

info MEDICUS

The essence of medical practice

Volume 12 Issue 3

Management of sepsis

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Intensive insulin
corticosteroids
with sepsis.

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‡ Elastase
§ Interleukin
|| Corticosteroids
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... 120 g per liter) and those who did
... (70 to 90g per liter).

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Editorial

Dear Doctor,

We are happy to present to you another issue of our Info Medicus. Through Info Medicus, we are always trying to fulfill your desk with the latest developments in medical science and in doing that, we take extreme care to provide you with the information from most authentic sources.

From the clinical prospective, in this issue we have presented 'Management of Sepsis' in the Review Article section. Here pathophysiology, causes, risk factors and treatment of sepsis are discussed briefly.

Knowing how to perform suprapubic bladder aspiration is important for clinicians who care for children. When a sterile urine specimen from a patient is required and the performance of urethral catheterization is difficult, suprapubic bladder aspiration is the next preferred method. That's why we have discussed about 'suprapubic bladder aspiration' in clinical method.

In this particular article we have discussed about 'Multiple Myeloma' which is a neoplasm of plasma cells. Multiple myeloma is a blood cancer that develops in the bone marrow. This disease predominantly affects older adults, and because of the protean manifestations of the disease patients can initially present to their primary care physicians with vague and confusing symptoms. So, it is important to diagnose the case which has been discussed in 'View Point'.

Pelvic inflammatory disease (PID) is an infection of the upper genital tract which primarily affects young, sexually active women. Delay in treatment may lead to major sequel, including chronic pelvic pain, ectopic pregnancy, and infertility. That's why we are concerned about this in 'Practice'.

We always welcome and count your valuable comment regarding 'Info Medicus' that helps us to make continuous improvement as we propel forward with new issues.

Thanks and best regards,



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Management of sepsis

A better understanding of the inflammatory, procoagulant, and immunosuppressive aspects of sepsis has contributed to rational therapeutic plans from which several important themes emerge. First, rapid diagnosis (within the first 6 hours) and expeditious treatment are critical, since early, goal directed therapy can be very effective. Second, multiple approaches are necessary in the treatment of sepsis. Third, it is important to select patients for each given therapy with great care, because the efficacy of treatment as well as the likelihood and type of adverse results will vary, depending on the patient.



Definition

Sepsis is a potentially life threatening complication of an infection. Sepsis occurs when chemicals released into the bloodstream to fight the infection trigger inflammatory responses throughout the body. This inflammation can trigger a cascade of changes that can damage multiple organ systems, causing them to fail. If sepsis progresses to septic shock, blood pressure drops dramatically, which may lead to death.

Pathophysiology

Sepsis is the culmination of complex interactions between the infecting microorganism and the host immune, inflammatory, and coagulation responses. The rationale for the use of therapeutic targets in sepsis has arisen from concepts of pathogenesis (Table 1).

Both the host responses and the characteristics of the infecting organism influence the outcome of sepsis. Sepsis with organ dysfunction occurs primarily when host responses to infection are inadequate. In addition, sepsis often progresses when the host cannot contain the primary infection, a problem most often related to characteristics of the microorganism, such as a high burden of infection and the presence of super antigens and other virulence factors, resistance to opsonization and phagocytosis, and antibiotic resistance.

Causes and risk factors

Bacterial infections are the most common cause of sepsis. However, sepsis can also be caused by other infections. It can result from something as seemingly harmless as a scraped knee or nicked cuticle or from a more serious medical problem such as appendicitis, pneumonia, meningitis, or a urinary tract infection. Sepsis may accompany infection of the bone, called osteomyelitis. In hospitalized patients, common sites of initial infection include IV lines, surgical incisions, urinary catheters, and bed sores.

Although anyone can get sepsis, certain groups of people are at greater risk. They include:

- People whose immune systems are not functioning well due to illnesses such as HIV/AIDS or cancer or use of drugs that suppress the immune system, such as steroids and those used to prevent rejection of transplanted organs
- Very young babies
- The elderly, particularly if they have other health problems
- People who have recently been hospitalized and/or had invasive medical procedures
- People with diabetes

Diagnostic criteria

Certain clinical features can be observed in case of sepsis. They are:

- Body temperature above 101° F (38.3° C) or below 96.8° F (36° C)
- Heart rate higher than 90 beats per minute
- Respiratory rate higher than 20 breaths per minute
- Probable or confirmed infection

In case of severe sepsis following signs and symptoms occurs:

- Significantly decreased urine output
- Abrupt change in mental status
- Decrease in platelet count
- Difficulty in breathing
- Abnormal heart pumping function
- Abdominal pain



Table 1: Pathways and mediators of sepsis, potential treatments

Pathway	Mediators	Treatment
Innate immunity	Super antigens: TSST-1 Streptococcal exotoxins (e.g., streptococcal pyrogenic exotoxin A) Lipopolysaccharide (endotoxin) TLR-2, TLR-4 Monocytes, macrophages Neutrophils	Anti-TSST-1 Antistreptococcal exotoxins Antilipopolysaccharide TLR agonists and antagonist GM-CSF, interferon gamma G-CSF †
Adaptive immunity	B cells (plasma cells and immunoglobulins) CD4+ T cells (Th1, Th2)	IgG
Proinflammatory pathway	TNF- α Interleukin-1 β Interleukin-6 Prostaglandins, leukotrienes Bradykinin Platelet activating factor Proteases (e.g., elastase) Oxidants Nitric oxide	Anti-TNF- α Interleukin-1-receptor antagonist Interleukin-6 antagonist Ibuprofen, high dose corticosteroids Bradykinin antagonist Platelet activating factor acetyl hydrolase Elastase inhibitor ‡ Antioxidants (e.g., N-acetylcysteine) Nitric oxide synthase inhibitor
Procoagulant pathway	Decreased protein C Decreased Protein S Decreased antithrombin III Decreased tissue factor pathway inhibitor Increased tissue factor Increased plasminogen activator inhibitor 1	Activated protein C Protein S Antithrombin III Tissue factor pathway inhibitor Tissue factor antagonist Tissue plasminogen activator
Anti inflammatory	Interleukin-10 TNF- α receptors	Interleukin-10 § TNF- α receptors
Hypoxia	Hypoxia inducing factor 1a, vascular endothelial growth factor	Early, goal directed therapy Supernormal oxygen delivery Erythropoietin
Immunosuppression or apoptosis	Lymphocyte apoptosis Apoptosis of intestinal epithelial cells	Anticaspases Anticaspases
Endocrine	Adrenal insufficiency Vasopressin deficiency Hyperglycemia	Corticosteroids ψ Vasopressin Intensive insulin therapy θ

* TSST denotes staphylococcal toxic shock syndrome toxin 1, GM-CSF granulocyte macrophage colony stimulating factor, G-CSF granulocyte colony stimulating factor, Th1 type 1 helper T cells, and Th2 type 2 helper T cells. Organism features means components of bacteria that are toxic to the host and that are potential therapeutic targets in sepsis.

† G-CSF is effective in patients with sepsis who have profound neutropenia.

‡ Elastase inhibitor was ineffective in a phase 2 trial involving patients with acute lung injury.

§ Interleukin-10 was ineffective in a phase 2 trial involving patients with acute lung injury.

ψ Corticosteroids had no effect on overall 28 day mortality but decreased mortality in a subgroup of patients with no response to corticotrophin. Additional trials of corticosteroids in patients with septic shock are in progress.

θ Intensive insulin therapy decreased the mortality rate among critically ill surgical patients but has not yet been evaluated in patients with sepsis.



