Chapter 9 – Fever in the Adult Patient

NOTE: CONTENT CONTAINED IN THIS DOCUMENT IS TAKEN FROM ROSEN'S EMERGENCY MEDICINE 9th Ed.

Italicized text is quoted directly from Rosen's.

Key Concepts:

1. *Younger adults with fever usually have benign self-limited disease, with low mortality. The challenge in this group is to identify the rare meningitis or septic condition when confronted with a predominance of self-limited viral and focal bacterial illness.*
2. *For older patients, immunosuppressed patients, or those with chronic disease, fever indicates a high risk for serious disease. Temperature elevation may be minimal in these patients, who often are unable to mount a significant febrile response to serious infection. Bacterial infection is the most common cause of fever in these patients. Three body systems—the respiratory tract, urinary tract, and skin and soft tissue—are the target for more than 80% of these infections.*
3. *Atypical symptoms of illness are common in older febrile patients. Altered mental status, difficulty with ambulation, frequent falls, and general functional decline may be the only signs of serious infection in older patients.*
4. *The white blood cell count is not a discriminatory test for patients with fever, may incorrectly indicate serious infection when none is present, or may be normal in the presence of life-threatening infection.*
5. *In febrile patients with serious signs and symptoms, early empirical antibiotic therapy is often appropriate. The choice of antibiotics is based on the likely cause of the fever as well as concomitant conditions, such as absolute neutropenia and end-stage renal disease.*

Rosen's In Perspective

You pick up a chart, look at the vitals, and you have a temp of 38.3ºC staring back at you? Do you care? What do you do? Young, healthy adults with fever rarely have serious disease as a cause. However, older patients and immunocompromised patients (or IVDU patients, if you work in a center like ours) can have serious underlying disease with fever. Additionally, MRSA patients, patients with indwelling catheters/devices, and neutropenic patients represent some additional high-risk subsets of our patient population who can be harbouring serious pathology. Aside from infectious causes of fever, one must also consider whether or not this patient has an elevated temperature because of an autoimmune of malignant process. While more uncommon,

these conditions often cause fevers in our most vulnerable patients. So, with all of that in mind, WHAT WILL YOU DO?

The answer: do not fret. Owen and I have got you covered. Today's podcast will give you a solid foundation of knowledge to inform your approach to the febrile patient. We will review the pathophysiologic process behind fever, common infectious and non-infectious aetiologies of fever, and core information about the febrile patient that will allow you to risk stratify your next elderly man with a temperature of 38.6ºC.

As always, these podcasts are meant to serve as a jumping off point. We encourage you guys to read the chapter in Rosen's and use our flashcard decks to reinforce the concepts you learn with us today. Additionally, we want you guys to push to expand your knowledge by reviewing the most current and up-to-date literature surrounding the topics we present. Spaced repetition is KEY, so make sure you are doing the best to consistently expose and re-expose yourselves to these topics.

Core Questions:

1. What structure controls body temperature and how does it go about controlling it?
2. What are pyrogens and how are they classified?
3. What is the difference between fever and hyperthermia?
4. What is the role of PGE2 in fever and what medications can you give to combat its effects?
5. List four factors that blunt the febrile response.
6. What are the benefits and pitfalls of the febrile response?
7. List five infectious and five non-infectious causes of fever. (see Box/Table 9.1)
8. Describe your approach to the febrile patient. (see Figure 9.1/9.2)

Wisecracks:

1. What is the most accurate temperature measurement site?
2. How are heart rate and body temperature related?
3. How are respiratory rate and body temperature related?
4. How high must a fever be to necessitate rapid cooling interventions?

Core Questions:

[1] What structure controls body temperature and how does it go about controlling it?

Alright, let's hop in our Delorean and gun it back 4-8 years to the first months of medical school. We are starting off the episode right with some good old neuroanatomy.

Body temperature is controlled by the preoptic region of the hypothalamus. This region accomplishes this by utilizing neurons that directly monitor body temperature. If an alteration in temperature must be made, the hypothalamus can alter peripheral vasomotor tone, induce or quell the shivering response, augment baseline metabolic heat production, and prompt behavioural changes that can either reduce or enhance heat production/loss.

