# Intern Bootcamp: Fever

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# Learning Objectives

Definition of fever & pathophysiology

Practical Points

History/Exam/Differential/Workup

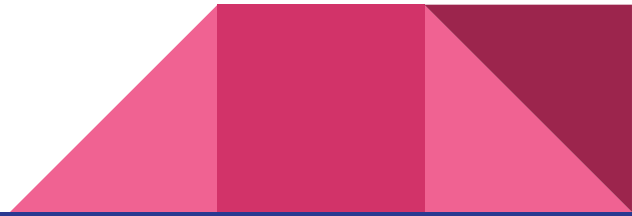
Culture or no culture?

Neutropenic Fever

Fever of Unknown Origin

Drug Fever

Hyperthermia



# Fever or No fever?

You’re glancing at a patient’s vitals and you notice they had a temperature of 100F overnight. The patient is a 57 yo M with history of HTN and HLD who was admitted for syncope evaluation. He has no new symptoms since admission, no further episodes of syncope so far.

# Fever Definition

One temperature of 38.3C or above

OR

T of 38C (100.4F) that persists for over 1 hour

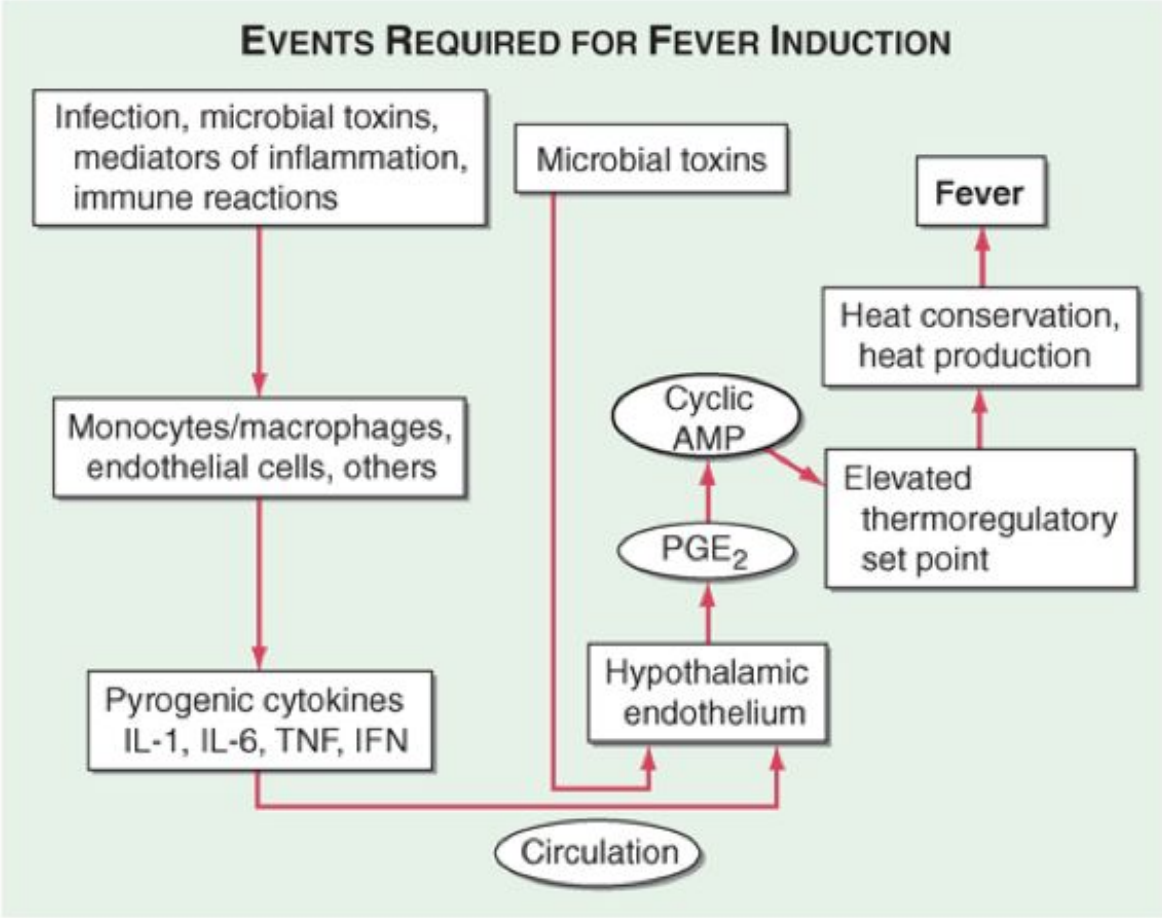
# Pathophysiology

Where do common anti-pyretics act?