Treatment according to the early and later stages of sepsis

Early goal directed therapy

The cornerstone of emergency management of sepsis is early, goal directed therapy, plus lung protective ventilation, broad spectrum antibiotics, and possibly activated protein C (Table 2). A randomized controlled trial was conducted in which patients with severe sepsis and septic shock received early, goal directed, protocol guided therapy during the first 6 hours after enrollment or the usual therapy. In the group receiving early, goal directed therapy, central venous oxygen saturation was monitored continuously with the use of a central venous catheter. The level of central venous oxygen saturation served to trigger further interventions recommended in the protocol. Crystalloids were administered to maintain central venous pressure at 8 to 12 mm Hg. Vasopressors were added if the mean arterial pressure was less than 65 mm Hg; if central venous oxygen saturation was less than 70%, erythrocytes were transfused to maintain a hematocrit of more than 30%. Dobutamine was added if the central venous pressure, mean arterial pressure, and hematocrit were optimized yet venous oxygen saturation remained below 70%. Early, goal directed therapy in that study decreased mortality at 28 and 60 days as well as the duration of hospitalization. Patients in the early, goal directed therapy group received more fluids, transfusions, and dobutamine in the first 6 hours; whereas control subjects received more fluids and more control subjects received vasopressors, transfusion, and mechanical ventilation for a period of 7 to 72 hours. The mechanisms of the benefit of early, goal directed therapy are unknown but may include reversal of tissue hypoxia and a decrease in inflammation and coagulation defects.

Ventilation

Once early, goal directed therapy has been initiated, lung protective ventilation should be considered. Acute lung injury often complicates sepsis, and lung protective ventilation meaning the use of relatively low tidal volumes is thus another important aspect of management. Furthermore, lung protective ventilation decreases mortality and is beneficial in septic acute lung injury. Excessive tidal volume and repeated opening and closing of alveoli during mechanical ventilation cause lung injury. Lung protective mechanical ventilation, with the use of a tidal volume of 6 ml per kilogram of ideal body Weight (or as low as 4 ml per kilogram if the plateau pressure exceeds 30 cm H₂O) as compared with 12 ml per kilogram of ideal body weight has been shown to decrease the mortality rate (from 40 to 31%), to lessen organ dysfunction, and to lower levels of cytokines.

Broad spectrum antibiotics

Because the site of infection and responsible microorganisms are usually not known initially in a patient with sepsis, cultures should be obtained and intravenous broad spectrum antibiotics administered expeditiously while the host immune status is

ascertained. The rising prevalence of fungi, gram positive bacteria, highly resistant gram negative bacilli, methicillin resistant *Staphylococcus aureus*, vancomycin resistant enterococcus, and penicillin resistant pneumococcus, as well as local patterns of antibiotic susceptibility should be considered in the choice of antibiotics. Observational studies indicate that outcomes of sepsis and septic shock are worse if the causative microorganisms are not sensitive to the initial antibiotic regimen.

Activated protein C

Once goal directed therapy, lung protective ventilation, and antibiotic therapy have been initiated, the use of activated protein C should be considered. Therapy with activated protein C (24 µg per kilogram per hour for 96 hours) has been reported to decrease mortality and to ameliorate organ dysfunction in patients with severe sepsis. Activated protein C is approved for administration to patients with severe sepsis and an increased risk of death. However, a subsequent trial of activated protein C in patients with a low risk of death was halted after an interim analysis for lack of effectiveness. This outcome suggests that activated protein C is not beneficial in low risk patients. The mechanism of action by which activated protein C improves the clinical outcome is unknown. Activated protein C was shown to increase protein C and decrease markers of thrombin generation (e.g., d dimer, a marker of disseminated intravascular coagulation) in one study. Although activated protein C prevents hypotension, it has little effect on coagulation in a human intravenous endotoxin model of sepsis, suggesting that modulation of coagulation may not be the primary mechanism underlying the cardiovascular benefit. Other anticoagulant therapies have included antithrombin III and tissue factor pathway inhibitor, yet only activated protein C was effective, perhaps because of its complex anti-inflammatory, antiapoptotic, and anticoagulant actions.

Treatment of anemia in sepsis

Anemia is common in sepsis in part because mediators of sepsis (TNF- α and interleukin-1 β) decrease the expression of the erythropoietin gene and protein. Although treatment with recombinant human erythropoietin decreases transfusion requirements, its use in randomized controlled trials failed to increase survival. Erythropoietin takes days to weeks to induce red cell production and thus may not be effective. Two trials used different transfusion strategies in different stages of sepsis. Using a hematocrit of 30% as a threshold for transfusion in early sepsis as part of a 6 hour protocol. Transfusion was associated with an improved outcome. Compared hemoglobin values of 70 and 100g per liter as a threshold for transfusion later in the course of critical care. Patients were expected to stay in the intensive care unit (ICU) for more than 3 days, and two transfusion strategies were compared during their entire ICU stay. There was no significant difference in mortality between patients who received transfusion on the basis of higher hemoglobin levels (100 to 120 g per liter) and those who did so on the basis of lower levels (70 to 90g per liter).

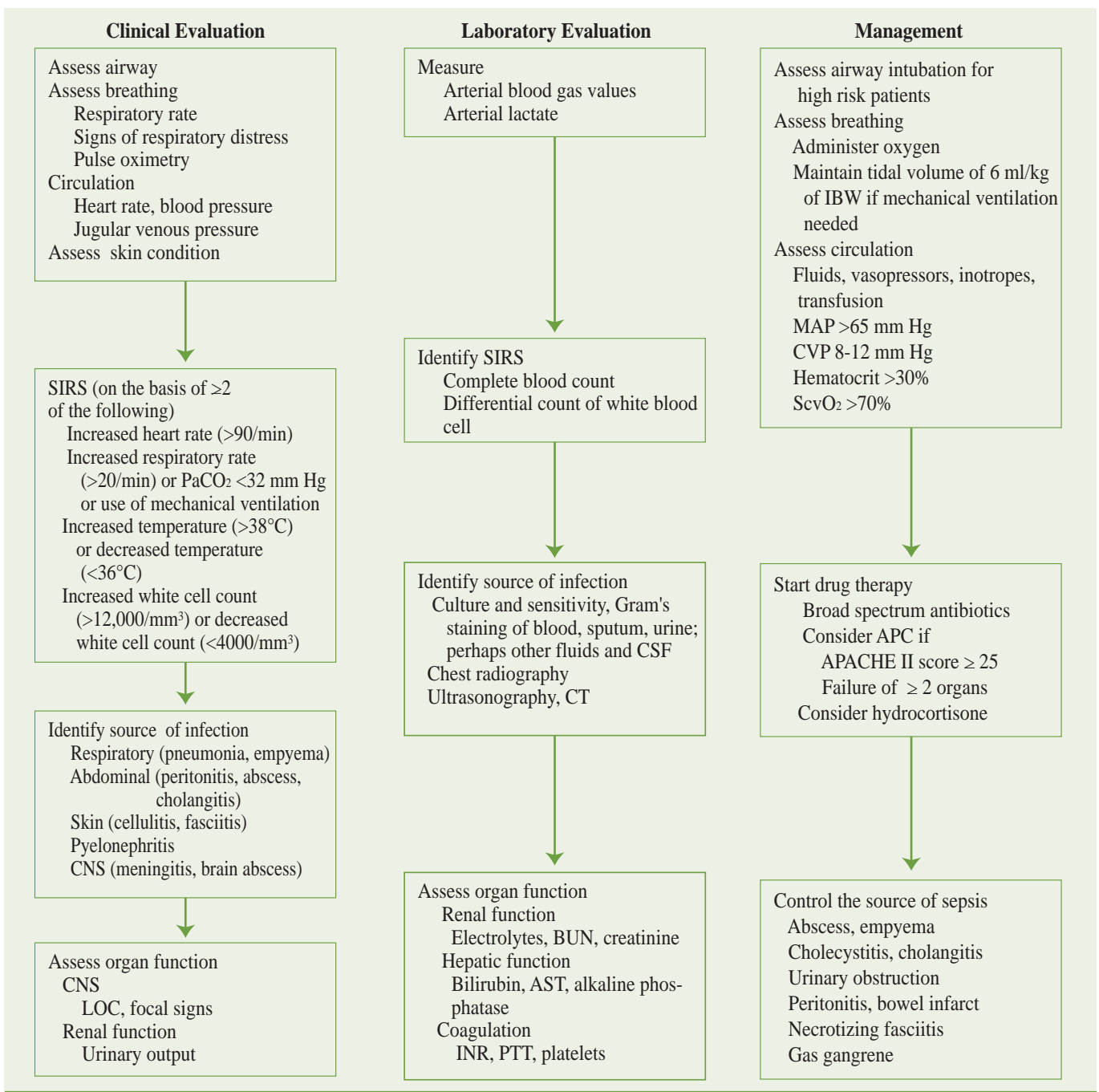


Corticosteroids in patients who require critical care

The exact mechanisms whereby corticosteroids or mineralocorticoids exert their effects on tissue function are unknown. However, in therapies other than adrenal replacements, the anti-inflammatory and/or immunosuppressive actions of the glucocorticoids are the principal desired qualities. Because of their anti-inflammatory effects, the glucocorticoids were previously thought to improve the course and reduce the mortality of septic

shock. They were reported to be able to perform a number of beneficial functions, such as disaggregating clumps of granulocytes, stabilizing lysosomal enzymes and capillary membranes, minimizing capillary permeability, improving oxygenation by altering ventilation or perfusion mismatches, increasing cardiac contractility, antagonizing complement and reducing complement mediated granulocytic aggregation,

