INTRODUCTION

Intensive care units are specialized wards in hospitals to offer close monitoring and personalized care to very sick patients who are in need of haemodialysis and respiratory monitoring. In ICU fever is always alarming sign. Often fever indicates an emerging infection in ICU but all of us know infection can exist without fever and fever can exist without infections.

In healthy individuals, this temperature varies by 0.5 to 1.0°C, according to circadian rhythm and menstrual cycle. With heavy exercise, temperature can rise by 2 to 3°C. Whereas many biological processes can alter body temperature, a variety of environmental forces in an ICU can also alter temperature, such as specialized mattresses, hot lights, air conditioning, cardiopulmonary bypass, peritoneal lavage, dialysis, and continuous hemofiltration, drugs or by damage to the central or the autonomic nervous systems.

Temperature is most accurately measured by an intravascular, esophageal, or bladder thermistor, followed by rectal, oral, and tympanic membrane measurements, in that order. Avoid axillary measurement 1.

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**Fig. 1: Events Required For Fever Induction**

Fever is an elevation of the body temperature that exceeds the normal diurnal variations and occurs in conjunction with an increase in the hypothalamic set point i.e. from 37°C to 39°C. Very high fever with chills and rigors can occur following a pyrogen reaction from an IV infusion, while patients with life threatening sepsis can have a mild elevation or even subnormal temperatures. Infants, elderly patients, alcoholics and uremic patients may not respond with expected temperature pattern even in serious infections.

CAUSES OF FEVER IN ICU

A. Infectious Causes
   - Bacterial
   - Non Bacterial
B. Noninfectious Causes

Infectious causes:

Spectrum of the condition of patients with infections in hospital

Bacteremia: presence of bacteria in the blood, as evidenced by blood cultures.

Septicemia: Presence of microbes or their toxins in blood

SIRS: Two or more of the following conditions
1) Fever (Oral temperature > 38°C) or hypothermia (<36°C)
2) Tachypnea (>24 breaths/min)
3) Tachycardia (heart rate > 90 beats/min)
4) Leucocytosis (>12,000/microl), Leucopenia (<4,000/microl), 10% bands.

May have an infections or noninfectious etiology.

Sepsis: SIRS that have a proven or suspected microbial etiology.

Severe sepsis: Sepsis with one or more signs of organ dysfunction (such as metabolic acidosis, acute encephalopathy, oligouria, hypoxemia, or disseminated intravascular coagulation) or hypotension.

Septic shock: Sepsis with hypotension (arterial blood pressure of <90 mmHg systolic or 40 mmHg (less than patient’s normal blood pressure) that is unresponsive to fluid resuscitation, along with organ dysfunction.

Refractory septic shock: Septic shock that lasts for > 1 hr and does not respond to fluid or pressor administration.

MODS: Dysfunction of more than one organ, requiring intervention to maintain hemostasis

A. Common Clinical Types of Infections In ICU

1. Pneumonia is the Most dreaded complication with a high mortality rate of 30-50%. Patients at risk are those with altered sensorium, patient with nasogastric tubes, elderly patients, COPD patients, post operative patients. Patients on Ventilator and any of the above patients taking H2 blockers or antacids.

Pneumonia should be suspected when a patient develops a new cough, fever, leucocytosis, sputum production and a new infiltration on chest x-ray. Chest x-rays are difficult to interpret, because fluid overload, congestive heart failure and ARDS are all common findings in hospitalized patients. An important clue to pneumonia is a change in the output or character of these secretions. A subtle sign of pneumonia in the intubated patient is requirement for frequent change in ventilator settings.

