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IMPORTANT NOTICE FOR READERS

Dear Readers,

We have been regularly publishing the Pulmonary and Critical Care Bulletin (four issues per year) for the past several years. We have now felt that most of the articles that have been published in the recent issues have been written by our D.M. Fellows based on the seminars presented by them in our departmental academic meetings. These seminars are being directly uploaded per se to our website (www.indiachest.org) and can be freely viewed and downloaded. We, therefore, feel it would be unnecessary to have the same repeated in the online version of the Bulletin. Further, the rising concerns about the environmental effects of paper publications and the recent trend towards completely online journals have prompted us to consider discontinuing the print issue of this bulletin.

We, however, would be pleased to receive original contributions from our readers in any form (review articles, original articles and case reports). We encourage you to submit the same to Lung India (the official journal of the Indian Chest Society) at its online submission website (www.journalonweb.com/lungindia). We are hopeful for a good response to our appeal in the times to come and look forward to receiving your contributions.

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ULTRASOUND IN CRITICAL CARE

INTRODUCTION

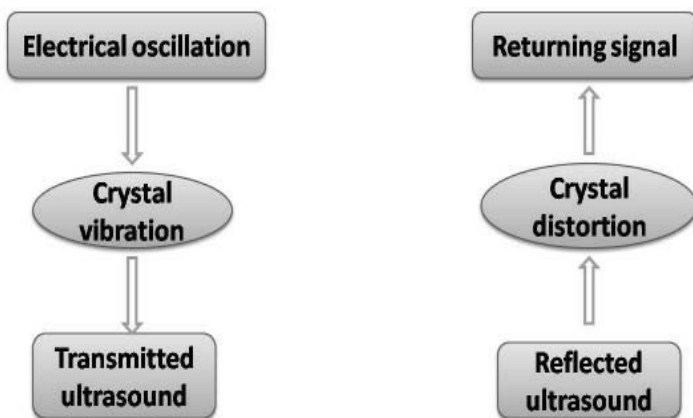
When evaluated scientifically, physical examination is quite limited and inaccurate in critically ill patients. Ultrasound (USG) has the potential to reinvigorate the physical examination, thereby improving accuracy and clinical utility and enhancing the teaching of physiology. The important attributes of ultrasound are its portability, lack of radiation, repeatability, absence of consumables and being battery powered. Further, this information is now available for storage and documentation, transmission, consultation, manipulation or fusion to other medical informatics.

The basic ultrasound skills should be a part of the armamentarium of critical care. Infact far from being competitive or conflicting, it is complementary. In one study, after a brief formal training in handheld Echocardiogram (ECHO) system (for about 10 hours), intensivists were able to perform limited transthoracic echocardiography (TTE) in 94% and interpret correctly in 84%. It changed the management in 37% of patients. The American College of Emergency Physicians (ACEP) and Society of

Critical Care Medicine (SCCM) have already included the use of ultrasound in the training of intensivists.

Sound of a frequency greater than 20,000 Hz is called ultrasound. Diagnostic USG usually uses 2.5- 14 MHz frequency sound waves. The frequency of a sound wave depends upon the sound source only and not by the medium in which the sound is traveling. Ultrasound production depends upon the property of piezoelectric effect. When electrical current passes through a piezoelectric substance, crystal vibrates. These waves are transmitted through the body. Most of these waves are scattered or absorbed by tissues, while a small proportion is reflected back, which again distorts the piezoelectric substance and produces an electric current (Figure 1).

Figure 1: Mechanism of ultrasound examination



The reflected signal gives information about the depth and the nature of the tissues. On the grey scale, high reflectivity (e.g. bone) is white; low reflectivity (e.g. muscle) is grey; no reflectivity (e.g. air) is black. With high frequency probes, better is the image resolution and lesser is the penetration, so better for superficial structures. Since low frequency probes provide better penetration, they can be applied for deeper structures and in adults.

The principle of Doppler is similar to that of sounds from moving vehicles. The pitch of the horn sound is higher when it approaches a person than when it goes away. The change of frequency (Doppler shift) depends on the speed of automobile and the original frequency of horn sound. In the human body, a Doppler study is based on the utilization of ultrasound waves reflected by moving red blood cells. It tells us about the flow velocity and flow direction as well.