Table 2. Therapeutic plan based on the early and later stages of sepsis



SIRS - Systemic inflammatory response syndrome, LOC - Level of consciousness, BUN - Blood urea nitrogen, AST - Serum aspartate aminotransferase, INR - International normalized ratio, IBW - Ideal body weight, MAP - Mean arterial pressure, CVP - Central venous pressure, ScvO₂ - Central venous oxygen saturation, APC - Activated protein C, PTT - Partial thromboplastin time.



diminishing coagulopathy, antagonizing endotoxin effects, decreasing local inflammatory responses and release of mediators, altering the migratory patterns of inflammatory cells, reducing toxic oxygen radical release, and vasoconstricting the capillary bed either directly or indirectly through the potentiation of the adrenergic system. Most of these effects are probably mediated through the effects of glucocorticoids on cellular lipocortins, which interfere with the release and metabolism of arachidonic acid. Although, high dose corticosteroids should not be administered in severe sepsis. Consequently, high dose corticosteroid therapy for the treatment of severe sepsis was abandoned.

Evaluation and control of the source of sepsis

Successful management of the critical care stage of sepsis requires support of affected organs. If a causative organism is identified (20% of patients with sepsis have negative cultures the antibiotic regimen should be narrowed to decrease the likelihood of the emergence of resistant organisms. A thorough search for the source of sepsis may require imaging (e.g., ultrasonography or computed tomography) and drainage (e.g., thoracentesis).

Vasopressin

Vasopressin deficiency and down regulation of vasopressin receptors are common in septic shock. Vasopressin dilates renal, pulmonary, cerebral and coronary arteries. Intravenous infusion of low dose Vasopressin (0.03 to 0.04 U per minute) has been reported to increase blood pressure, urinary output, and creatinine clearance, permitting a dramatic decrease in vasopressor therapy. However, vasopressin therapy may cause intestinal ischemia, decreased cardiac output, skin necrosis, and even cardiac arrest, especially at doses greater than 0.04 U per minute.

- Norepinephrine as the first choice vasopressor.
- Dopamine as an alternative vasopressor agent to norepinephrine only in highly selected patients (e.g., patients with low risk of tachyarrhythmias and absolute or relative bradycardia).

Hyperglycemia and intensive insulin therapy

Hyperglycemia and insulin resistance are virtually universal in sepsis. Hyperglycemia is potentially harmful because it acts as a procoagulant, induces apoptosis, impairs neutrophil function, increases the risk of infection, impairs wound healing, and is associated with an increased risk of death. Conversely, insulin can control hyperglycemia and improve lipid levels; insulin has anti-inflammatory, anticoagulant, and antiapoptotic actions. The appropriate target glucose range and insulin dose in patients with sepsis are unknown, because no randomized controlled trial has been conducted to specifically study patients with sepsis.

- A protocolized approach to blood glucose management in ICU patients with severe sepsis commencing insulin dosing when 2 consecutive blood glucose levels are >180 mg/dL. This protocolized approach should target an upper blood glucose 180 mg/dL rather than an upper target blood glucose 110 mg/dL .
- Blood glucose values be monitored every 1-2 hours until glucose values and insulin infusion rates are stable and then every 4 hrs thereafter. Glucose levels obtained with point-of-care testing of capillary blood be interpreted with caution, as such measurements may not accurately estimate arterial blood or plasma glucose values.

Renal dysfunction and dialysis

Acute renal failure is associated with increased morbidity, mortality and resource use in patients with sepsis. Continuous renal replacement therapy decreases the incidence of adverse biomarkers, but there is little evidence that it changes outcomes. Low dose dopamine (2 to 4 µg per kilogram per minute) neither decreases the need for renal support nor improves survival and, consequently, is not recommended. Lactic acidosis is a common complication of septic shock; however, sodium bicarbonate improves neither hemodynamics nor the response to vasopressor medications.

Support and general care

The goal of cardiovascular support should be adequate perfusion, though whether it is beneficial to try to maintain central venous oxygen saturation above 70% after the first 6 hours is unknown. Respiratory support requires continued application of a tidal volume of 6 ml per kilogram and a well defined weaning protocol. Because sepsis increases the risk of deep venous thrombosis, prophylactic heparin which can be added to activated protein C is recommended for patients who do not have active bleeding or coagulopathy.

Enteral nutrition is important because it is generally safer and more effective than total parenteral nutrition. However, total parenteral nutrition may be required in patients who have had abdominal sepsis, surgery, or trauma. For patients with sepsis who are receiving mechanical ventilation, stress ulcer prophylaxis with the use of histamine H2 receptor antagonists may decrease the risk of gastrointestinal hemorrhage. Proton pump inhibitors may be effective but have not been fully evaluated for stress ulcer prophylaxis.

Use of sedation, neuromuscular blocking agents, and corticosteroids should be minimized because they can exacerbate the septic encephalopathy, polyneuropathy, and myopathy of sepsis. The use of immune support benefits specific subgroups of patients with sepsis (e.g., patients with neutropenia benefit from treatment with granulocyte colony stimulating factor). The risk of nosocomial infection in patients with sepsis may be decreased by using narrow spectrum antibiotics, weaning patients from ventilation, avoiding immune suppression, and removing catheters.

Summary

Optimal management of sepsis requires early, goal directed therapy; lung protective ventilation; antibiotics; and possibly activated protein C. The use of corticosteroids, vasopressin, and intensive insulin therapy requires further study. Later in the course of sepsis, appropriate management necessitates organ support and prevention of nosocomial infection. Studies focused on novel targets, mechanisms of action, and combination therapy may improve current treatment.

- References:**
1. *N. Eng. J. Med.*, 19 October 2006; 355:1699-713
 2. *IMAJ*, January 2003; 51:55
 3. *Int. Care. Med.*, 2013; 39(2):165-228
 4. *Crit. Care. Med.*, 2013; 41(2):580-637
 5. www.webmd.com
 6. www.mayoclinic.org

Suprapubic bladder aspiration in children

Suprapubic bladder aspiration in children is a simple, safe, and useful technique for collection of sterile urine. The procedure can be performed in the emergency department of hospital. Suprapubic bladder aspiration of urine is the preferred method of collecting urine for culture. The technique is also indicated to verify urinary tract infection in children. Suprapubic bladder aspiration is contraindicated in the presence of abdominal distension or an empty bladder. Carefully and properly performed, the risk of complications should be negligible, and the success rate in obtaining urine is 90%.



Indications

Suprapubic bladder aspiration is performed to obtain a sterile urine sample from children when the urethra cannot be adequately visualized, such as in girls with labial adhesions or labial edema, in uncircumcised boys with unretractable foreskins, in children with conditions such as severe, protracted diarrhea that may make it difficult to obtain a sterile specimen, in children in whom multiple unsuccessful attempts have been made to obtain urine through urethral catheterization, and in children with a history of urethral or introital surgery in whom it may be difficult to perform catheterization.

Contraindications

Contraindications to suprapubic bladder aspiration include major genitourinary abnormalities, infections of the abdominal wall, clinically significant bleeding disorders, and massive organomegaly.