It is important to note that there is a normal physiologic circadian variation in body temperature. Body temperature tends to be lower in the morning and higher in the late afternoon.

[2] What are pyrogens and how are they classified?

A pyrogen is any substance that has the capacity to trigger a febrile response. These substances are classified as either being an endogenous or exogenous pyrogen. Endogenous pyrogens are produced by the body whereas exogenous pyrogens are either directly from outside the body or produced by a microorganism. Endogenous pyrogens include any number of cytokines produced by leukocytes in response to infectious, neoplastic, inflammatory processes (think interleukins, tumor necrosis factor, interferon). Exogenous cytokines include all of the weird and wonderful viruses, bacteria, exotoxins, and endotoxins that your friendly neighbourhood microbiologist obsesses about on a daily basis.

[3] What is the difference between fever and hyperthermia?

Oh my lanta. This is something that is asked not infrequently as a good ol' pimper. Do not fear - we have a concise answer to get you those points on shift.

Fever is an issue with internal heat generation whereas hyperthermia is an issue with heat dissipation.

When an individual is suffering from hyperthermia (e.g., Kenyan marathoner running in 45ºCheat) they are unable to effectively lose body heat. Their problem is not in the hypothalamus, their issue is that they cannot cool themselves down. As a result, core body temperatures soar, with measured temperatures often reading >41.0ºC.
When you see temperatures this high, always keep hyperthermia on your differential, but do not forget the other causes of fever that we will review later.

[4] What is the role of PGE2 in fever and what medications can you give to combat its effects?

Prostaglandin E2 (PGE2) is perhaps the most important substance to consider when attempting to understand the pathogenesis of fever. This magical molecule provides the hypothalamus with the means to alter body temperature. When needed, the hypothalamus will produce PGE2 to raise core body temperature. This substance increases basal metabolic heat production, changes peripheral vasomotor tone, prompts shivering, and prompts changes in behaviour to increase heat production/conservation. As long as PGE2 levels remain high, the fever is maintained. Once they fall, the fever will dissipate.

Induction of prostaglandin production in the hypothalamus is the primary mechanism by which pyrogens bring about fever. All of those endogenous and exogenous substances push the hypothalamus out of its comfort zone, and bring about systemic changes to make your patient hot and sweaty. Exposure to PGE2 will similarly bring about fevers in your patients. Think about that obstetrical patient who gets a fever after receiving cervidil...it may simply be a side effect of the medication.

So, what medications can we give for this? Simple - give them medications that inhibit PGE2 production. Both acetaminophen and NSAIDs do this. There is no evidence to suggest that giving these medications affects morbidity and mortality in our febrile patients; however, patients often feel more comfortable after their fever is broken, so consider ordering some Tylenol the next time you encounter the febrile patient.

It is important to note that there are other substances and pathways that regulate body temperature. However, understanding the role of PGE2 in fever is essential; so, commit this stuff to memory.

[5] List four factors that blunt the febrile response.

Four factors that blunt the febrile response:

1. Advanced Age
2. Immunosuppression
3. Malnutrition
4. Chronic Disease

[6] What are the benefits and pitfalls of the febrile response?

Benefits of the febrile response include:

- Increased chemotaxis
- Decreased microbial replication
- Improved lymphocyte functioning
- Direct inhibition of bacterial or viral growth

Pitfalls of the febrile response include:

- Increased oxygen consumption
- Increased metabolic demands
- Protein breakdown
- Increased gluconeogenesis

These are problematic in patients with poor physiologic reserve.

[7] List five infectious and five non-infectious causes of fever. (See Box/Table 9.1)

Alright, time to get into the tables, figures, and boxes of Rosen's. Specifically, this question will be answered using the information contained within Box 9.1 and Table 9.1 in Rosen's 9th Edition. Along with giving us the answers we seek, these seemingly endless lists force us to consider a wide differential for every febrile patient. So often, we view every fever as the consequence of some infectious process; however, you need to think about other critical diagnoses like neoplasm or autoimmune disease when you see those triage vitals.