USG IN VENOUS THROMBOSIS

The incidence of deep venous thrombosis (DVT) in the intensive care unit (ICU) is about 10%. Pulmonary embolism is amongst the most common preventable causes of death in hospitalized patients, ranging from 20-29%. USG is helpful in diagnosing DVT, to know the extent of DVT and to differentiate acute and chronic DVT. Compression USG can be easily done in the ICU to diagnose DVT, which can be confirmed by Doppler.

USG IN THORACIC DISEASES

As against the previous dogma, USG is quite helpful in thoracic diseases. Acute respiratory disorders amenable to diagnosis with ultrasound are pleural effusion, alveolar consolidation, acute interstitial syndrome and pneumothorax. The seven principles of lung ultrasound are :

1. A simple unsophisticated USG machine is perfectly adequate
2. The artifacts are due to air-water mixing. There are two main types of diseases - 'dependent' e.g. effusion and 'non-dependent' e.g. pneumothorax
3. All lung patterns arise from the pleural line
4. Interpretation is mainly based on the analysis of artifacts
5. Lung patterns are largely dynamic
6. The majority of acute lung disorders about the lung surface
7. Precise areas are to be defined with physical examination

A micro-convex probe is generally used, which allows satisfactory analysis of the intercostal space and veins. In a normal scan of the lung, the pleural line is located 0.5 cm below the rib line in the adult. The upper rib, pleural line and lower rib outline a characteristic pattern called the '*bat sign*'. The horizontal lines arising from the pleural line are separated by regular intervals that are equal to the distance between the skin and the pleural line. These were called A lines. Lung dynamics generate '*lung sliding*' (sandy) pattern. This pattern is called the '*seashore sign*'. B line is the name given to a vertical comet-tail artifacts which arise strictly from the pleural line, are well defined (laser-like), hyperechoic, move with lung sliding, spread to the edge of the screen without fading and erase A lines. Three or more B lines in a single view are called B + lines.

The A profile designates anterior predominant bilateral A lines associated with lung sliding (with possible focalized B lines). The A' profile is an A profile with abolished lung sliding and without lung point. The B profile designates anterior-predominant bilateral B + lines associated with lung sliding (with possible focalized A lines). The B' profile is a B profile with abolished lung sliding. The A/B profile designates anterior predominant B + lines on one side and predominant A lines on the other. The C profile designates anterior alveolar consolidation(s). The normal profile associates the A profile without posterolateral alveolar and/or pleural syndrome (PLAPS) (regardless of posterior A or B lines). These have been summarized in Table 1.

Table 1 : Profiles seen on ultrasound examination of the lung

| Profiles | Description | Suggestive of | Rules out |
|-------------|--|---|--|
| A profile | Predominant A lines plus lung sliding at the anterior surface | COPD, pulmonary embolism, posterior pneumonia | Pulmonary edema |
| B profile | Predominant B lines | Pulmonary edema | COPD, pulmonary embolism, pneumothorax |
| A/B profile | Anterior-predominant B lines at one side, predominant A lines at other | Pneumonia | |
| C profile | Anterior alveolar consolidation | | |

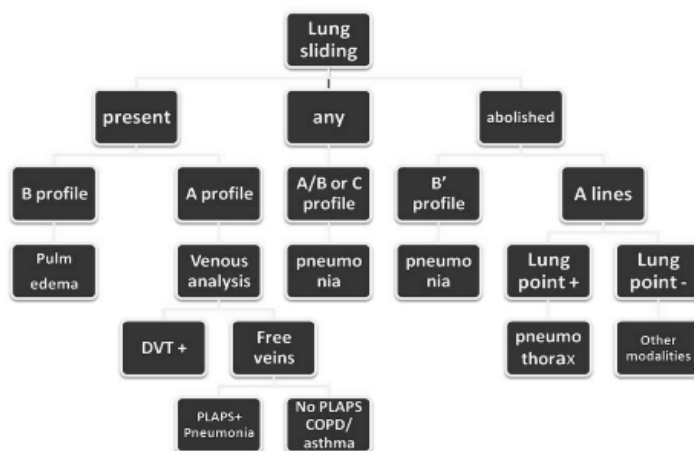
Predominant A lines plus lung sliding indicate asthma or COPD while multiple anterior diffuse B lines with lung sliding indicate pulmonary edema. A normal anterior profile plus deep venous thrombosis suggests pulmonary embolism. Anterior absent lung sliding plus A lines plus lung point indicate pneumothorax. Anterior alveolar consolidations, anterior diffuse B lines with abolished lung sliding, anterior asymmetric interstitial patterns, posterior consolidations or effusions without anterior diffuse B lines indicate pneumonia. The sensitivity and specificity of the above findings in relation to the diagnosis being suggested are depicted in Table 2.