Equipment

To perform suprapubic bladder aspiration, topical anesthetic cream and an adhesive bandage, 1% lidocaine (with or without epinephrine), a 25 gauge 5/8 in. or 1 in. needle, a 22 gauge or 23 gauge 1.5 in. needle, two sterile 5 ml syringes, Sterile gloves, a sterile drape or towel, antiseptic solution with sterile gauze, a sterile specimen container, and a bandage is needed.

Analgesia

Apply the topical anesthetic to the skin 1 to 2 cm superior to the pubic symphysis and cover with an adhesive bandage. The anesthetic will be most effective if applied approximately 20 to 30 minutes before the procedure begins. In case of performing the procedure in an infant, dip a pacifier into an oral sucrose solution and allow the infant to suck the pacifier during the procedure to decrease discomfort. Alternatively, the care provider can dip a finger into the solution. In older children, who have thicker abdominal walls, use a subcutaneous injection of lidocaine.

Anatomy

To perform the procedure safely and successfully, a clear understanding of pelvic anatomy is must. The bladder lies posterior to the pubic symphysis and anterior to the uterus in girls and anterior to the rectum in boys.

Procedure

The procedure can be performed with or without ultrasound guidance. Both approaches are described.

Without ultrasound guidance

Place the child on his or her back, in the frog-leg position. One assistant should keep standing at the child's head. To maintain control of the arms and a second assistant to restrain the legs. Wash hands with soap and water, and should wear sterile gloves. Cleanse the child's skin from the umbilicus to the pubic symphysis, using an antiseptic solution. Next, infiltrate the subcutaneous tissues

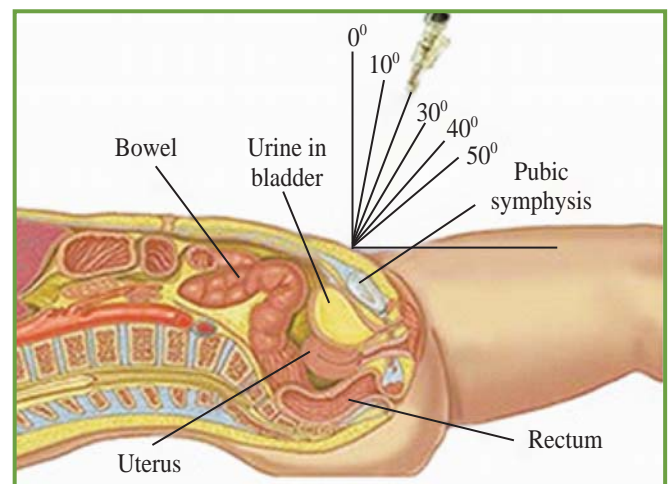


Figure 1. First attempt at bladder aspiration

approximately 1 to 2 cm above the pubic symphysis with 1 ml of lidocaine. Use the 1.5 inches needle to perform bladder aspiration.



The needle should be placed at an angle that is perpendicular to the abdominal wall, which means the needle will be approximately 10 to 20 degrees from true vertical (Figure 1). Penetrate the skin and immediately apply negative pressure to the syringe as the needle through the skin until urine is visible. A change can be felt as the needle penetrates the bladder wall. If no urine is obtained after the initial attempt, withdraw the needle to the edge of the needle tip, but do not remove the needle from the skin. Then change the angle of needle entry so that the needle tip is more caudad. The needle should be oriented in a true vertical position (Figure 2). Once sufficient urine collected in the syringe, immediately transfer the urine to a sterile container.

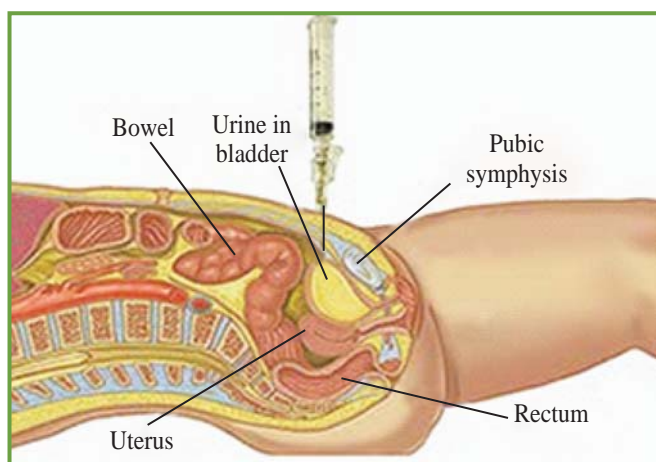


Figure 2. Second attempt at bladder aspiration

In the first attempt at bladder aspiration, the needle should be placed at an angle that is perpendicular to the abdominal wall, which means the needle will be approximately 10 to 20 degrees from true vertical.

With ultrasound guidance

Ultrasonography is increasingly used for diagnostic and procedural guidance. The use of ultrasonography to assess bladder volume and to guide aspiration can increase the likelihood that the procedure will be successful. The most common reason for failing to obtain urine with suprapubic bladder aspiration is a lack of sufficient urine in the bladder, which may be the case if the child has urinated within the past hour or if the child is dehydrated. Performing ultrasonographic evaluation of the bladder to ensure an adequate urine volume before attempting the procedure can increase the likelihood that urine will be obtained. A high frequency (5 to 10 MHz) linear array transducer is ideal for imaging the superficial pediatric bladder. Obtain a transverse view and measure the size of the bladder. Measurements of at least 2 cm in each dimension will provide sufficient volume for analysis.

If there is an inadequate amount of urine in the bladder, provide the patient with oral or intravenous hydration, as appropriate to the patient's clinical state, and try using ultrasound guidance to locate the bladder 30 minutes afterward. The amount of fluid administered will depend on the size of the patient, the level of dehydration, if present, and whether there is any known cardiac or renal disease.

If no urine is obtained after the initial attempt, withdraw the needle to the edge of the needle tip, but do not remove the needle from the skin. Then change the angle of needle entry so that the needle tip is more caudad. The needle should be oriented in a true vertical position.

Once there is sufficient urine in the bladder, the procedure may begin again. Prepare a small amount of sterile gel and put on sterile gloves. Cleanse the skin with antiseptic solution, and place a sterile cover on the ultrasound probe.

Locate the bladder again. If ultrasonography is not used for real time guidance of bladder aspiration, use a sterile pen to mark the skin site where the bladder is best visualized and proceed with bladder aspiration. When performing real time ultrasound guidance, leave the probe on the abdomen and insert the needle midline and just inferior to the edge of the probe at an angle that is perpendicular to the abdominal wall. The needle tip clearly on the ultrasound screen as it advances through the skin and into the anterior wall of the bladder. When the needle is seen in the bladder, aspirate the urine. The procedure can also be performed with the transducer along the long axis of the needle, such that the length of the needle is visualized.

Complications

Complications of suprapubic bladder aspiration are rare. They include gross hematuria, cellulitis of the abdominal wall, and perforation of the bowel, which may occur when a loop of bowel overlies the bladder. The use of ultrasound guidance decreases the likelihood of bowel perforation. If bowel perforation is suspected, withdraw the needle and reattempt the procedure with a fresh needle and syringe. Intestinal penetration is usually not clinically significant and generally requires no follow up.

Summary

Knowing how to perform suprapubic bladder aspiration is important for clinicians who care for children who are not toilet trained or who are unable to provide a clean catch urine specimen. When a sterile urine specimen from a patient is required and the performance of urethral catheterization is difficult or unfeasible, suprapubic bladder aspiration is the next preferred method.

Reference: N. Engl. J. Med., 4 September, 2014, Vol. 371, N(10)

Info Quiz Answers (April-June 2015)

1. b 2. a 3. d 4. d 5. b 6. a 7. b, c, e 8. c,d,e 9. a 10. a, c, e

Tuberculosis presenting as multiple intramuscular nodules in a child

A 9 year old girl presented with multiple painless, gradually progressive swellings over different parts of her body for 3 months with no history of contact with tuberculosis. Her physical examination was normal except for multiple swellings in her right forearm, a single swelling in her interscapular region and multiple swellings in her right calf. Ultrasonography of swellings revealed multiple nodules in the intramuscular layer. Excisional biopsies performed from two different sites revealed swellings in muscular layers and histopathology showed granulomatous inflammation with caseous necrosis consistent with tuberculosis. She was started on antitubercular therapy after which the swellings resolved and kept on regular follow up.