HEAT Trial

When to treat fevers?

-MI, Stroke, Arrest, underlying CV and/or pulmonary disease, elderly, delirium




Source: Longo DL, Fauci AS, Kasper DL, Hauser SL, Jameson JL, Loscalzo J: *Harrison's Principles of Internal Medicine, 18th Edition*: www.accessmedicine.com

# How the human body responds

# Practical Points

Know the context of the fever

Not all infection will present with fever

Not all fever means infection

Some people have different baseline temperatures

Ex: Dysautonomia/spinal cord injury, hypothyroidism,

hx stroke

# Fever and its Broad Differential

Infectious

Autoimmune/Rheumatologic

Vascular

-Vasculitis (goes along with autoimmune)

-PE/DVT

Medication-related

Malignancy

Transfusion reaction

“Chemical” ex: pancreatitis

# History: Points to Consider

Recent Travel

Sick Contacts

Recent antibiotics and/or other drugs

Occupation/exposure

Sexual history

PMH: Immune system (HIV, splenectomy, sickle cell, BMT, chronic steroids, chemo, other immunosuppression)

Surgeries/Hardware

Culture History

Animals/insects

Recent hospitalization

# The Exam

**General**: Flushed? Dehydrated? Warm to touch?

**HEENT**: Conjunctival injection/drainage?

Ear erythema/pain? TM?

Nasal discharge?

Oropharyngeal erythema/exudates?

Meningismus? Photophobia/phonophobia?

**Cardio**: Tachycardia? New murmur?

**Respiratory**: Crackles? Increased WOB? Sputum?

**Skin**: Rashes? Lesions?

**GI**: N/v/d? Mucosal lesions?

Abdominal tenderness? Enlarged liver/spleen?

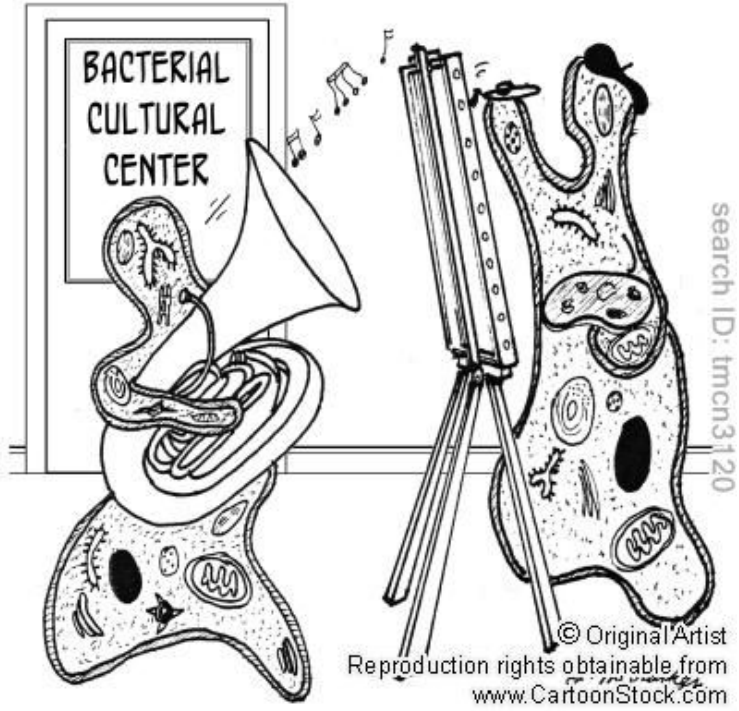
**Musculoskeletal**: Joint swelling/erythema?

**Lymph**: Nodes?

**GU**: Rashes or lesions? Discharge?

# Culture or No culture?

42 yo F with history of hypothyroidism, depression, anxiety who was admitted for hypertensive emergency. Blood pressure improving with treatment. You walk in on rounds and she's not feeling very well- she feels warm during exam. You take her temperature and T 38.5C. She has had chills/rigors overnight. Mentions her urine is cloudy and smells more concentrated.



# Culture or no culture?

68 year old M with history of alcohol abuse, HTN, anxiety/depression admitted for hyponatremia. He was an extremely “difficult stick” and has a PICC for monitoring his electrolytes. His nurse calls you as he has a temperature of 39C.

What if you get called on night float with a fever in this patient? Keep in mind, he had a fever earlier that day- what do you want to check?