Adapted from Table 9.1 in Rosen's 9th Edition

Infectious Causes of Fever - Differential Diagnoses			
Organ System	**Critical Diagnoses**	**Emergent Diagnoses**	**Non-emergent Diagnoses**
Respiratory	Bacterial pneumonia with respiratory failure	Bacterial pneumonia, peritonsillar abscess, retropharyngeal abscess, epiglottitis	Otitis media, sinusitis, pharyngitis, bronchitis, influenza, tuberculosis
Cardiovascular	nil	Endocarditis, pericarditis	nil
Gastrointestinal	Peritonitis	Appendicitis, cholecystitis, diverticulitis, intraabdominal abscess	Colitis or enteritis

Genitourinary	nil	Pyelonephritis, tuboovarian abscess, pelvic inflammatory disease	Cystitis, epididymitis, prostatitis
Neurologic	Meningitis, cavernous sinus thrombosis	Encephalitis, brain abscess	nil
Skin and Soft Tissue	Nil	Cellulitis, infected decubitus ulcer, skin tissue abscess	nil
Systemic	Sepsis or septic shock, meningococcemia	nil	Nil

Adapted from Box 9.1 in Rosen's 9th Edition

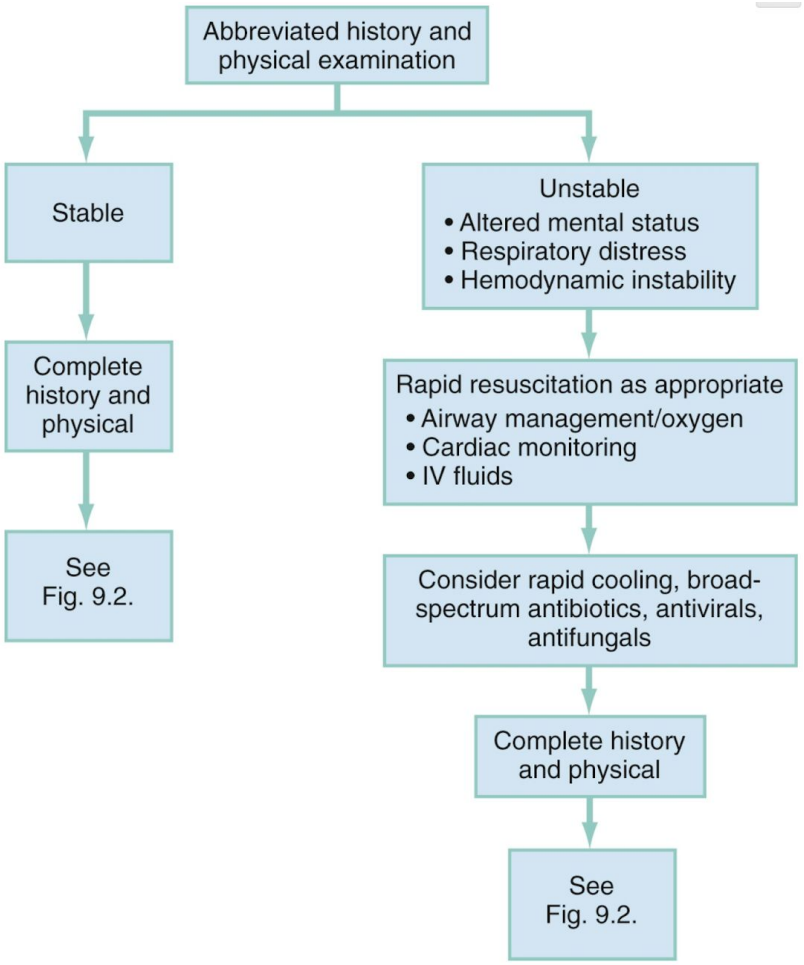
Differential Diagnosis - Noninfectious Causes of Fever		
Critical Diagnoses	**Emergent Diagnoses**	**Non-emergent Diagnoses**
• Acute myocardial infarction • Pulmonary embolism or infarction • Intracranial hemorrhage • CVA • NMS • Thyroid Storm • Acute Adrenal Insufficiency • Transfusion reaction • Pulmonary Edema	• CHF • Dehydration • Recent seizure • Sickle cell disease • Transplant rejection • Pancreatitis • DVT	• Drug fever • Malignancy • Gout • Sarcoidosis • Crohn Disease • Postcardiotomy syndrome