Intramuscular nodules in multiple muscular sites may be the presenting symptoms of tuberculosis of the muscles. Tuberculosis of skeletal muscles should be considered in a differential diagnosis when presented with single or multiple masses even when a chest X-ray is normal and there is no evidence of tubercular foci elsewhere in the body. She has no history of fever, trauma, joint pain, rashes, prolonged cough, decreased appetite, weight loss as well as no known or traceable history of contact with tuberculosis. On examination her weight and height were appropriate for her age. There were no signs of pallor, icterus, generalized lymphadenopathy, rashes, discharging sinus or features suggestive of osteomyelitis and joint involvement. The systemic examination was unremarkable except for presenting swellings. There was a small swelling in her back (Figure 1A), swellings in her right forearm (Figure 1B) and multiple swellings in her right calf (Figure 1C and Figure 1D) of varying size which were soft, raised, non tender, mobile, not fixed with skin and had normal overlying skin.



Figure 1: Photograph of swellings. A. Interscapular region. B. Forearm. C and D. Right calf.

A radiological investigation showed normal chest X-ray and limbs radiography for osteomyelitis was negative and there were no calcifications in chest and limb radiographs. A Mantoux test revealed no induration after 72 hours. Ultrasonography of her swellings revealed well defined hypoechoic intramuscular lesions and there were also a few calcifications and cystic degeneration in some of the lesions. Ultrasound guided fine needle aspiration cytology (FNAC) of the swelling revealed features suggestive of parasitic cysts based on the finding of bluish fibrillary structures with interspersed small nuclei in a background of mixed inflammatory cells consisting of neutrophils, eosinophils, lymphocytes and histiocytes. Acid fast bacilli staining of aspirate was negative for tubercular bacilli and aspirate culture was also negative. Intraoperatively the swelling was located in the muscular layer and histopathology showed features of granulomatous inflammation with caseous necrosis, consistent with tuberculosis. An excision biopsy was repeated again at a different site from her right forearm after 10 days. There were no characteristic histopathological findings of neurocysticercosis, filarial infections, hydatid cysts of muscles and sarcoidosis on both biopsy specimens. Based on her history, clinical examination and biopsy report from two different sites showing granulomatous inflammation with caseous necrosis suggestive of tuberculosis plus high prevalence of tubercular infection, diagnosis of tubercular infection was made. She was started on an antitubercular regimen and all the swellings resolved during the intensive phase and she is now on the continuation phase of the antitubercular regimen.

Reference: Journal of Medicine, March 2015; Vol. 9:72



Scientists find chemical clues on obesity in urine samples

Scientists have identified chemical markers in urine that are linked to body mass, offering clues about why people who are obese are more likely to develop illnesses such as cancer, stroke, diabetes and heart disease. Urine contains various chemicals known as metabolites that come from a range of biochemical processes in the



body. A study was published in the journal *Science Translational Medicine*, scientists led by a team at Imperial College London analyzed urine samples from more than 2,000 volunteers in the United States and Britain. They found 29 different metabolic products whose levels correlated with the person's body mass index. Some of these metabolites are produced by bacteria that live in the gut, the researchers said, highlighting the potentially important role they play in obesity.

It may be possible to identify non obese people who have such patterns in their urine profile. These people could be at risk of developing obesity and metabolic diseases, and might benefit from personalized preventative interventions.

Reference: www.foxnews.com/health

New ovarian cancer screening method can detect twice as many cases

Researchers say they've developed a new screening method that can detect ovarian cancer in twice as many women as traditional



strategies. The trial, led by the University College London, used a new algorithm to evaluate the levels of the blood protein CA125, known as a tumor marker or biomarker, which is found in greater concentration in tumor cells than in other cells of the body. CA125 has a particularly strong presence in ovarian cancer cells and is often tested in women at a high risk for the disease. Although CA125 testing is not new, the statistical calculation method, called ROCA algorithm and gave accurate ovarian cancer detection in 86 percent of women, compared to the conventional screening method that identifies fewer than half, between 41 and 46 percent.

Reference: www.foxnews.com/health

Kids of obese moms have risk of attention deficit hyperactivity disorder (ADHD)

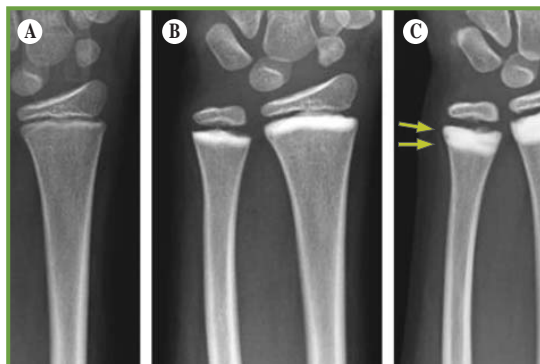
Six years old kids whose mothers were severely obese before pregnancy are more likely to have developmental or emotional problems than kids of healthy weight moms, according to a new study. The researchers had found evidence of this link in two



previous studies, an epidemiologist with CDC's National Center on Birth Defects and Developmental Disabilities. A study show data on 1,311 mother-child pairs collected between 2005 and 2012, including the mothers' body mass index before pregnancy and their reports of the children's psychosocial difficulties at age six. Kids of moms who were severely obese, with a BMI greater than 35, were twice as likely to have emotional symptoms, problems with peers and total psychosocial difficulties compared to kids of moms who had a healthy BMI, between 18.5 and 25. They were three times as likely to have a diagnosis of autism spectrum disorder and more than four time as likely to have attention deficit hyperactivity disorder (ADHD). So, Pre gestational weight loss is recommended for severely obese women. The healthier a woman can be entering pregnancy, the better it will be for children

Reference: www.foxnews.com/health

Problem 1



A 10 year old boy, 144 cm tall, was referred to hospital, with a 2 month history of persistent pain in the buttocks. He had altered gait due to pain, but no disturbance of bladder or bowels. Radiographs, CT, and MRI showed a large osteolytic lesion in the sacrum, and examination of a bone biopsy sample confirmed a giant cell tumour of bone, which considered to be unresectable because of the potential risk of neurological deficit and massive bleeding. Informed consent from the patient and his parents was obtained and the review board for use of denosumab, a potent inhibitor of osteoclastic bone resorption, to reduce the tumour mass.

What is the diagnosis?

Reference: The Lancet, 7 February 2015; Vol. 385

Problem 2

A 37 year old man with a history of bicuspid aortic valve surgically replaced at age 31 years was admitted to hospital, with 6 weeks of fever and 4 weeks of mild left mandibular pain. On examination he had short stature (155 cm) and shortened fourth and fifth fingers without fourth or fifth metacarpophalangeal knuckles bilaterally. Hand radiographs confirmed symmetric abnormalities of both hands with shortening of the first and third distal phalanges and fourth and fifth metacarpals bilaterally consistent with Albright's hereditary osteodystrophy. He had no ectopic calcifications on chest radiograph, serum calcium and phosphate were normal, and he had intact parathyroid hormone (PTH) levels.

What is the diagnosis?



Reference: The Lancet, 21 March 2015; Vol. 385


Problem 3



A 70 year old woman was admitted to hospital, for symptomatic atrial fibrillation. She had a history of oxacillin resistant coagulase negative staphylococcal endocarditis complicated by aortic root abscess, needing surgery and aortic valve re-replacement with a bioprosthesis, few years back. Since then, she had been on long term suppressive antibiotic therapy with minocycline 100 mg twice a day.

What is the diagnosis?

Reference: The Lancet, 31 January 2015; Vol. 385

Please see the answers  Page 15



Multiple myeloma

Multiple myeloma is a blood cancer that develops in the bone marrow. In myeloma, normal antibody producing plasma cells transform into malignant myeloma cells. Myeloma cells produce large quantities of one antibody (or immunoglobulin) called monoclonal (M) protein. These malignant cells also crowd out and inhibit the production of normal blood cells and antibodies in the bone marrow. In addition, groups of myeloma cells cause other cells in the bone marrow to remove the solid part of the bone and cause osteolytic lesions, or soft spots in the bone. This disease predominantly affects older adults, and because of the protean manifestations of the disease patients can initially present to their primary care physicians with vague and confusing symptoms.