Table 2 : Diagnosis based on ultrasound examination of the lung

| Diagnosis | Ultrasound findings | Sensitivity | Specificity |
|--------------------|--|-------------|-------------|
| COPD/ asthma | A lines + lung sliding | 89% | 97% |
| Pulmonary edema | Multiple B lines + lung sliding | 97% | 95% |
| Pulmonary embolism | Normal profile + DVT | 81% | 99% |
| Pneumothorax | Absent lung sliding | 81% | 100% |
| Pneumonia | Anterior alveolar consolidation, B lines - sliding | 89% | 94% |

The use of this profile provides correct diagnoses in approximately 90% of cases. The routine use of this algorithm called Bedside Lung Ultrasound in Emergency- the BLUE protocol (Figure 2) provides a direct approach to acute respiratory failure.

Figure 2 : Bedside Lung Ultrasound in Emergency- the BLUE protocol



USG also helps in differentiating elevated diaphragm and pleural effusion from mass lesions, atelectasis and consolidation. Presence of septations, debris, echogenic material and thickened pleura almost always indicates a complicated pleural effusion. It is specially indicated in patients on mechanical ventilation (MV), obese patients and those with loculated or small fluid collections. USG is also helpful in pleural catheter manipulation or redirecting it and changing or upsizing the drain.

Using lung ultrasound saves time and decreases the need for CT, whose drawbacks include delayed care implementation, irradiation, cost and the required supine position. Lung ultrasound is nearly equivalent to CT in detecting most disorders, can be repeated at will and provides additional information.

BEDSIDE ECHOCARDIOGRAPHY

It is indicated in patients with hemodynamic instability, infective endocarditis, aortic dissection or rupture, unexplained hypoxemia or source of embolus and to diagnose complications after cardiothoracic surgery. In ICU patients, TTE is generally considered inferior to transesophageal echo (TEE) because of poor acoustic window, which may be because of MV interposing the inflated lung between the heart and chest wall, surgical emphysema, obesity, chronic obstructive pulmonary disease (COPD), surgical wounds, dressings, tapes, tubings, lack of patient cooperation and difficulty in moving patients. Usually failure rates of TTE are 30-40% and of TEE 10-15%. The main indications of TEE in the ICU are when high image quality is vital (e.g. aortic dissection), structures which are inadequately imaged by TTE (e.g. left atrial appendage, prosthetic valves), situations where TTE is associated with inadequate image clarity (e.g. obesity, emphysema, application of high positive end-expiratory pressure (PEEP) during MV, presence of surgical drains and dressings) and acute hemodynamic instability in the peri-operative period.

Five commonly used echo windows are left parasternal, apical subcostal, right parasternal, and suprasternal. These days, echo examination is mandatory in all critically ill hemodynamically unstable patients and in suspected cases of aortic dissection. Echo leads to change in therapy in about 25% of patients. It is helpful in diagnosing cardiogenic shock (by assessing the contractility), hypovolemic shock (by assessing preload), pericardial tamponade and pulmonary embolism. TTE is successful in 50% whereas TEE in 90% of the patients.