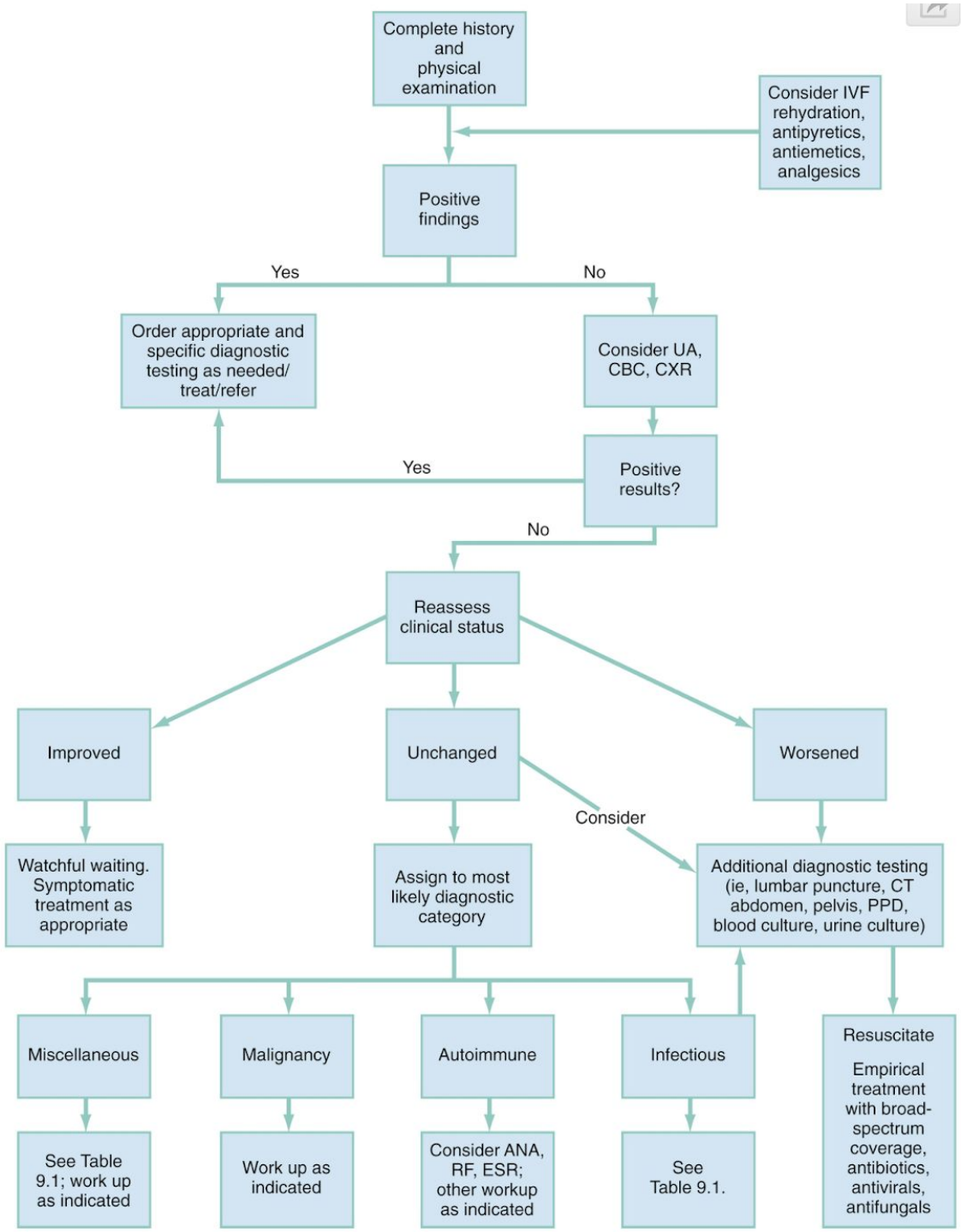
[8] Describe your approach to the febrile patient. (see Figure 9.1/9.2)

We are yet again peeling into another couple of lovely Rosen's figures. To be fair, these figures give you a pretty solid approach to the febrile patient, so we have elected to include them in the shownotes. Please take some time to look over these figures, as they will better equip you for your next shift.