Causes of multiple myeloma

The exact causes of multiple myeloma still unknown. But it is found that there are certain changes in DNA that can make plasma cell cancerous. Recent studies have found that abnormalities of some oncogenes (such as MYC) develop early in the course of plasma cell tumors. Changes in other oncogenes (such as the RAS genes) are more often found in myeloma cells in the bone marrow after treatment, and changes in tumor suppressor genes (such as the gene for p53) are associated with spread to other organs. Myeloma cells also show abnormalities in their chromosomes. Although normal human cells contain 46 chromosomes, some cancer cells may have extra chromosomes (called duplication) or have all or part of a chromosome missing (called a deletion). One fairly common finding in myeloma cells is that parts of chromosome number 13 are missing. These deletions appear to make the myeloma more aggressive and resistant to treatment.

Risk Factors

Scientists have found few risk factors that may affect someone's chance of getting multiple myeloma.

Age

The risk of multiple myeloma goes up as people age. Less than 1% of cases are diagnosed in people younger than 35 years old. Most people diagnosed with this cancer are at least 65 years old.

Gender

Men are slightly more likely to develop multiple myeloma than women.

Race

Multiple myeloma is more than twice as common in African Americans as in white Americans.

Radiation

People who were exposed to radiation from an atomic bomb blast had a higher risk of multiple myeloma. Exposure to lower levels of

radiation may also increase the risk of multiple myeloma. At most, this accounts for a very small number of cases.

Family history

Multiple myeloma seems to run in some families. Someone who has a sibling or parent with myeloma is 4 times more likely to get it than would be expected. Still, most patients have no affected relatives, so this accounts for only a small number of cases.

Workplace exposures

Studies looking at workplace exposures and multiple myeloma risk have found no clear links.

Obesity

A study by the American Cancer Society has found that being overweight or obese increases a person's risk of developing myeloma.

Having other plasma cell diseases

Many people with monoclonal gammopathy of undetermined significance (MGUS) or solitary plasmacytoma will eventually develop multiple myeloma.

Importance of early diagnosis

The common manifestations of multiple myeloma such as bone pain, fatigue, and weight loss may be nonspecific and are often initially ignored or missed by patients and medical practitioners. Patients with untreated myeloma can develop debilitating complications such as pathological fractures from lytic lesions, irreversible renal failure requiring long term haemodialysis, or more rarely spinal cord compression from extramedullary plasmacytomas. Delays in diagnosis are associated with a higher rate of complications and reduced disease free survival. Timely diagnosis of myeloma may prevent the potentially serious complications of the disease.



Diagnosis

Symptoms and signs

The symptoms and signs of myeloma result from malignant plasma cells infiltrating the bones or other organs (such as myelosuppression from marrow infiltration, hepatosplenomegaly) as well as from an increased amount of paraprotein (which causes, for example, hyper viscosity symptoms or paraesthesia from peripheral neuropathy) or light chains in the serum (which result, for example, in renal failure from light chain nephropathy). Patients with early stage disease may remain completely asymptomatic until complications arise. Table -1 lists the most common presenting symptoms or signs, according to a large, single centre retrospective analysis.

Table 1: Most common presenting signs & symptoms

● Normochromic, normocytic anaemia
● Bone pain
● Renal impairment
● Fatigue
● Weight loss
● Hypercalcaemia
● Hyper viscosity symptoms, such as headache, visual disturbance, cognitive impairment
● Paraesthesia
● Spinal cord compression
● Hepatomegaly
● Splenomegaly
● Lymphadenopathy
● Fever

Investigations

When myeloma is suspected in a patient, the baseline screening investigations should include:

- A full blood count to detect cytopenias resulting from marrow infiltration
- Inspection of the peripheral blood film to look for rouleaux, which may suggest underlying paraproteinaemia
- Serum biochemistry to detect the presence of renal impairment, hypercalcaemia (from widespread bony destruction, as cytokine expression by myeloma cells results in osteoclastic bone resorption), and raised uric acid (from increased tumor cell turnover)
- Liver function tests to look at the total protein concentration

Managements

Patients with myeloma are broadly divided into two main groups—those who are or are not eligible for an autologous stem cell transplant. This division is important as cytotoxic agents form the backbone of modern treatment for myeloma, and in patients eligible for transplantation the excessive use of alkylating agents may jeopardise a successful stem cell collection. Patients often receive repeated cycles of induction chemotherapy, usually in combination with thalidomide, lenalidomide or bortezomib, before stem cell mobilization and autologous transplantation.

Patients who are not eligible for transplantation are typically treated with combination chemotherapy until resolution of end organ damage and absence of detectable paraprotein. All patients with myeloma require bisphosphonates, which reduce pathological fractures and skeletal related events in myeloma. A recent randomised controlled trial suggests that zoledronic acid may be the bisphosphonate of choice. Adjuvant treatments in the form of localized radiotherapy may also be used for patients with symptomatic lytic lesions. Patients with recurrent infections resulting from secondary hypogammaglobulinaemia may benefit from regular intravenous immunoglobulin replacement.

Complications

The possible complications of multiple myeloma are:

- Kidney failure
- Bone fractures
- High levels of calcium in the blood, which can be very dangerous
- Increased chances for infection, especially in the lungs
- Weakness or loss of movement due to tumor pressing on spinal cord

Prevention

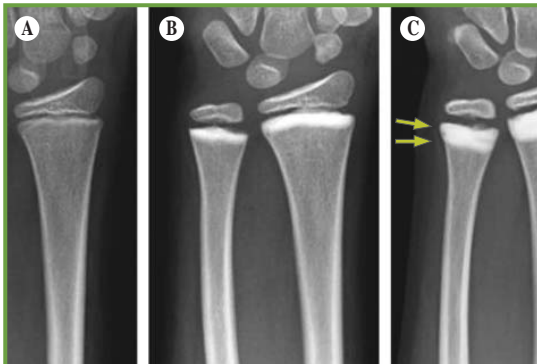
For some types of cancer, risk factors are known for the majority of cases. For example, smoking causes most lung cancers. This provides an opportunity for prevention. For other cancers, such as cervical cancer, pre cancers can be detected early by a screening test (such as the Pap test) and treated before they develop into an invasive cancer.

With multiple myeloma, few cases are linked to risk factors that can be avoided. There is no known way to prevent multiple myeloma from developing in those people with monoclonal gammopathy of undetermined significance or solitary plasmacytomas.

Reference: 1. *BMJ*, 5 January 2012; 344:d7953
2. www.cancer.org



Answer 1



Subcutaneous denosumab 120 mg every 4 weeks, with loading doses on days 8 and 15 of the first cycle was given. Due to the excellent clinical response and the obvious sclerotic changes along the growth plates stopped treatment after five cycles (seven injections). The sclerosing bands were seen in almost all the radiographs of metaphyses, most prominently in the distal radius and ulna, and also in the proximal humerus, proximal femur, and phalanges of the fingers. During the 5 months of treatment the tumour grew again, so restarted treatment with denosumab for 4 months until the tumour had reduced enough in size for surgery to be safely carried out. Before surgery repeat radiographs showed double layered sclerotic bands at the metaphysis reflecting the longitudinal bone growth during the periods on and of denosumab. At last follow up the patient showed no signs of growth retardation (151 cm tall), was able to participate in sports without pain, and showed no evidence of tumour recurrence.

Reference: The Lancet, 7 February 2015; Vol. 385

Answer 2

The diagnosis is pseudopseudo hypoparathyroidism. Patients with pseudohypoparathyroidism who had short stature, obesity, round facies, shortened metacarpals and metatarsals, and PTH resistance causing hypocalcaemia and hyperphosphataemia. This condition is caused by loss of function mutations in the subunit of the Gs protein encoded by the first 13 exons or intervening introns of the complex GNAS gene locus. Maternal transmission causes pseudohypo parathyroidism type 1a whereas paternal transmission leads to pseudopseudo hypoparathyroidism, a phenomenon known as genomic imprinting. Pseudopseudo hypoparathyroidism needs no treatment, but genetic counselling is recommended.