# Blood Cultures

Blood Cultures

-Great idea in a new onset true fever

-Remember 2 sets of cultures means 4 vials

-Ideally 60 minutes apart from two peripheral sites

Patients with Lines

-Ideally want one from their catheter (each port)

and one peripheral set

PPV of true bacteremia if 2 sets of blood cultures are +

Both peripherally drawn: 98%

One catheter + one peripheral: 96%

Two catheter: 50%

# Other Cultures

Urine Culture

-Usually if patient is sick, you'll cover empirically and narrow based on culture

-When do you treat asymptomatic bacteruria?

Sputum Culture

-When your patient has diagnosis of PNA and an organism is isolated, can be clinically useful

-Look back at previous cultures- colonized?

# What do I do with this culture?

65 yo M with history of COPD, DMII, HTN admitted for DKA. Admission blood culture is growing gram positive cocci in clusters. His highest temp since admission was 37.5C overnight two nights prior. He’s feeling much better overall than when he first was admitted.

# Empiric Antibiotics

If you’re suspicious for/have diagnosed sepsis or septic shock, optimal doses of appropriate IV antibiotic therapy should be initiated, ideally within one hour of presentation, **after cultures have been obtained**

-SIRS, qSOFA

Otherwise...

Use your clinical judgement- if you don’t feel they need empiric antibiotics, you may be right- this is a good discussion to be had! Unless...

40 year old F with recently diagnosed AML who underwent induction chemotherapy via a newly placed port. She called her oncologist after feeling “shakes” at home and was told to come to the ED for evaluation. Vitals on arrival reveal T 38.5C.

What else do you need to know at this point?

# Neutropenic Fever

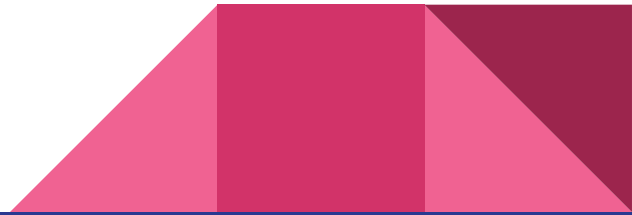
**Mild**: ANC 1000 - 1500 **Moderate**: ANC 500 - 1000 **Severe**: ANC 0 - 500

RF's: catheters, skin breakdown, GI mucositis, obstruction anywhere, immune deficiency

Most common organisms? -Recently gram positives, but historically GNR's (pseudomonas)

Prolonged neutropenia and/or antibiotic use? -Think fungal

Diagnosis: Exam! (*No DRE*), Labs, Imaging



# Neutropenic Fever

Empiric Antibiotic Coverage

-You want pseudomonal coverage

-If patient VRE colonized, want to cover this as well

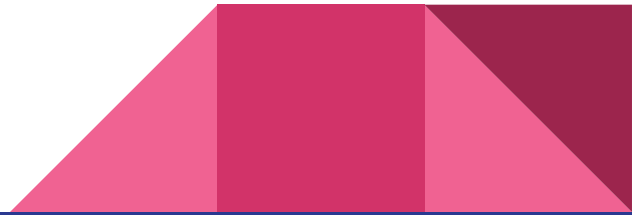
IV regimens

Monotherapy: ceftazidime (3rd), cefepime (4th), zosyn, imipenem, meropenem

2 drugs: aminoglycoside + anti-pseudomonal beta lactam

When to add Vanc? When to add fungal coverage?

PO for Low risk: Ciprofloxacin + Augmentin



# Neutropenic Fever

Who gets prophylactic antibiotics?

If likely to have >1 week neutropenia or severe <100 ANC

-Levofloxacin has been shown to decrease febrile episodes and bacterial infections in hemo-related high risk neutropenic patients, no difference in mortality

It’s 6:58pm on your long call Saturday night and you’re called for your final admission!

70 yo F with PMH dementia, HTN, HLD, COPD who was found to be febrile to 39C by her caregiver. She is an outside hospital transfer and comes with one week worth of paper charts detailing her workup thus far. Long story short, per report, they still have not found the source of her fevers. Cultures have been drawn. She is on vancomycin and zosyn from OSH and she’s on her way to Lakeside.


Oh…
you said
FUO…
not UFO.