Ventilator Associated Pneumonia:

a. National Nosocomial Infection Surveillance System Clinical Criteria for the Diagnosis of Nosocominal Pneumonia

Radiographic

Two or more serial chest radiographs with new or progressive and persistent infiltrate or cavitation or consolidation

One of the following:

- Fever - 38°C (100.4°F) with no other recognized cause
- WBC count > 12,000/mm.
- For adults to 70 yr old, altered mental status with no other recognized cause

And at least two of the following:

- New-onset purulent sputum or change in character of sputum, or increase in respiratory secretions or suctioning requirements
- New-onset or worsening cough, dyspnea, or tachypnea
- Rales or bronchial breath sounds
- Worsening gas exchange, increased oxygen requirements, increased ventilatory support
- Microbiology (optional)
- Positive culture result (one): blood (unrelated to other source), pleural fluid, quantitative culture by BAL or PSB

Health Care Acquired Pneumonia (HCAP)

Hospital acquired pneumonia: pneumonia that occurs 48 hours or more after admission, which was not incubating at the time of admission.

ICU-acquired pneumonia: pneumonia that arise more than 48 hours after ICU admission.

Ventilator-associated pneumonia (VAP): pneumonia that arises more than 48-72 hours after endotracheal intubation. Early onset HAP & VAP: occurring within the first 4 days of hospitalization.

Late onset HAP & VAP: at 5 days or more of hospitalization.
2. Sinusitis:

**Pathophysiology**
- impaired drainage of the sinus cavities in the supine position,
- slowed venous drainage due to positive-pressure ventilation,
- obstructive devices such as nasogastric or nasotracheal tubes

**Risk factors**
- Nasal colonization with enteric Gram-negative bacilli feeding via nasoenteric tube
- sedative use
- Glasgow coma scale of _ 8

Nasotracheal and nasogastric tubes are risk factors. 85% in patients with nasotracheal tube for >1 wk may develop. Maxillary sinus - commonly involved.

3. Diarrhea:
- suspect any patient with fever and diarrhea who has received an antibacterial agent or chemotherapy within 3 weeks before the onset of the diarrhea
- A tissue culture assay for *C. difficile* toxin is the diagnostic "gold standard"
- *C. difficile*-associated diarrhea and enterocolitis are important factor for causing diarrhea. Pseudomonas and *Cl. septicum* in neutropenic patients.

4. Urinary tract infection:

**Symptomatic infection**: a positive result on urine culture (_ 10^5 microorganisms/mL) and one of the following clinical signs: fever _ 38°C; urgency; frequency; dysuria; loin pain; loin/suprapubic tenderness.

**Asymptomatic bacteriuria**: urine culture of _ 10^5 microorganisms/mL of no more than two species, in the presence or absence of a catheter, no fever present (_ 36°C), urgency, frequency, dysuria, or loin/suprapubic tenderness.

**Risk factors**
the duration of catheterization, the absence of systemic antibiotic treatment, diabetes mellitus, and renal failure.

**Causative organisms**
Gram negative bacilli, *Streptococcus faecalis*, and yeasts. Urinary tract infection usually follows instrumentation of the urinary tract, most often with a catheter. After 10 to 14 days, about half of catheterized patients have bacteriuria. Urinary tract infections account for between 30 and 40% of all health care-associated infections.

5. Vascular Catheter related infection (VCRI):

**The risk factors**
Vary according to the type of catheter; the hospital size, unit, or service; the location of the site of insertion; and the duration of catheter placement

**Pathogenesis**
1. **Nontunneled CVC infection**: is often related to (1) extraluminal colonization of the catheter, which originates from the skin and, less commonly, from hematogenous seeding of the catheter tip, or (2) intraluminal colonization of the hub and lumen of the CVC.
2. **Tunneled CVCs or implantable devices**: Contamination of the catheter hub and intraluminal infection is the most common route of infection. *S. aureus* and *Candida* are more virulent and associated with a much higher probability of true blood stream infection.

6. CNS infection:
A prospective study of fever in neurocritical care patients indicates that although fever occurs in about 25% of such patients, almost half are noninfectious in etiology.