Presence of a dilated inferior vena cava (IVC) (>20 mm in diameter) without a normal inspiratory decrease in caliber (>50% with gentle sniffing) usually indicates elevated right atrial pressure. It is less specific in mechanically ventilated patients. However, a small IVC virtually rules out elevated right atrial pressure. In the study by Feissel et al, cardiac output (CO) and a change in the IVC diameter before and immediately after administering a volume load (8 mL/kg 6% hydroxyethylstarch over 20 minutes) was assessed by echo. It was found that, in patients who responded to volume loading (increase in \geq CO by 15%), the variation in the IVC diameter before the fluid challenge was greater than in non-responders. A 12% cutoff value in IVC diameter variation before volume loading identified those patients who would respond to a fluid challenge, with positive and negative predictive values of 93% and 92%, respectively.

In pericardial tamponade, heart chambers collapse when pericardial pressure exceeds chamber pressure. It occurs in diastole before systole and on the right side before left side. The most sensitive two dimensional (2D) echo finding is right ventricular (RV) collapse during diastole. Right atrial collapse lasting longer than a third of the R-R interval is a specific sign for pericardial tamponade.

Pulmonary embolism should be considered in a patient with increased alveolar arterial oxygen gradient, hemodynamic instability and no other obvious explanation. Presence of pulmonary emboli decreases the pulmonary blood flow and can lead to increased pressures in the right side of the heart. The echo findings suggestive of pulmonary embolism are often those which indicate both pressure and volume overloads including increased size of the pulmonary arteries, RV dysfunction of varying degrees, flattening of the inter-ventricular septum, tricuspid regurgitation, dilated right atrium (RA) and increased size of IVC. In the absence of these findings, the diagnosis of pulmonary embolism is unlikely. The sensitivity and specificity of the McConnell sign (akinesia of the mid-free wall but normal motion of the apex) is about 77% and 94% respectively.

There should be a high index of suspicion for infective endocarditis (IE) as the classical findings are absent in critically ill patients. They are at increased risk for IE because of multiple indwelling catheters, total parenteral nutrition (TPN), severe underlying disease, altered gastrointestinal mucosal permeability and prolonged MV duration all of which increase the likelihood of bacteremia. The echo features

highly suggestive of IE are large or mobile vegetations, valvular insufficiency, suggestion of perivalvular extension, intracardiac abscesses and new dehiscence of prosthetic valve. TEE should be reserved for patients with a high clinical likelihood and negative TTE, prosthetic valve IE, complications of IE, unknown source of *S aureus* bacteremia and positive blood cultures despite antibiotics.

USG IN ICU – OTHER INDICATIONS

USG in patients with renal disease helps mainly to characterize the type of renal disease - acute versus chronic and in acute kidney injury to rule out hydronephrosis. It is also being used as a possible monitor of splanchnic perfusion.

The interventions which can be done with ultrasound guidance are central line placement, thoracentesis, paracentesis, drainage of abscesses at various sites, percutaneous nephrostomy and cholecystostomy, IVC filter placement and arterial catheterization. The advantages are that it is portable, allows imaging in numerous planes, allows real time visualization of needle and catheter and reduces the need for other imaging modalities that are associated with radiation exposure or use of nephrotoxic substances. USG guide central venous catheter placement significantly decreases the need for multiple attempts, failure rates for cannulation and complication rates as well as allows more rapid access. There are two methods of placement- trocar method and Seldinger technique.

SUMMARY

USG marries the human hand to the digital age, allowing the examiner to interrogate the anatomy and physiology with instantaneous visual gratuity. It may appear complex at first sight but simply requires a change in thinking. Once the process has been learned, a step-by-step use will make it a routine tool for intensivists and improve the management of critically ill patients.