# Fever of Unknown Origin

Fever on more than one occasion over at least 3 weeks and no diagnosis despite 1 week of evaluation

Or if you want to get technical…

| | CLASSIC FUO | NOSOCOMIAL (HEALTH CARE –ASSOCIATED) FUO | NEUTROPENIC (IMMUNE-DEFICIENT) FUO | HIV-RELATED FUO |
|---|---|---|---|---|
| **Definition** | >38.3° C (100.9° F), >3 wk, >2 visits or 3 days in hospital | >38.3° C (100.9° F), >3 days, not present or incubating on admission | >38.3° C (100.9° F), >3 days, negative cultures after 48 hr | >38.3° C (100.9° F), >3 wk for outpatients, >3 days for inpatients, HIV infection confirmed |

# Back to the differential-

Infectious

Autoimmune/Rheumatologic

Vascular

-Vasculitis (can do along with autoimmune)

-PE/DVT

Medication-related

Malignancy

Transfusion reaction

“Chemical” ex: pancreatitis

# Recommended Workup (beyond H&P)

-CBC w/differential
-RFP/LFT's- if LFT's abnormal, hepatitis workup
-ESR/CRP
-LDH, lactate
-ANA, RF
-Cryoglobulin
-CK
-SPEP
-3 sets blood cultures (off of antibiotics)
-UA/Urine cultures
-PPD or IGRA
-HIV Ab +/- PCR
-Heterophile Ab or EBV/CMV titers

Imaging depends on patient (CXR, CT chest/abdomen, TTE, tagged WBC scan)

**Remember, empiric antibiotics are not always indicated**

# Persistent Fevers

For the patient who does not defervesce on antibiotics...

Think about what you may not be covering

-> MRSA, pseudomonas, anaerobes, fungal

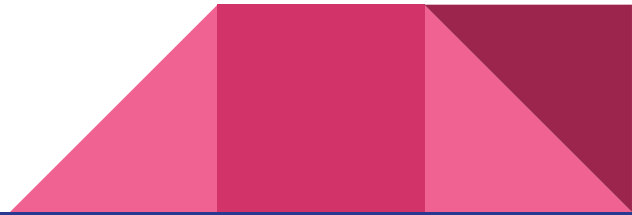
Do you have source control?

Are you suspecting an abscess/empyema somewhere?

Non-infectious causes of fever?

56 yo F with history of HTN, HLD, and recent necrotizing fasciitis in gluteal region s/p antibiotic treatment and surgical debridement x3 who is transferred from the floor for T 38.8C and persistently low BP. She was placed on vancomycin and zosyn after her first fever 3 days ago. Colorectal surgery evaluated her- it's not recurrent necrotizing fasciitis. She developed hives which was thought to be due to zosyn, so she was switched to meropenem. BP's are 80s systolic/60s diastolic despite fluid boluses. Patient is completely asymptomatic other than some lightheadedness. Exam is unremarkable other than gluteal region - though not concerning for any new process.

What to do...



No source of infection despite thorough workup?

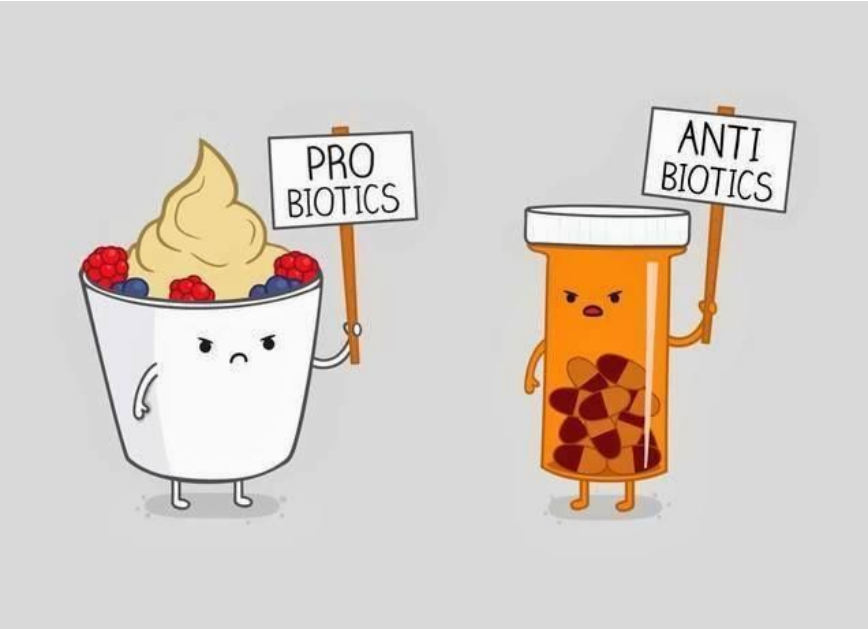
Culture NGTD?

Patient developing systemic signs but they don’t seem infected?

Eosinophils creeping up?

STOP THE ANTIBIOTICS.

