POST-OPERATIVE FEVER
~ An Brief Overview and Practical approach

Lee Kaing
DEFINITION

- Fever is an increase in normal core temperature that exceeds normal daily variation and occurs in association with an increase in the hypothalamic set point.

- Measurement of body temperature:
  Rectal Temp \(\sim 0.5^\circ C\) > Oral Temp \(\sim 0.5^\circ C\) > Axillary
  Rectal temperature is considered core.

- Postoperative fever is defined as a temperature >38°C on 2 consecutive postoperative days, or >39°C on any 1 postoperative day (Best Practice).
PATHOPHYSIOLOGY

- Fever → cytokine release in response to a variety of stimuli. Fever-associated cytokines include: IL-1, TNFα, and IFNγ, IL-6

- Released due to tissue trauma; do not necessarily mean infection. Degree of trauma correlates with degree of fever response.

- Bacterial endotoxins & exotoxins → stimulate cytokine release to cause postop fever
Infectious agents and/or microbial products, as well as cytokines and other inflammatory processes, induce macrophages, endothelial cells, and the reticuloendothelial system to produce and secrete pyrogenic cytokines into the circulation. These pyrogenic cytokines induce the synthesis of prostaglandin E2 (PGE2) in the hypothalamus. In addition, microbial toxins, acting as ligands to the toll-like receptors in the hypothalamus, stimulate the synthesis of PGE2 by the hypothalamus. PGE2 raises the thermostatic set point in the hypothalamus to febrile levels. The vasomotor center sends signals for heat conservation (vasoconstriction) and heat production (shivering). Corticosteroids reduce the peripheral synthesis of pyrogenic cytokines, whereas antipyretics reduce PGE2 levels in the brain. TLR: toll-like receptor; IL-1: interleukin-1; IL-6: interleukin-6; TNF: tumor necrosis factor; IFN: interferon; PGE2: prostaglandin E2.
LIST OF DIFFERENTIAL DIAGNOSIS

- **Infectious**
  - Surgical site infection
  - Pneumonia (ventilator-associated and aspiration)
  - Urinary tract infection (usually with an indwelling bladder catheter)
  - Intravascular catheter-associated infection
  - Antibiotic-associated diarrhea
  - Sinusitis
  - Otitis media
  - Parotitis
  - Intraabdominal abscess
  - Meningitis
  - Acute cholecystitis
  - Transfusion-associated viral infections
  - Foreign body infection (orthopedic hardware, endovascular devices eg, prosthetic heart valves, grafts, and stents)
  - Osteomyelitis
  - Endocarditis

- **Noninfectious**
  - Surgical site inflammation without infection
  - Hematoma/seroma
  - Suture reaction
  - Thrombosis
  - Deep vein thrombosis
  - Pulmonary embolism (thrombotic or fat embolism)
  - Inflammatory
  - Gout/pseudogout
  - Pancreatitis
  - Vascular
  - Cerebral infarction/hemorrhage
  - Subarachnoid hemorrhage
  - Myocardial infarction
  - Bowel ischemia/infarction

- **Other**
  - Medications
    - Antimicrobials: Penicillins, Cephalosporins, Fluoroquinolones, Vancomycin, Sulfonamides, Nitrofurantoin, Rifampin, Amphotericin B; Cardiovascular med: thiazide diuretics, Furosemide, Spironolactone, Hydralazine, Quinidine, Procainamide; Anticonvulsants: Phenytoin; Other: Heparin (especially unfractionated), Salicylates, Allopurinol, Immunoglobulins, Iodides, Propylthiouracil, Hydroxyurea, Mycophenolate mofetil
  - Drug/alcohol withdrawal
  - Transfusion reactions
  - Transplant rejection
  - Hyperthyroidism (including thyroid storm)
  - Hypoadrenalism
  - Cancer/neoplastic fever
THE 5 ‘W’ OF POST-OP FEVER

1. Wind – eg. atelectasis, pneumonia
2. Water – eg. UTI
3. Wound – eg. Wound/Surgical site infection, Abscess, Anastomotic leak, Lines (eg IVC, CVC, drains, heamatoma etc)
4. Walking – eg. DVT / PE
5. Wonder drugs
IMMEDIATE POST-OP FEVER

- Onset in the OT or within hours after surgery

- Medications - eg: immune mediated reactions such as reaction to antimicrobials

- Blood products - transfusion reaction; may p/w vasodilation, hypotension; rash

- Trauma - eg surgical: self-limited; usu resolves in 2-3 days; severity & duration related to length and extensiveness of procedure

- Infections (pre-existing to surgery)