7. Surgical site Infections SSI:
Wound infections account for up to 20-30% of nosocomial infections but contribute up to 57% of extra hospital days and 42% of extra costs. The average wound infection has an incubation period of 5-7 days. The most common risks for postoperative wound infection are related to the surgeon’s technical skill, the patient’s underlying diseases (e.g., diabetes mellitus, obesity) or advanced age, and inappropriate timing of antibiotic prophylaxis, the presence of drains, shaving of the operative site by razor the day before surgery, a long duration of surgery, and infection at remote sites (e.g., untreated UTI). *S. aureus*; coagulase-negative staphylococci; enterococci; gram-negative bacilli such as *E. coli*, *Enterobacter*, *Klebsiella*, and *Serratia*; and *Candida* are the common pathogens. (Fig.2)

B. Nonbacterial infections:
Persistence of fever on antibiotics should also alert the physician to the possibility of fungal disease, especially if the patient continues to deteriorate clinically. Central hyperalimentation lines may be a source of fungal infection. Systemic fungal infections carry a high mortality rate and are difficult to diagnose. Cultures for fungi are often unrevealing, and serologic tests may be helpful.

Cellulitis in immunosuppressed patients may represent
fungal disease and should not be assumed to be bacterial in origin. Careful serial ophthalmoscopic examinations are necessary.
Evidence of Candida colonisation should be sought by obtaining cultures and if multiple sites are positive then empiric amphotericin B should be considered.
Aspergillus (or Mucor) must be suspected when a new chest infiltrate develops in a granulocytopenic patient being treated with antibiotics. An invasive procedure is usually necessary for diagnosis. Systemic amphotericin should be started as soon as the diagnosis is established.

The protozoan Pneumocysti carini cause pulmonary compromise in immunosuppressed hosts. Seasonal of infection of the locality like Malaria, dengue cannot be

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**Table I. Noninfectious Causes of Fever**

<table>
<thead>
<tr>
<th>Noninfectious Causes</th>
<th>Therapies</th>
<th>Inflammatory States</th>
<th>Endocrine Emergencies &amp; Others</th>
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<tbody>
<tr>
<td>1. Most often attributed to antimicrobials, antiepileptic drugs, antiarrhythmics and antihypertensives</td>
<td>1. Transfusion of blood products and Blood.</td>
<td>1. Pulmonary infarction</td>
<td>Hyperthyroidism Acute adrenal insufficiency</td>
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<td>2. Local inflammation at the site of administration</td>
<td>2. Fever in association with the Jarisch-Herxheimer phenomenon</td>
<td>2. Fibroproliferative phase of ARDS</td>
<td>Others</td>
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<tr>
<td>3. Malignant hyperthermia</td>
<td>3. Tumor lysis syndrome</td>
<td>3. Acute or chronic pancreatitis</td>
<td>Subarachnoid hemorrhage, gout, fat emboli, transplant rejection, Deep venous thrombosis, in association with indwelling catheters or occurring spontaneously</td>
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<td>6. Alcohol and opiates withdrawal</td>
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<td>7. Drugs or their delivery systems (diluent, intravenous fluid, or intravascular delivery devices) may also contain pyrogens or, rarely, microbial contaminants.</td>
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<td>8. Heat production (thyroxine),</td>
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<td>9. Limit heat dissipation (e.g., atropine or epinephrine),</td>
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<td>10. Alter the moregulation</td>
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forgotten. Reactivation of TB Infections are not uncommon in Indian ICUs. (Table I & Fig.3)

**APPROACH TO THE PATIENT**

The evaluation of a hospitalized patient with new fever should include a careful history. History should be focused on the possible causes of fever both infective and noninfective. Particular attention should be paid to symptoms of headache, cough, abdomen pain, diarrhea, flank pain, dysuria and leg pain. Past or current use of urinary catheter, surgical procedure should be questioned.

Clinical examination should be directed at potential sources of infection like skin rashes, pustules, signs of phlebitis, surgical wounds and signs of infection in lungs and abdomen. The laboratory evaluation should include a complete blood count, chest X-ray, blood and urine cultures.