*Diagnosis of exclusion*



# DRESS

**Scoring system for classifying drug reactions with eosinophilia and systemic symptoms (DRESS)**

| Item | | Present | Absent |
|---|---|---|---|
| Fever ≥38.5°C (101.3°F) | | 0 | −1 |
| Enlarged lymph nodes (>1 cm size, at least two sites) | | 1 | 0 |
| Eosinophilia: ≥700 or ≥10 percent (leucopenia) | ≥1500 or ≥20 percent (leucopenia) | 1 \| 2 | 0 |
| Atypical lymphocytes | | 1 | 0 |
| Rash ≥50 percent of body surface area | | 1 | 0 |
| Rash suggestive (≥2 of facial edema, purpura, infiltration, desquamation) | | 1 | 0 |
| Skin biopsy suggesting alternative diagnosis | | −1 | 0 |
| Organ involvement: one | two or more | 1 \| 2 | 0 |
| Disease duration >15 days | | 0 | −2 |
| Investigation for alternative cause (blood cultures, ANA, serology for Hepatitis viruses, mycoplasma, Chlamydia) ≥3 done and negative | | 1 | 0 |

Total score <2: excluded; 2-3: possible; 4-5: probable; ≥6: definite.

# The Drug Fever Match Game

Hypersensitivity reaction

Altered thermoregulatory mechanisms

Reactions directly related to administration of the drug (phlebitis, pyrogenic contaminants)

Reactions that are direct extensions of the pharmacologic action of the drug (cell lysis, necrosis, Jarisch-Herxheimer reaction)

Idiosyncratic reactions (malignant hyperthermia, NMS, serotonin syndrome)

Solid tumor chemo agents

Post-Syphilis Tx

Haloperidol

Carbamazepine, Phenytoin

Anticholinergics

**Table 2.** Manifestations of Severe Serotonin Syndrome and Related Clinical Conditions.

| Condition | Medication History | Time Needed for Condition to Develop | Vital Signs | Pupils | Mucosa | Skin | Bowel Sounds | Neuromuscular Tone | Reflexes | Mental Status |
|---|---|---|---|---|---|---|---|---|---|---|
| Serotonin syndrome | Proserotonergic drug | <12 hr | Hypertension, tachycardia, tachypnea, hyperthermia (>41.1°C) | Mydriasis | Sialorrhea | Diaphoresis | Hyperactive | Increased, predominantly in lower extremities | Hyperreflexia, clonus (unless masked by increased muscle tone) | Agitation, coma |
| Anticholinergic "toxidrome" | Anticholinergic agent | <12 hr | Hypertension (mild), tachycardia, tachypnea, hyperthermia (typically 38.8°C or less) | Mydriasis | Dry | Erythema, hot and dry to touch | Decreased or absent | Normal | Normal | Agitated delirium |
| Neuroleptic malignant syndrome | Dopamine antagonist | 1–3 days | Hypertension, tachycardia, tachypnea, hyperthermia (>41.1°C) | Normal | Sialorrhea | Pallor, diaphoresis | Normal or decreased | "Lead-pipe" rigidity present in all muscle groups | Bradyreflexia | Stupor, alert mutism, coma |
| Malignant hyperthermia | Inhalational anesthesia | 30 min to 24 hr after administration of inhalational anesthesia or succinylcholine | Hypertension, tachycardia, tachypnea, hyperthermia (can be as high as 46.0°C) | Normal | Normal | Mottled appearance, diaphoresis | Decreased | Rigor mortis–like rigidity | Hyporeflexia | Agitation |

# Hyperthermia (vs Fever)

-Heat stroke, metabolic, drug-induced

-Risk for heat stroke increases with T> 40C

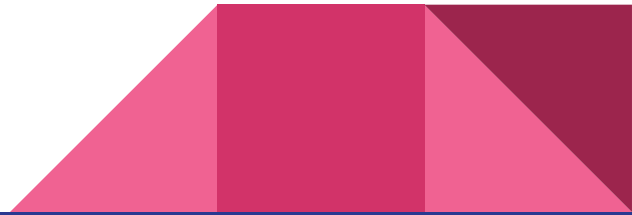
-Unchanged thermoregulatory setting, so your body isn't responding properly to lose heat

-Exogenous heat exposure and/or endogenous heat production can lead to dangerously high temperatures

-Rapidly fatal so important to differentiate from fever!

Treatment: Rapid reduction of body temperature by

*physical* means, tx underlying cause



# Summary

Fever doesn’t always mean infection- there’s a broad differential

Your exam is still your most valuable data

Not everyone needs cultures and/or empiric antibiotics

...except if you’re neutropenic. Or septic. Or your clinical judgement says so.

If all else fails, blame the drugs.

Cleveland is the new Ibiza.

# Thank You!

# Questions?