- Malignant hyperthermia (RARE) - hypercarbia within 30 mins of triggering agent (eg, inhaled anesthetics, succinycholine), but have been reported later in the operative course. P/w - high fever due to hypermetabolism. Tx: Dantrolene
ACUTE POST-OP FEVER

- Onset within the first week after surgery; Nosocomial infections are common

- Pneumonia
  - Hospital Acquired vs Community
  - Ventilator associated
  - Aspiration (depressed mental state, reduced gag reflex, NGT, GORD)
  - Atelectasis leading to chest infection

- UTI
  - Indwelling urethral catheters. Risk increases with length of catheterization

- Surgical site infection
  - Necrotizing infection (within 48hrs): Clostridium perfringens, Group A streptococcus (GAS)
  - Often occurs in subacute period

- Anastomotic leak (Day 3-5 Post-op)

- IVC

- DVT & PE

- Other: acute gout, acalculous cholecystitis, pancreatitis, alcohol withdrawal
SUBACUTE POST-OP FEVER

- Onset from one to four weeks following surgery

- Patients needing critical care post-op are at higher risk of developing subacute fever - Nosocomial infections are more common because of their treatment with invasive medical devices.

- Surgical Site Infection – Common cause

- Antibiotic related – eg diarrhea due to C. Difficile

- Febrile drug reactions eg Beta-lactam Abs, sulfa-containing, others such as H2-blockers, phenytoin, procainamide, and heparin

- Lines - CVC, Thrombophlebitis

- DVT & PE
A  Surgical considerations
- Surgical classification
- Skin preparation
- Site, duration and complexity of surgery
- Presence of suture or foreign body
- Suturing quality
- Pre-existing local or systemic infection
- Prophylactic antibiotics
- Haematoma
- Mechanical stress on wound

B  Anaesthetic considerations
- Tissue perfusion
- Normovolaemia/hypovolaemia
- Perioperative body temperature
- Concentration of inspired oxygen
- Pain
- Blood transfusion

C  Patient-related factors
- Diabetes
- Smoking
- Poor nutrition
- Alcoholism
- Chronic renal failure
- Jaundice
- Obesity
- Advanced age
- Poor physical condition
- Medication
- Previous radiotherapy or chemotherapy

Decreased collagen synthesis
Affected by B and C

Increased vasoconstriction
Affected by B and C

Increased immunosuppression
Affected by A, B and C

Decreased tissue perfusion

Decreased PtO2

Decreased neutrophil bactericidal activity

Increased wound infection

Decreased wound tensile strength

Wound breakdown

Poor wound healing
DELAYED POST-OP FEVER

- Onset more than one month after surgery
- Mostly due to Infection
- Viral - from blood products, eg CMV, Hepatitis, HIV
- Parasitic infections via transfusion (eg, Toxoplasmosis, Plasmodium malariae infection) are very RARE
- Surgical Site Infection by more indolent microorganisms (eg, coagulase-negative staph) - implanted medical devices (will need r/o device)
- Delayed cellulitis – Surgery that disrupted venous or lymphatic drainage; can be recurrent
- Infective Endocarditis – due to perioperative bacteremia
<table>
<thead>
<tr>
<th>Category</th>
<th>0-48 hours</th>
<th>3-7 days</th>
<th>2-4 weeks</th>
<th>&gt;4 weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infectious</td>
<td>Toxic shock syndrome</td>
<td>Urinary tract infection</td>
<td>Clostridium difficile</td>
<td>Foreign body infection</td>
</tr>
<tr>
<td></td>
<td>Pneumonia</td>
<td>Pneumonia</td>
<td>Deep wound infection</td>
<td>Viral hepatitis</td>
</tr>
<tr>
<td></td>
<td>Wound cellulitis</td>
<td>Intra-abdominal abscess</td>
<td>Intra-abdominal abscess</td>
<td>HIV</td>
</tr>
<tr>
<td></td>
<td>Catheter-related intravascular infection</td>
<td>Foreign body infection</td>
<td>Foreign body infection</td>
<td>Infective endocarditis</td>
</tr>
<tr>
<td></td>
<td>Superficial thrombophlebitis</td>
<td>Leaking anastomosis with peritonitis</td>
<td>Leaking anastomosis with peritonitis</td>
<td>Osteomyelitis</td>
</tr>
<tr>
<td></td>
<td>Acalculous cholecystitis</td>
<td>Urinary tract infection</td>
<td>Urinary tract infection</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Transfusion-related acute infection</td>
<td>Pneumonia</td>
<td>Pneumonia</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Otitis media</td>
<td>Wound cellulitis</td>
<td>Wound cellulitis</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Bacterial meningitis</td>
<td>Catheter-related intravascular infection</td>
<td>Catheter-related intravascular infection</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Superficial thrombophlebitis</td>
<td>Superficial thrombophlebitis</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Acalculous cholecystitis</td>
<td>Acalculous cholecystitis</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Transfusion-related acute infection</td>
<td>Transfusion-related acute infection</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Otitis media</td>
<td>Otitis media</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Bacterial meningitis</td>
<td>Bacterial meningitis</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Toxic</td>
<td>Drug fever</td>
<td>Drug fever</td>
<td>Drug fever</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Malignant hyperthermia</td>
<td>Alcohol withdrawal</td>
<td>Alcohol withdrawal</td>
<td></td>
</tr>
<tr>
<td>Vascular</td>
<td>Myocardial infarction</td>
<td>Fat embolism</td>
<td>Deep venous thrombosis</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Stroke</td>
<td>Cavernous sinus thrombosis</td>
<td>Pulmonary embolism</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Infarction of tissue operated</td>
<td>Myocardial infarction</td>
<td>Cavernous sinus thrombosis</td>
<td></td>
</tr>
<tr>
<td>Immune</td>
<td>Inflammatory response to surgery</td>
<td>Delayed transfusion reaction</td>
<td>Acute transplant rejection</td>
<td>Acute transplant rejection</td>
</tr>
<tr>
<td></td>
<td>Transfusion reaction</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Hyperacute transplant rejection</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Traumatic</td>
<td>Haematoma</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Seroma</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Subarachnoid haemorrhage</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inflammatory</td>
<td>Suture reaction</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Aseptic meningitis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Suture reaction</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Underlying disease-related</td>
<td>Hyperthyroidism</td>
<td>Gout</td>
<td>Underlying malignancy</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Phaeochromocytoma</td>
<td>Pseudogout</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Pancreatitis</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Adrenal insufficiency</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Hyperthyroidism</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
APPROACH TO FEBRILE PATIENT

