proportion of survivors with and without TM rupture have blast lung injury.

Ossicle disruption or damage to the sensory structures may cause permanent conductive hearing deficits; perilymph fistulas can cause vertigo or dizziness.

TM ruptures that involve > 5% of the membrane surface will probably need surgical intervention.

Central nervous system

Secondary and tertiary blast-related brain injuries that involve ICH, direct parenchymal damage, and cerebral contusion represent most CNS injuries.

After explosions, cerebral concussive syndromes are common and associated with PTSD, and affected people experience substantial memory dysfunction and cognitive deficits.

Recent studies suggest that TM perforation might be a predictor for concussive brain injury although not necessarily for other primary blast injuries.

Musculoskeletal system

Compartment syndrome:

- common after exposure to an explosion since fractures, direct tissue damage, and burns can elevate extremity compartmental pressures.
- can occur in apparently uninjured blast-exposed extremities
- delayed compartment syndrome has been reported in people after explosions and is postulated to be associated with several factors, including the presence of severe diffuse injury, pelvic fractures, and burns covering a large body surface-area that raise the need for large-volume or extended resuscitation.

Traumatic amputations are mostly regarded as primary blast injuries; they are associated with immediate mortality rates of 10% - 85%, and are a marker for poor prognosis as they are seen in 10% of delayed deaths. Hence, traumatic amputations mandate a high suspicion for additional primary blast injury.

Manthous CA. Avoiding circulatory complications during endotracheal intubation and initiation of positive pressure ventilation. J Emerg Med. 2010;38(5):622-631.

Endotracheal Intubation (ETI)

General Principles

- Perform serial vital signs every 2–3 min for the first 20–30 min after ETI.
- Interrupt BMV for no more than 30 s and attain maximum oxygen saturation possible before each attempt.
- National guidelines suggest no more than 3 ETI attempts before either inviting more skilled personnel or employing “difficult airway” tools.
- Keep in mind that during RSI when the patient is completely dependent upon caregivers to maintain sufficient ventilation in the peri-intubation period, metabolic acidosis and high CO₂ production, which occur in many critical illnesses, often require a high minute ventilation to maintain a safe pH.

Initiation of Positive Pressure Ventilation: Common and Preventable Complications

Insufficient venous return

> 25% of patients develop transient hypotension after emergent ETI.

Venous return is proportional to the driving pressure outside the thorax minus the upstream pressure in the thorax; ETI commonly affects both:

Respiratory failure is accompanied by stress and catecholamine excess. Dyspnea and tachypnea are often accompanied by poor PO intake. IV medications administered to relax patients during ETI reduce catecholamines, which may cause abrupt arterial and venous dilatation. Although there are known direct cardiovascular effects of medications (e.g. benzodiazepines, etomidate, barbiturates) used to facilitate emergent ETI, the transient effects to reduce catecholamines are more likely responsible for the hypotension.

In addition, PPV raises intrathoracic pressure and venous return decreases, often outstripping cardiovascular reflexes that maintain an adequate BP

In one large study, systolic BP < 70 mm Hg complicated 13 of 136 (10%) intubations of critically ill patients; another study demonstrated a 2% risk of cardiopulmonary arrest during ETI.

Patients at greatest risk are those with: hypotension or tachycardia with normotension before ETI; excess catecholaminergic states (e.g., withdrawal syndrome, severe pain) with rapid relaxation; morbidly obese patients (i.e., large vascular capacitance); and high intrathoracic pressure after institution of PPV (as may occur with severe obstructive lung disease).

Consider the following to avoid hypotension:

- Rather than bolusing a single large dose of sedative, if the patient's condition permits, attempt ETI with verbal commands (talking a patient through the procedure) and local anesthesia. When resorting to sedatives, use multiple small doses (or increments) of IV medication (e.g., 1–2 mg of midazolam or lorazepam; 0.3 mg/kg lean body mass propofol) every 5–10 min when time allows.

- Begin volume resuscitation -wide open, normal saline - in all but evidently hypervolemic patients expectantly during ETI, especially when patients are very catecholamine-driven before ETI.
- Ensure that a pure vasoconstrictor (e.g. phenylephrine) is rapidly available in case the rate of fluid resuscitation is insufficient to refill the system until more vascular tone returns with awakening.
- Commence PPV with PEEP = 5 cm H₂O (no PEEP for obstructive lung disease) and an initial tidal volume of 8 mL/kg. Then titrate the TV to achieve a plateau airway pressure of 20 - 30 cm H₂O shortly after starting PPV.

Only assist control, volume-cycled ventilation with tidal volumes aimed to achieve plateau (static) airway pressures < 30 cm H₂O has been shown to improve patient outcomes.

For severe ARDS and asthma (but not COPD), choose initial tidal volumes of 6–8 mL/kg, which are then customized to maintain safe plateau pressures (20–30 cm H₂O maintains sufficient but not barotraumatic tidal recruitment).

High resistance (> 20 cm H₂O/L/s) and high minute volumes (> 20 L/min), common in acutely ill patients, promote gas trapping (i.e., “auto-PEEP”). Thus, initial tidal volumes are best delivered with a constant (square) waveform of 60 L/min, which maximizes expiratory time, until the patient can be stabilized.

Acid-base failure

The hallmark of respiratory- or metabolic-related cardiac arrest = tachycardia giving way to sudden bradycardia and asystole. This may lead to severe acidosis, resulting in failure to choose an initial PPV rate sufficient to compensate for the patient’s pre-ETI metabolic acidosis.