Reference: The Lancet, 21 March 2015; Vol. 385

Answer 3

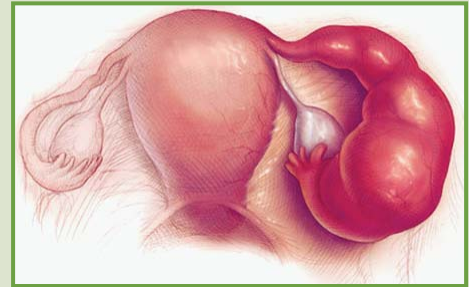


On examination, she had black hyper pigmentation of the shins and blue black scleral Hyper pigmentation. Despite the dyschromia, she was recommended to continue taking minocycline for life because of her previous endocarditis. She was electrically cardioverted for symptomatic atrial fibrillation. Although the mechanism is unknown, minocycline when oxidised turns black. It can discolour skin, bulbar conjunctiva, nails, and teeth. Sunlight and concomitant use of oestrogen, amitriptyline, and phenothiazines can exacerbate hyper pigmentation. Resolution of the hyper pigmentation takes months to years after discontinuation of therapy and can persist indefinitely.

Reference: The Lancet, 31 January 2015; Vol. 385

Pelvic inflammatory disease

Pelvic inflammatory disease (PID) is a polymicrobial infection of the upper genital tract. It primarily affects young, sexually active women. The diagnosis is made clinically; no single test or study is sensitive or specific enough for a definitive diagnosis. Pelvic inflammatory disease should be suspected in at risk patients who present with pelvic or lower abdominal pain with no identified etiology, and who have cervical motion, uterine, or adnexal tenderness. *Chlamydia trachomatis* and *Neisseria gonorrhoeae* are the most commonly implicated microorganisms; however, other microorganisms may be involved. The spectrum of disease ranges from asymptomatic to life threatening tubo ovarian abscess. Patients should be treated empirically, even if they present with few symptoms. Most women can be treated successfully as outpatients with a single dose of a parenteral cephalosporin plus oral doxycycline, with or without oral metronidazole. Delay in treatment may lead to major sequelae, including chronic pelvic pain, ectopic pregnancy, and infertility. Hospitalization and parenteral treatment are recommended if the patient is pregnant, has human immunodeficiency virus infection, does not respond to oral medication, or is severely ill. Strategies for preventing pelvic inflammatory disease include routine screening for chlamydia and patient education.



Pathophysiology

Most cases of PID are presumed to occur in 2 stages. The first stage is acquisition of a vaginal or cervical infection. This infection is often sexually transmitted and may be asymptomatic. The second stage is direct ascent of microorganisms from the vagina or cervix to the upper genital tract, with infection and inflammation of these structures. The mechanism by which microorganisms ascend from the lower genital tract is unclear. Although cervical mucus provides a functional barrier against upward spread, the efficacy of this barrier may be decreased by vaginal inflammation and by hormonal changes that occur during ovulation and menstruation.

In addition, antibiotic treatment of sexually transmitted infections can disrupt the balance of endogenous flora in the lower genital tract, causing normally nonpathogenic organisms to overgrow and ascend. Opening of the cervix during menstruation, along with retrograde menstrual flow, may also facilitate ascent of microorganisms.

Intercourse may contribute to the ascent of infection through rhythmic uterine contractions occurring during orgasm. Bacteria may also be carried along with sperm into the uterus and fallopian tubes.

In the upper tract, a number of microbial and host factors appear to influence the degree of inflammation that occurs and thus the amount of subsequent scarring that develops. Infection of the fallopian tubes initially affects the mucosa, but inflammation may rapidly become transmural. This inflammation, which appears to be mediated by complement, may increase in intensity with subsequent infections. Inflammation may extend to uninfected parametrial structures, including the bowel. Infection may extend via spillage of purulent materials from the fallopian tubes or via lymphatic spread beyond the pelvis to produce acute peritonitis and acute perihepatitis.

Pregnancy related factors: PID rarely occurs in pregnancy. However, chorioamnionitis can occur in the first 12 weeks of gestation, before the mucous plug solidifies and seals off the uterus from ascending bacteria. Fetal loss may result. Concurrent pregnancy influences the choice of antibiotic therapy for PID and demands that an alternative diagnosis of ectopic pregnancy be excluded. Uterine infection is usually limited to the endometrium but may be more invasive in a gravid or postpartum uterus.

Genetic factors: Genetically mediated variation in immune response plays an important role in susceptibility to PID. Variants in the genes that regulate toll like receptors (TLRs), an important component in the innate immune system, have been associated with an increased progression of *C. trachomatis* infection to PID. The microorganisms that are implicated in PID are thought to spread in three ways which is given in (Table 1).

Table 1: Way of spread of microorganism in PID

- Intra abdominally, traveling from the cervix to the endometrium, through the salpinx, and into the peritoneal cavity (causing endometritis, salpingitis, tubo ovarian abscess, or pelvic peritonitis)
- Through the lymphatic systems, such as infection of the parametrium from an intrauterine device (IUD)
- Through hematogenous routes, such as with tuberculosis, although this is rare

Etiology

The organisms most commonly isolated in cases of acute PID are *N. gonorrhoeae* and *C. trachomatis*. *C. trachomatis* is an intracellular bacterial pathogen and the predominant sexually



transmitted organism that causes PID. This can happen after intra uterine device (IUD) insertion, childbirth, miscarriage or abortion.

Risk factors

There are several things which would put a woman at risk for PID, including:

- Being a sexually active woman younger than 25 years old
- Having multiple sexual partners
- Being in a sexual relationship with a person who has more than one sex partner
- Having sex without a condom
- Having had an IUD inserted recently
- Douching regularly, which upsets the balance of good versus harmful bacteria in the vagina and may mask symptoms
- Having a history of pelvic inflammatory disease or a sexually transmitted infection

Clinical features

Symptoms

Patients with acute PID presents with a wide range of non specific clinical symptoms. The lower genital tract infection preceding salpingitis may be passed unnoticed. History of exposure may or may not be present. Symptoms usually appear at and immediately following the menstruation.

- Bilateral lower abdominal and pelvic pain which is dull in nature. The onset of pain is more rapid and acute in gonococcal infection (3 days) than in chlamydial (5-7)
- There is fever, lassitude and headache of varying intensity
- Irregular and excessive vaginal bleeding is usually due to associated endometritis
- Abnormal vaginal discharge which becomes purulent or copious. This is usually due to associated lower genital tract infection
- Nausea and vomiting
- Dyspareunia
- Pain and discomfort in the right hypochondrium due to concomitant perihepatitis may occur in 5-10 percent of cases of acute salpingitis. The liver is involved due to transperitoneal or vascular dissemination of either gonococcal or chlamydial infection

Signs

- The temperature is elevated to beyond 38⁰ C
- Abdominal palpation reveals tenderness on both the quadrants of lower abdomen. The liver may enlarged and tender
- Vaginal examination reveals - (1) Abnormal vaginal discharge to extent of purulent. (2) congested external urethral meatus or openings of Bartholin's ducts through which pus may be seen escaping out of pressure. (3) Speculum examination shows

congested cervix with purulent discharge from the canal. (4) Bimanual examination reveals bilateral tenderness on fornix palpation, which increases more with movement of the cervix. There may be thickening or a definite mass felt through the fornices

Treatment and Management

The treatment of PID must be empiric because a definitive diagnosis is rarely known or confirmed at the time of presentation. Empiric treatment may result in adverse effects from the antibiotics, including allergic reactions, gastrointestinal symptoms, or drug resistance; however, the benefits are thought to outweigh the risks. Because these infections are polymicrobial, broad spectrum antimicrobial agents are recommended to cover the most likely pathogens.