- FEBRILE PATIENT
  - STABLE
  - UNSTABLE
    - RESUSCITATE – remember your ABC

- History
  - Examination

- Consider DDX

- Investigation

- Treat accordingly
EVALUATION

- Fever is a common scenario – as an intern or HMO, you will be paged about a febrile post-op patient

- Look from the end of the bed
  - Is this patient well or unwell?

- Look at the Vitals/Observation Chart
  - GCS (is pt confused/delirious – baseline vs new)
  - Is this patient stable or unstable (look at baseline and trend) – COMMENCE RESUS IF PATIENT IS UNSTABLE
  - Beware the Beta-blocked patient
HISTORY

- Do not forget to take a history from the patient!

- Remember your differentials – target your history taking

- Resp questions (eg. cough, sputum, hemoptysis, CP)
- Cardiac questions (eg. CP, palpitation, dizziness, N/V)
- Urinary questions (eg. dysuria, freq, urgency, hematuria)
- GIT questions (eg. N/V/D, abdo pain, PR bleed)
- Related to surgery – Surg site pain/symptoms, specific to surgery (eg. H/A, meningism (N/Surg), abdo symptoms (HB, CR), etc)
- Beware the transplant patient – Immunosuppression, Rejection
EXAMINATION

- Be systematic – LOOK, LISTEN, FEEL

- Surgical Site - Take off any dressings, discharge, fluctuance
- Drains
- Lines – eg IVC, CVC
- Any pressure sore?
- Chest - ? Tachypnea, creps, wheeze, AE, pleural effusions
- Heart - ?murmurs, tachycardia
- Abdo - ?tenderness, peritonism, BS
- Calf - ?calf tenderness, peripheral odema
- Skin - ?rash, jaundice, echymosis, erythema, haematoma
Look at the Patient’s File
- Anaesthetic Record
- Surgical/Operation Record
- Preoperative State
- Drug chart/transfusion chart/allergies
- PMHx, D+A Hx, etc
INVESTIGATION

- “Septic Screen”
  - Blood Culture (x2)
  - Basic Bloods – FBE, U+E, CRP (trend), LFT
  - Urinalysis – always do! Easy, Fast, Cheap
  - Urine MSU
  - Sputum
  - CXR
  - Others – specific to clinical suspicion
    - Eg.
      - Wound infection: swab
      - C.Diff: C. Diff culture, toxin
      - PE: CTPA (Ultrasound for DVT)
      - Anastomotic leak: CT A/P w contrast
    Etc.
MANAGEMENT

- Depends on Diagnosis
- Infective causes (eg Pneumonia, Surgical site infection, UTI, line infections) – treat with antibiotics after cultures (broad spectrum while awaiting sensitivities), remove/replace lines (CVC – send tip off for culture), debridement, imaging-guided drainage of abscess
- Thrombo-embolic – treat with anticoagulation (note – bleeding risk; IVC filter?)
- Transfusion/Drug related - Cease transfusion, Cease drug that you suspect is causing fever
CASE 1

- 65 yo F with RA, D4 post-op right total hip replacement
- ATSP : Febrile 38.5
- PMHx : RA, otherwise well
- Med: Methotrexate
POSTOPERATIVE COURSE:
- Catheter is placed during surgery
- Post-op, pt went to orthopedic unit
- A fever of 38.1°C is noted on D1PO
- Her Foley catheter is removed on D2PO
- Her temperature is normal on D2-3PO
- D4PO, her temp is 38.5°C
- Wound healing well
- Pt ambulating the day following surgery
What is the most likely cause of her fever D1PO?