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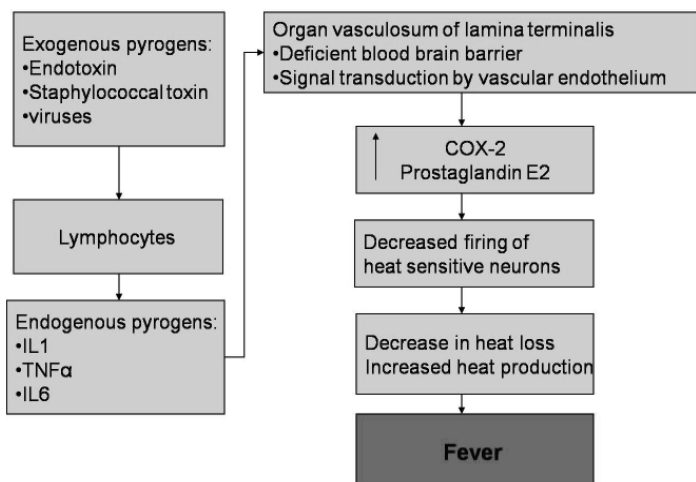
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FEVER IN THE INTENSIVE CARE UNIT

INTRODUCTION

Fever is a complex physiologic reaction to disease involving a cytokine mediated rise in core temperature, generation of acute-phase reactants, and activation of numerous physiological, endocrinological and immunological systems (Figure 1). Normal body temperature in human beings is considered to be 37.0°C (98.6°F) with a circadian variation of between 0.5 to 1.0°C.

Figure 1 : Pathogenesis of fever



The definition of fever is arbitrary and depends on the purpose for which it is being defined. The Society of Critical Care Medicine (SCCM) and Infectious Diseases Society of America (IDSA) suggested that a temperature of above 38.3°C (101°F) should be considered as fever and should prompt a clinical assessment. Frequency of fever in the intensive care unit (ICU) has been variably quoted between 26% and 44%. Presence of high grade fever (39.5°C) at admission or during ICU stay is associated with poor outcome.

Although infections are a common cause of fever, various environmental factors in the ICU like specialized mattresses, hot lights and air conditioning can alter body temperature.. Also one should remember that fever, an important sign of infection and sepsis, can be absent in the elderly, patients with open abdominal wounds and burns, patients receiving extra-corporeal membrane oxygenation (ECMO), cardiopulmonary bypass, peritoneal lavage, dialysis, continuous renal replacement therapy (CRRT) or continuous hemofiltration, patients with chronic cardiac, renal or liver disease as well as in patients taking anti-inflammatory or antipyretic drugs.

Various methods of measuring body temperature are mentioned in literature, which are tabulated below in table 1

Table 1 : Different methods for temperature measurement in the ICU

| Method | Merits | Demerits /Limitations |
|--|---|---|
| Axillary temperature measured by thermometer | | Underestimates core temperature |
| Sublingual temperature measured by thermometer | | Influenced by food, liquids and respiratory devices |
| Infrared ear thermometry | | Potential for inflammation or blockade of external ear |
| Rectal temperature measured by thermometer | Few tenths of °C above core temperature | Potential for rectal trauma and <i>Clostridium difficile</i> transmission |
| Mixed venous blood from pulmonary artery | Optimal site for core temperature | Requires presence of pulmonary artery catheter |
| Thermistor in urinary bladder | Represents core temperature | Expensive and needs to be monitored |
| Thermistor in distal esophagus | Represents core temperature | Position difficult to confirm Uncomfortable Risk of perforation |

IDSA guidelines mention that measuring axillary temperature is less desirable and oral temperature is acceptable although pulmonary artery catheter, rectal or esophageal probes give the most accurate temperature readings.

NON-INFECTIOUS CAUSES OF FEVER IN THE ICU

Apart from various nosocomial infections, there are a number of non-infectious causes of fever. Fever due to non infectious causes rarely reaches 39°C (102°F). Occasionally drug fever and transfusion reactions can cause high grade fever. Table 2 lists common non infectious causes of fever in ICU. The common causes are discussed here in detail.