Summary:

- Determine if stable or unstable
    - If stable - complete a full history and physical examination
    - If unstable (defined by altered mental status, respiratory distress, or hemodynamic instability) - resuscitate ABC's, administer broad spectrum ABx +/- antivirals +/- antifungals, and cool the patient
        - After stabilization, complete a full history and physical examination
- After a complete history and physical examination, initiate IV fluids and antimicrobial agents +/- other medications aimed at reducing burden of symptoms (anti-nauseants, anti-pyretics etc.) if not done already
- Order appropriate diagnostic tests based on positive findings
    - If exam or history is non-contributory, consider evaluating the most commonly infected systems (e.g., GU, RESP, DERM) with CXR, UA, CBC
- If no apparent cause or diagnosis made with investigations, reassess patient
    - If improved, consider watchful waiting and symptomatic management
    - If unchanged, consider work ups for malignancy, autoimmune disease, other infectious process
    - If worsening, actively resuscitate and consider LP/other lab workup and higher-order imaging studies




Complete history and physical examination
Consider IVF rehydration, antipyretics, antiemetics, analgesics
Positive findings
Yes
No
Order appropriate and specific diagnostic testing as needed/ treat/refer
Consider UA, CBC, CXR
Yes
Positive results?
No
Reassess clinical status
Improved
Unchanged
Worsened
Consider
Watchful waiting. Symptomatic treatment as appropriate
Assign to most likely diagnostic category
Additional diagnostic testing (ie, lumbar puncture, CT abdomen, pelvis, PPD, blood culture, urine culture)
Miscellaneous
Malignancy
Autoimmune
Infectious
Resuscitate
Empirical treatment with broad-spectrum coverage, antibiotics, antivirals, antifungals
See Table 9.1; work up as indicated
Work up as indicated
Consider ANA, RF, ESR; other workup as indicated
See Table 9.1.

Wisecracks:

[1] What is the most accurate temperature measurement site?

All you guys that thought that rectal temperatures were the most accurate are WRONG. The most accurate site for measuring core body temperature is the pulmonary artery using a pulmonary artery catheter. Crazy, I know. ICU just got real excited.

In all reality, we will likely never have the luxury of pulmonary artery catheters in the ED. Thus, for practicality's sake, we have to use other sites. Both rectal temperatures and bladder temperatures are the most accurate temperatures we can take in the ED. Tympanic and axillary temperatures are unreliable, and oral temperatures can be unduly influenced by recent ingestions.

[2] How are heart rate and body temperature related?

As a general rule, heart rate will increase by approximately 10 beats per second for every 0.55ºCincrease in temperature. For all of our American followers out there, that is a increase in 10 beats per minute for every 1ºF increase in body temperature.

Remember, this is a general rule. There are many situations in which you will not see this corresponding rise.

[3] How are respiratory rate and body temperature related?

The respiratory rate typically increases in the setting of fever as well. As a general rule, your patient will experience an increase in their respiratory rate by 2-4 breaths per minute with every 1ºC increase in body temperature.

[4] How high must a fever be to necessitate rapid cooling interventions?

As per Rosen's 9th Edition:

"Sustained temperatures above 41.0ºC are rare but can be damaging to neural tissues and require rapid cooling (eg. misting, fans, cooling blankets)"

While there may be some disagreement on the exact temperature above while you need to urgently cool the patient, keeping this threshold in mind is important. Above this temperature, proteins begin to denature and physiologic functioning deteriorates.