**INVESTIGETIONS**

**Routine Hematological Evaluation may reveal polymorph leucocytosis and parasite infection**

 Blood Cultures: One blood culture is defined as a sample of 20-30 mL of blood drawn at a single time from a single site. Drawing three to four blood cultures with appropriate volume from separate sites of access within the first 24 hrs of the onset of fever is the most effective. ICU clinicians routinely culture central venous catheters on removal, Microbial growth can be quantitated using a quantitative blood culture system, or by using the differential time to positivity for peripheral vs. catheter blood cultures drawn simultaneously. If both sets of cultures are positive for the same organism and the set drawn through the catheter becomes positive _120 mins_ earlier than the culture drawn peripherally, this is highly suggestive of catheter-related bloodstream infection.

Posterior- anterior chest radiographs with lateral view or **CT scan** offer more information and should be obtained when clinically indicated, in HAP or VAP both immunocompetant and immunocompromised patients. (Fig.4)

Obtain one sample of lower respiratory tract secretions for direct examination and culture before initiation of or change in antibiotics. Expectorated sputum, induced sputum, tracheal secretions, or bronchoscopic or nonbronchoscopic alveolar lavage material can be used effectively.

**Pleural fluid** may be obtained with ultrasound guidance for Gram-negative stain and routine culture.

**Stool sample** for *C. difficile* common antigen, EIA for toxin A and B, or tissue culture assay. If severe illness is present and rapid tests for *C. difficile* are negative or unavailable, consider flexible sigmoidoscopy.

A specimen of **urine** should be obtained and evaluated by direct microscopy, Gram-negative stain, and quantitative culture. The specimen should not be collected from the drainage bag because multiplication of bacteria to high
levels can occur while the urine is in the bag. Rather, a specimen of urine should be aspirated from the catheter sampling port aseptically.

*Acute sinusitis* can be suggested by plain radiographs, ultrasound, CT, or magnetic resonance imaging.

*Surgical wounds* should be examined daily for infection. They need not be cultured if there is no symptom or sign suggesting infection.

*Imaging studies* and culture of the cerebrospinal fluid are the cardinal features of a diagnostic evaluation. A non-contrast CT scan is adequate to exclude mass lesions or obstructive hydrocephalus, which might contraindicate a lumbar puncture.

**Infectious Vs non-infectious fever**
- Procalcitonin can be used as an adjunctive to microbiological tests for identifying infective diseases.
- Tumor necrosis factor, interleukin-6, C-reactive protein, and triggering receptor expressed on myeloid cells-1 (TREM-1) have been tested as methods to discriminate true infection from other inflammatory states but have not yet been validated.
- Endotoxin activity assay = EA had a sensitivity of 85.3% and a specificity of 44.0% for the diagnosis of gram-negative infection. High negative predictive value (98.6%) for Gram-negative Infection.

**MANEGMENT**

**Rational use of antimicrobials in the ICU**
1. Empirical antibiotic regimens should cover most likely pathogens, should be initiated after taking suitable cultures and should be given in high doses.
2. Antimicrobial resistance patterns must be factored in the initial choice of antibiotic(s),
3. The results of culture and susceptibility tests should be utilised to make suitable changes to initial empiric antibiotic regimens.
4. Protocol driven antibiotic cycling in which specific antibiotics are periodically withdrawn and replaced by drugs from a different class should be considered for prevention of emergence of drug resistant organisms.
5. Combination microbial regimens should be used in the treatment of mixed infections or organisms like *Pseudomonas aeruginosa* which are often resistant to multiple antibiotics.
6. Shorter courses of antibiotics e.g. 8 days versus 15 days to treat VAP may be equally efficacious.
7. Monitoring of antibiotic therapy should include clinical response, changes in organ function requiring changes in drug dosing, drug related adverse events, drug interactions and monitoring of serum antibiotic levels.
8. Initial route of administration should be IV.