Table 2 : Noninfectious Causes of Fever in the ICU

Abdomen

- Acalculous cholecystitis
- Pancreatitis

- Adrenal insufficiency
- Gastrointestinal bleeding

Thorax

- Acute myocardial infarction
- Dressler syndrome (pericardial injury syndrome)
- Pneumonitis without infection (including aspiration pneumonitis)
- Pulmonary embolism
- Pulmonary infarction
- Fat embolism
- ARDS (both acute and late fibroproliferative phase)

Brain

- Cerebral infarction/hemorrhage
- Subarachnoid hemorrhage

Musculoskeletal system and limbs

- Deep venous thrombosis
- Phlebitis/thrombophlebitis
- Gout/pseudogout

Intervention or Therapy Related

- Postoperative fever
- Transplant rejection
- Blood product transfusion
- IV contrast reaction
- Drug fever
- Immune reconstitution inflammatory syndrome

Miscellaneous

- Decubitus ulcers
- Hematoma
- Neoplastic fevers
- Alcohol/drug withdrawal

Drug Fever

Drug fever presents as unexplained high spiking temperatures, usually in the second week of administration of the culprit drug. It may be associated with leukocytosis and eosinophilia. Relative bradycardia, although commonly cited, is uncommon. There may be associated skin rash. It resolves rapidly within 72 hours of discontinuation of the drug (if no rash is present) but occasionally may take up to 7 days. The causative drugs are enumerated in table 3.

Table 3 : Offending agents implicated in drug fevers

Common offenders : Atropine, Amphotericin B, Asparaginase, Barbiturates, Bleomycin, Methyldopa, Penicillins, Cephalosporins, Phenytoin, Procainamide, Quinidine, Salicylates, Sulfonamides (including sulfa-containing laxatives), Interferon

Uncommon offenders : Allopurinol, Azathioprine, Cimetidine, Hydralazine, Iodides, Isoniazid, Rifampin, Streptokinase, Imipenem, Vancomycin, Nifedipine, NSAIDs

Rarecauses : Corticosteroids, Aminoglycosides, Macrolides, Tetracyclines, Clindamycin, Chloramphenicol, Vitamin preparations

Other drug related syndromes include neurolept malignant syndrome, serotonin syndrome and malignant hyperthermia.

Transfusion Reactions

These complicate about 0.5% of blood transfusions and occur more commonly following platelet transfusion. Antibodies against membrane antigens of transfused leukocytes and/or platelets are responsible. Fever usually begins within 30 minutes to 2 hours after a blood-product transfusion. The fever generally lasts between 2 to 24 hours and may be preceded by chills. Acute leukocytosis lasting up to 12 hours occurs commonly.

Acalculous Cholecystitis

Up to 1.5% of patients admitted in the ICU can develop this complication. Right upper abdominal pain, nausea, vomiting are non specific symptoms and so are the laboratory investigations. Gallbladder ischemia and cholestasis with bile salt inspissation play a role in the pathogenesis. It is associated with total parenteral nutrition (TPN) and application of positive end-expiratory pressure (PEEP) during mechanical ventilation. Untreated, it can progress to gangrene and perforation. Ultrasonography and computed tomography (CT) scan of the abdomen are sensitive imaging modalities. Percutaneous cholecystostomy is the treatment of choice and surgical methods are reserved for patients not responding to minimally invasive methods.

INFECTIOUS CAUSES OF FEVER IN THE ICU

The EPIC study conducted across ICUs in the European continent suggested a 20% point prevalence of nosocomial infections. The most common infection in ICU is ventilator associated pneumonia (VAP) and others are urinary tract infections (UTI), sinusitis, catheter related blood stream infections (CRBSI) and Clostridium difficile colitis.

Ventilator Associated Pneumonia (VAP)

New onset or worsening chest infiltrates associated with fever, purulence of respiratory secretions and leucocytosis is necessary for a clinico-radiological diagnosis of VAP. All patients should preferably be evaluated by sampling of the lower respiratory secretions with either bronchoscopy or non bronchoscopic techniques like endotracheal (ET) aspirate. Gram stain and quantitative bacterial cultures should be obtained. Blood and pleural fluid cultures are also recommended. All patients, unless there is a low clinical probability or Gram stain does not show any organism, should receive empirical antibiotics according to the probable causative organism(s) and suspected antibiotic resistance pattern. Patients should be re-evaluated at 48 hours in the light of available bacterial cultures and managed

accordingly. Microbiological and serological tests for fungal, viral, atypical bacterial and mycobacterial infections should be done as guided by the clinical picture.

A clinical pulmonary infection score (CPIS) (Table 4) has been developed and used to predict the presence of VAP. If the CPIS is less than 6 both at baseline and at 72 hours, most clinicians would safely allow stopping antibiotics.