A. Transfusion reaction
B. Malignant hyperthermia
C. Trauma from surgery
D. Adrenal Insufficiency
What is the most likely cause of her fever now?

A. Joint hemarthrosis
B. Urinary tract infection
C. Superficial wound infection
D. Prosthesis infection
CASE 2

- 60 yo F, D3 post-op laparoscopic to open cholecystectomy
- ATSP: Abdo pain, Fever 40\(^\circ\)C
- PMHx: Obesity, Poorly controlled T2DM, HTN, Hchol
Considerations:

- Diabetic Patient
  - Poor healing response, infection risk

- Laparoscopic to Open?
  - You review operation notes – gangrenous gallbladder
ASSESSING PATIENT

Obs:
- Temp 40°C
- HR 140
- BP 80/50
- RR 25
- O2 Sat 94%
EXAMINATION

- Flushed, restless, unwell looking
- Wound – blistered, weeping, ?crepitation
- Drain - ~100ml, dirty dishwater
- Abdo – tender, reduced bowel sounds
- Chest – shallow rapid breaths, some basal creps
FEBRILE PATIENT

STABLE

UNSTABLE

RESUSCITATE – remember your ABC

History
Examination

Consider DDX

Investigation

Treat accordingly
This patient is septic

***SEPTIC SHOCK***
(hypotensive, tachycardic, tachypneic)

RESUSCIATE!
(Remember your ABC!)
SEPTIC SHOCK

SIRS
T° > 38°C or <35°C
Heart rate of >90 bmp
Respiratory rate >20 breaths per minute or PaCO₂ <32mm Hg
Abnormal WCC >12,000/µL or < 4,000/µL or >10% immature [band] forms
+ Infective organism
+ Organ Hypoperfusion, Organ Dysfunction
  (iotropic support)
MANAGEMENT

- Call for help
- IVC
- Bloods (BC, FBE, U+E, CRP, LFT, coag)
- IVT (assess response! ICU?)
- Antibiotics (*Surviving Sepsis* campaign guidelines/bundles)
- Further investigation – CT
- Return to theatre?
CASE 3

- 78 yo male D7 of admission, D4 post-op Craniotomy and resection of large frontal meningioma
- ATSP: Temp 37.8; desaturating to 88% on 4L NP
- PMHx: HTN, Hchol, Diet controlled DM, Ex-smoker ~80pack year history, Poor exercise tolerance
HISTORY

- “Feeling terrible doc”
- Not feeling particularly short of breath
- Normally not mobilise very far
- No CP, palpitation, dizziness, nausea
- Has chronic cough, no different
EXAMINATION

- BP 130/88
- HR 110
- RR 28
- SaO2 80% RA, 88% 4L
- Temp 37.8
- GCS 15
- Chest – Bibasal creps to midzone, scattered wheeze, soft breath sounds, decreased air entry bilaterally
- Cardiac – ESM at Aortic Region (found on admission, awaiting TTE)
- Peripheral – Bilateral pitting odema
What are you differential diagnosis?
DIFFERENTIAL DIAGNOSIS

- Fluid overload
- Exacerbation of COPD
- Hospital Acquired Pneumonia
- Pulmonary Embolus
- AMI
What investigations are you going to do?
INVESTIGATION

Initial
• ABG, FBE, U+E, CRP (trend)
• CXR

Other
• ECG
• CTPA
• LL USS
TREATMENT

Fluid Overload
- Diuretics (eg Frusemide)
- Monitor fluid status, JVP, peripheral oedema, daily weigh

Pneumonia
- Antibiotic (broad spectrum to cover HAP, await sensitivity from sputum)

Exacerbation of COPD
- Antibiotics, Inhalers/Nebulisers

Pulmonary Embolus
- Anticoagulation
  - Clexane
  - Warfarin
    (NB: Bleeding risk post-op)
- IVC filter
SUMMARY

• Remember your ‘5 Ws’
• Recognise Sepsis – remember your ABCs
• Full Patient Assessment
THANK YOU FOR YOUR TIME

END OF MEDICAL STUDENT TALK