Treatment regimens for pelvic inflammatory disease

Drug	Dosage
Option 1	
Ceftriaxone plus Doxycycline with or without Metronidazole	250 mg IM in a single dose 100 mg orally twice per day for 14 days 500 mg orally twice per day for 14 days
Option 2	
Cefoxitin plus Doxycycline with or without Metronidazole	2 g IM in a single dose administered concurrently with probenecid (1 g orally) 100 mg orally twice per day for 14 days 500 mg orally twice per day for 14 days
Option 3	
Other parenteral third generation cephalosporin (e.g., ceftizoxime, cefotaxime) plus Doxycycline with or without Metronidazole	100 mg orally twice per day for 14 days 100 mg orally twice per day for 14 days 500 mg orally twice per day for 14 day

Physicians should determine whether the patient requires inpatient or outpatient management. Randomized clinical trials have demonstrated effectiveness of parenteral and oral antimicrobial agents in patients with mild or moderate PID. The first option for oral treatment includes a one time 250 mg intramuscular dose of ceftriaxone plus 100 mg of doxycycline orally twice per day for 14 days. Women with mild to moderate PID may receive outpatient oral medical treatment without increased risk of long term sequelae. The patient's age does not affect the response to treatment, whether inpatient or outpatient.



If parenteral therapy is required, the patient should be transitioned to oral treatment 24 to 48 hours after clinical improvement. Women with tubo ovarian abscesses should have at least 24 hours of inpatient treatment, and may require additional treatment, such as surgery. There is widespread emergence of *N. gonorrhoeae* resistance to fluoroquinolones, and these agents are no longer recommended unless there is a positive culture with confirmed sensitivity. Otherwise, a parenteral cephalosporin is suggested.

Follow up is important to ensure that the patient is responding to outpatient treatment. Clinical symptoms should improve within 72 hours of treatment, and if not, further evaluation is advised. Some patients may require additional testing to rule out other diagnoses, such as a tubo ovarian abscess, and assessment is needed for additional antimicrobial therapy, parenteral antimicrobials, and hospitalization.

Male partners of women with PID should be evaluated and treated if they have had sexual contact within 60 days of a diagnosis of PID. Men are often asymptomatic even when their partners are positive for chlamydia or gonorrhea. To decrease the chance of recurrence, women and their partners should abstain from sexual intercourse until they have completed the course of treatment.

Women with PID should be counseled about the prevention of sexually transmitted infections and PID because there is a high risk of reinfection even when partners have been treated. Repeat testing for women with chlamydia or gonorrhea is suggested three to six months after treatment. Testing for human immunodeficiency virus (HIV) infection and syphilis should be performed to rule out coexisting infections.

Differential diagnosis of acute pelvic pain

Women of reproductive age

Gastrointestinal

Appendicitis, bowel obstruction, diverticulitis, gastritis, inguinal hernia, irritable bowel syndrome, mesenteric venous thrombosis, perirectal abscess

Gynecologic

Adenomyosis, degenerating uterine fibroid, ectopic pregnancy, endometriosis; mittelschmerz, ovarian torsion, pelvic inflammatory disease, ruptured ovarian cyst, tuboovarian abscess.

Urinary

Cystitis, pyelonephritis, ureterolithiasis.

Pregnant women

Corpus luteum hematoma; ectopic pregnancy, endometritis (postpartum), ovarian torsion, ovarian vein thrombosis (postpartum), placental abruption, uterine impaction.

Complications

PID infections can cause scarring of the pelvic organs. This can lead to:

- Chronic pelvic pain
- Ectopic pregnancy
- Infertility
- Tubo ovarian abscess

Clinical features of acute salpingitis, acute appendicitis and ectopic pregnancy

Symptoms and signs	Acute salpingitis	Acute appendicitis	Ectopic pregnancy
Pain	Acute lower abdominal on both sides	Starts near umbilicus but settles to right iliac fossa	Acute lower abdomen on one sides
Amenorrhoea and bleeding PV	Unrelated	Unrelated	Usually present
GI symptoms such as nausea, present vomiting	Inconsistently	Usual	Absent
General look	Face flushed	Toxic	Pale
Tongue	No significant change	Furred	Pale
Pulse	Rapid but proportionate with temperature	Rapid, out of proportion to temperature	Persistent rise even with normal temperature
Temperature	More raised	Slightly raised	Not raised
Tenderness	Lower abdomen on both side	On McBurney`s point may have muscle guard	Lower abdomen more on one side
Per vaginal	Tenderness on both fornices A mass may be felt	Tenderness on right fornix and high up	Mass may be felt through one fornix extending to pouch of Douglas

Reference: 1. *Am. Fam. Physician*, 2010; 82(2):141-147
 2. *Am. Fam. Physician*, 2012; 85(8):791-796
 3. *BMJ*, 2013; 346:f3189
 4. www.mayoclinic.com
 5. www.webmd.com
 6. *Text Book of Gynaecology* by D.C. Dutta



Refresh your memory

Please select the correct answer by (✓) against a, b, c, d, e of each question in the Business Reply Post Card and sent it through our colleagues or mail within 17 August 2015; this will ensure eligibility for the Raffle Draw and the lucky winners will get attractive prizes!

- 1. Which dietary substrate is broken down into glucose and galactose by the action of intestinal enzymes?**
 - a. Fructose
 - b. Lactose
 - c. Maltose
 - d. Mannose
 - e. Sucrose
- 2. A 46 year old man presented within 1 hour of ingesting 40 tablets of slow release theophylline. What is the most appropriate initial management?**
 - a. Activated charcoal
 - b. Alkaline diuresis
 - c. Gastric lavage
 - d. Observation only
 - e. Whole bowel irrigation
- 3. On removal of the renal arterial clamp following donor kidney transplantation, the surgeon noted changes suggestive of hyperacute rejection. Which immunoglobulin is likely to be responsible?**
 - a. IgA
 - b. IgD
 - c. IgE
 - d. IgG
 - e. IgM
- 4. A 50 year old woman presented with a 24 hour history of palpitations. An ECG revealed atrial fibrillation with a ventricular rate of 130 beats per minute. Which drug is most likely to restore sinus rhythm?**
 - a. Adenosine
 - b. Bisoprolol
 - c. Digoxin
 - d. Flecainide
 - e. Verapamil
- 5. A 27 year old man was referred with an acute hepatic illness. Which laboratory finding would indicate the need for inpatient management?**
 - a. Aspartate aminotransferase:alanine aminotransferase ratio >1.0
 - b. Prothrombin time 24 s (11.5-15.5)
 - c. Serum alanine aminotransferase 1400 U/L (5-35)
 - d. Serum alkaline phosphatase 1800 U/L (45-105)
 - e. Serum conjugated bilirubin 110 µmol/L (<3.4)
- 6. A 32 year old man was treated with combination chemotherapy for testicular cancer. Subsequent investigations confirmed a complete clinical remission. What is the dominant cellular process that explains why this therapy was successful?**
 - a. Apoptosis
 - b. Differentiation
 - c. Mutagenesis
 - d. Necrosis
 - e. Senescence
- 7. Herpes simplex infection:**
 - a. Is commonly associated with carcinoma of the uterus
 - b. May cause Kaposi's varicelliform eruptions
 - c. May cause keratoconjunctivitis
 - d. May cause subacute sclerosing panencephalitis
 - e. May cause acute gingivostomatitis
- 8. Which of the following conditions or drugs inhibit uric acid reabsorption?**
 - a. Low dose salicylate
 - b. Hyperlactacidemia
 - b. Phenylbutazone
 - d. Dicoumarol
 - e. Probenecid
- 9. A 45 year old man presented with recurrent epistaxis. Examination revealed telangiectasia on his lips and in the mouth. A diagnosis of hereditary haemorrhagic telangiectasia was made. What is the most likely mode of inheritance?**
 - a. Autosomal dominant
 - b. Autosomal recessive
 - c. Mitochondrial inheritance
 - d. Sporadic mutation
 - e. X-linked recessive
- 10. Which of the following may cause pain in the heel?**
 - a. Ankylosing spondylitis
 - b. Kohler's disease
 - c. Rheumatoid arthritis
 - d. Prolonged diazepam therapy
 - e. Gonococcal infection



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