**Choice of Antibiotics**
- *Ventilator Associated pneumonia* - piperacillin-carbapenem
- *I.V catheter* - Vancomycin for MRSA and positive blood culture of the cloxacillin for sensitive staph.
- *Urosepsis* change or remove catheter, carbapenems and ceftazidime are the drugs of choice for empiric antibiotic therapy of nosocomial UTIs.
- *Intraabdominal* by Antibiotics to cover aerobic infection.
- *Diarrhoea C.difficile* Oral metronidazole or antibiotics within last 3 weeks flexible sigmoidoscopy for vancomycin for *C.difficile* detection of pseudomembranes.
- *Fungal infection* amphotericin B or neutropenia. catheters voriconazole.
- *Meningitis* Vancomycin + Meropenem

**Controlling the fever**
- *Antipyretics are recommended* - Beware of Renal Impairment and Hypertension Hypothermic blankets are less effective in cooling Temp than antipyretics. Tepid/Ice
Fig. 5: Author’s Experience: Fever In Our ICU.
Temperature >38.3°C/101°F

2 sets blood cultures

Urine culture

S. Creatinine / Sputum culture

Clinically obvious source of infection

>39°C/102°F

Central lines >48 hrs

Nasal tubes

Diarrhea

Empirical ABx

Observe for 48 hrs

Non infectious causes
Alcohol withdrawal
Pancreatitis
GI Bleeding
Phlebitis
Hematoma
Post transfusion
Acalculous cholecystitis

Observe for 48 hrs

Persistence of fever or progressive signs of infection

Done

Appropriate Dx tests + Empirical ABx

Remove and culture

Remove tubes and CT sinuses

Stool WBC and C. difficile

?Antifungal Rx
Venoraphy
Abdominal imaging
?Drug fever
?TB Reactivation
Sponging is effective.

**Cooling** - central fever responds to cooling - External & Internal. (Fig 5)

**PREVENTION AND CONTROL**

The guidelines for prevention concern three main approaches

1. Methods and techniques are needed to prevent cross-contamination and to control the potential sources of pathogens that could be transmitted from patient to patient or from HCW to patients. These methods and techniques include appropriate protocols for cleansing, disinfecting, and caring for various pieces of equipment and devices.

2. Second, guidelines are needed for the appropriate use of surgical antibiotic prophylaxis or empirical therapy among selected groups of patients.

3. Strategies to limit the emergence of resistant microorganisms need to be developed

**Take Care**

- Aseptic introduction of urinary or vascular catheters and Maintenance
- Sedation vacation for ventilated patients.
- Use peptic ulcer disease and DVT prophylaxis early
- Alcohol Hand Rub for HCW is ideal than conventional Hand wash
- **Selective digestive decontamination (SDD)**, is to prevent the overgrowth of potentially pathogenic Gram-negative aerobic bacilli and yeasts by using oral, nonabsorbable antibiotics that preserve the endogenous anaerobic flora.
- Ask Daily. IS CATHETER NEEDED?

**CONCLUSION**

Infections in ICU are common Cause of Fever. In our ICU UTI is the commonest cause to be followed by Venus Catheter / wound infection / pneumonia. Parasites and TB Reactivation are to be remembered. We must effectively evaluate and control fever in ICU otherwise fever will control the sick patients. Infection control in ICU plays a vital role in Patient Safety.

**REFERENCES**

1. Naomi P. O’Grady, MD et al; Guidelines for evaluation of new fever in critically ill adult patients: Criti Care Med 2008 vol. 36, no. 4 pages:1330-1349
2. Charles A. Dinavello, Reuven Porat, Harrison internal medicine 17 edition, fever and hyperthermia Fig: 17.1 Page no. 119
9. Pramila Bajaj, Indian Journal of anesthesia, fungal infection in ICU year 2008/Volume 52/ issue 2/ Pages 221 · 222