Table 4 : Clinical pulmonary infection score (CPIS)

| | 0 | 1 | 2 |
|------------------------------------|---------------|---------------------|-------------------|
| Temperature (°C) | 36.5-38.4 | 38.4-39 | > 39 or < 36 |
| Leukocyte count | 4000-11000 | < 4000 or > 11000 | > 500 band forms |
| CXR | Normal | Diffuse infiltrates | Localized shadows |
| Secretions | Minimal | Moderate | Profuse |
| ET aspirate culture | Sterile | | Positive |
| PaO ₂ /FiO ₂ | > 240 or ARDS | | < 240, no ARDS |

Sinusitis

Nasogastric and nasotracheal tube placement is an established risk factor for sinusitis. Maxillary sinus is commonly involved, although ethmoid and sphenoid sinusitis may also be commonly associated with the former. Plain radiographs have a poor sensitivity for diagnosing sinusitis. Although CT scan of sinuses detects sinusitis with a high sensitivity rate, microbiological diagnosis with aspiration of the affected sinus is needed for confirmation of the diagnosis. Treatment includes removal of nasotracheal tube, surgical drainage of the affected sinus and antibiotics according to culture reports.

Clostridium difficile Colitis

C. difficile is the most common cause of nosocomial diarrhea. In neutropenic patients *C. septicum* and *Pseudomonas* spp. can also cause diarrhea. Other Gram negative bacilli which commonly cause community acquired infections are uncommon causes of nosocomial diarrhea. The clinical picture can vary from presence of abdominal pain, mild colitis to toxic megacolon. Diagnosis is achieved by stool examination for presence of toxin A and B using ELISA. In case, ELISA is negative and the clinical suspicion is high, stool can be tested with a cytotoxic assay for these toxins. Treatment options available are oral metronidazole and vancomycin. Vancomycin should be avoided unless metronidazole resistance or intolerance is present. Strict contact isolation of patient is essential for prevention of spread of infection.

Urinary Tract Infection

Bacteriuria or candiduria, defined as a quantitative culture of >1000 CFU/mL, has been reported in up to 30% of catheterized hospitalized patients. However it is

unclear how many catheterized patients with bacteriuria actually have UTI. Criteria have not been developed for differentiating asymptomatic colonization of the urinary tract from symptomatic infection. Bacteriuria should, however, be treated following urinary tract manipulation or surgery, in patients with kidney stones or urinary tract obstruction and neutropenic patients. Surveillance for and treatment of isolated bacteriuria in most ICU patients is currently not recommended.

Catheter Related Blood Stream Infections

CRBSI is seen in 5% of patients with indwelling vascular uncoated catheters. The estimated incidence is 2-5 infections/1000 catheter days. The risk is equal for arterial lines and peripherally inserted central venous catheters (CVC). The incidence of CRBSI increases with the length of time the catheter is *in situ*, the number of ports and the number of manipulations. The mortality rate attributed to catheter-related *S. aureus* bacteremia (8.2%) significantly exceeds the rates for other pathogens. Fever with inflammation with or without purulent discharge at the exit site or difficulty in aspirating or flushing from the CVC suggests CRBSI.

Various methods of diagnosing CRBSI have been described. Some require removal of the catheter (qualitative, semi-quantitative and quantitative cultures) while some can be done while retaining the catheter in place (qualitative or quantitative blood cultures from catheter or paired blood samples analyzed with quantitative cultures or time to culture positivity). Of all the above mentioned methods, the paired quantitative cultures method has the best performance.

All patients suspected to have CRBSI should have paired blood samples for quantitative cultures and central catheter should be removed if the patient has shock or organ dysfunction. Empirical antibiotics should be started in seriously ill patients. Once diagnosis is confirmed, appropriate antibiotics should be given and the catheter removed if not removed before. Duration of antibiotics is tailored according to the causative organism and by the presence or absence of any complication.

Fungal sepsis should be considered in patients with ICU stay of more than 10 days and who have received prolonged antibiotics. Epidemiological studies suggest that up to 15% of cases of sepsis in ICU are of fungal etiology.