Before ETI, patients hyperventilate to compensate or, as with sepsis and severe lung disorders, have a primary respiratory alkalosis with a metabolic acidosis. Failure to maintain the same level of respiratory compensation for metabolic acidosis can cause rapid drops of pH, which promote circulatory complications.

The rapid decrease in BP associated with ETI and metabolic abnormalities associated with critical illness potentiate seizures. Metabolic acidosis from peri-ETI seizures further exacerbate the circulatory and metabolic derangements associated with the ETI/PPV process. Unless such patients are hyperventilated or receive IV bicarbonate to “buy time” until lactic acid is metabolized, they are at risk for severe life-threatening acidosis.

Consider the following to avoid acidosis-related circulatory complications of ETI:

- Take preventative measures to avoid hypotension during ETI (see above).
- Choose initial ventilator settings that are similar to the patient’s pre-ETI rate (but not > 30 breaths/min because auto-PEEP increases with increasing respiratory frequency).
- Always obtain an ABG within 10–15 min of ETI/PPV.
- If ETI is complicated by seizure, hyperventilate (25–30 breaths/min) and draw an emergent ABG; consider IV bicarbonate only if the patient becomes unstable and there is insufficient time to document seizure-related acidosis as the cause.

Severe obstructive lung disease

Mechanism by which hyperventilation kills asthmatics: While on a vent exhalation is entirely passive. If airway resistance is very high, patients may not fully exhale before the next machine breath is delivered. In severe obstruction, breaths may “stack” to the point of increasing intrathoracic pressure and hypotension or pneumothorax.

Ventilators are typically set to stop tidal volume deliveries after exceeding a certain peak airway pressure (commonly 40–60 cm H₂O). In severe asthma, when peak airway pressures reflect resistance of the upper airways, the ventilator may truncate breaths to dangerously low volumes, barely sufficient to ventilate the dead space. To address this, peak pressure limits must be set higher, so long as plateau pressure is maintained < 30 cm H₂O. A high peak airway pressure is not harmful if tidal volumes are titrated to yield a plateau pressure < 30 cm H₂O.

In severe obstructive airways disease, exhalation times must be prolonged or dangerous breath-stacking occurs. I:E ratios should be 1:5 or less to promote full exhalation. Because respiratory frequency is the single greatest determinant of expiratory time, tachypnea is the greatest enemy of asthmatics on PPV.

The reduced respiratory frequency required to safely attenuate breath stacking can yield respiratory acidosis, that is, “permissive hypercapnia,” which can be life-saving in the worst cases. In order of effectiveness, reducing respiratory frequency, tidal volume (to achieve plateau pressure < 30 cm H₂O), and inspiratory time reduce intrinsic PEEP.

Note that these measures may cause a very high peak airway pressure that is indicative of the pressure required to drive gas across the conducting airways; patients are safe so long as plateau pressure remains < 30 cm H₂O.

Emphysema and bronchospasm provide a slightly different challenge. Passive recoil of the respiratory system is poor, thus promoting gas-trapping. Yet, if TVs are insufficient, atelectasis may ensue.

Early in a COPD exacerbation, bronchospasm may predominate, promoting intrinsic PEEP, and the emphasis must be to promote expiratory time. As bronchodilator therapy takes hold and airway resistance falls, tidal volumes may need to be increased lest atelectasis develop. Ensuring to always maintain plateau pressures of 20–30 cm H₂O is the safest way to approach such patients.

Sample Algorithm For Initial Ventilator Management In Status Asthmaticus

Initial Vent Settings: TV 8 ml/kg, RR = 10-16/min, square inspir flow = 60 L/min, PEEP = 0, FiO₂ = 100%

Plateau Pressure:

< 30 cm H₂O

with pH > 7.30 – continue same vent settings

with pH < 7.30 – increase rate until pH 7.30-7.40

> 30 cm H₂O

Intrinsic PEEP > 5 cm H₂O

Increase peak flow up to 100 L/min

Decrease RR by 2-3/min and check ABG

If intrinsic PEEP remains > 5 despite above, consider further decreases of RR; bicarb infusion if pH, 7.20

Intrinsic PEEP < 5 cm H₂O

Decrease TV until plateau pressure < 30 cm H₂O & Check ABG

Consider increasing RR or bicarb infusion if pH < 7.20

Severe hypoxemia

Approach to attenuate mortality of ARDS:

- Begin with tidal volumes of 6 mL/kg, PEEP = 5 cm H₂O, FiO₂ = 100%.
- When the patient is synchronous with the ventilator, check plateau pressure and titrate TV to maintain a plateau airway pressure < 30 cm H₂O.
- Increase PEEP by 3-5 cm H₂O every 2-3 mins to achieve > 90% O₂ Sat on FiO₂ = 60%; as PEEP increases, TV may need to decrease to ensure safe plateau pressure.
- Maintaining patient-ventilator synchrony is essential because PEEP is “defeated” with excessive over-breathing, coughing, and dys-synchrony.
- As the patient improves, PEEP can be reduced slowly (no more than 1 cm H₂O/hour because the lung de-recruits quickly and recruits slowly). As PEEP is reduced, airway pressures will fall; when plateau pressure < 15 cm H₂O, increments of TV may be required to avoid sustained atelectasis.