MANAGING A FEBRILE PATIENT IN THE ICU

As previously mentioned, patients with fever >38.3°C should be investigated with appropriate microbiological, radiological and serological tests guided by the clinical picture (Table 5). It must be remembered that fever and infection do not have a one-to-one relation and identification of non-infectious causes of fever is of paramount importance in avoiding inappropriate administration of antibiotics.

Table 5 : Investigating a febrile patient in the ICU

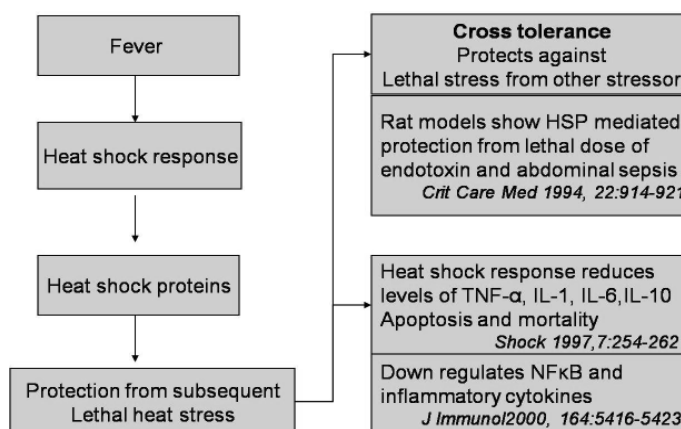
| Test | Comment |
|--|---|
| Blood cultures | Bacteremia (catheter related and others) |
| CVC tip culture | For CRBSI |
| Chest X ray | For VAP |
| ET/Mini-BAL/BAL quantitative culture | Will guide adjusting empiric antibiotics |
| CT paranasal sinuses | Needs to be followed by drainage and cultures |
| CT abdomen | More useful for diagnosis of abdominal sepsis than acalculous cholecystitis |
| Ultrasound abdomen | More useful for diagnosis of acalculous cholecystitis than abdominal sepsis |
| Cl. difficile toxin assay | Less sensitive than cytotoxic assay |
| Fungal cultures | Prolonged ICU stay, multiple antibiotics, TPN |
| Microbiological and serological tests for viral, fungal and bacteria | As epidemiological features guide |

Serum procalcitonin levels and endotoxin levels are recommended as adjunctive investigations in order to differentiate infectious from non-infectious causes of fever.

Whenever an infectious cause of fever is suspected, appropriate antibiotics (according to the suspected site of infection, suspected organism(s) and knowledge of local resistance patterns) should be started, especially if the patient is seriously ill or deteriorating. Empirical anti-fungals are to be considered in patients with a Candida score of >2.5 (score of 2 points for severe sepsis and 1 point each for TPN, surgery and multi-focal colonization by Candida spp).

Treating fever per se, with physical methods like cold sponging and drugs like acetaminophen is not mandated in all patients. Fever appears to be a beneficial phenomenon, as is evidenced by the fact that despite being a metabolically expensive phenomenon, it has been retained over the entire time period of evolution. It is also believed to exert a mortality benefit in patients with sepsis in previous observational studies. Experimental and animal studies suggest fever to be beneficial, as it protects cells from lethal stress and from its immuno-modulatory effects (Figure 2). Further, in controlled studies, cold sponging and acetaminophen failed to show any benefits in terms of patient comfort. Thus, treating fever is recommended only if fever is high grade (>39°C), or in patients with poor cardio-respiratory reserve and in patients with neurological insult to prevent secondary neurological injury.

Figure 2: Protective effects of fever



SUMMARY

Appropriately obtained temperature of >38.3°C in an ICU patient should prompt the clinician to take appropriate diagnostic tests. Fever has no one-to-one relation with infection. One has to consider both infectious and non-infectious causes for fever. Emphasis should be laid on appropriate microbiological and imaging studies as well as empirical antibiotics within 1 hour of identifying sepsis. Treatment of fever with physical and pharmacological methods is not mandatory and is recommended only if deemed essential.

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