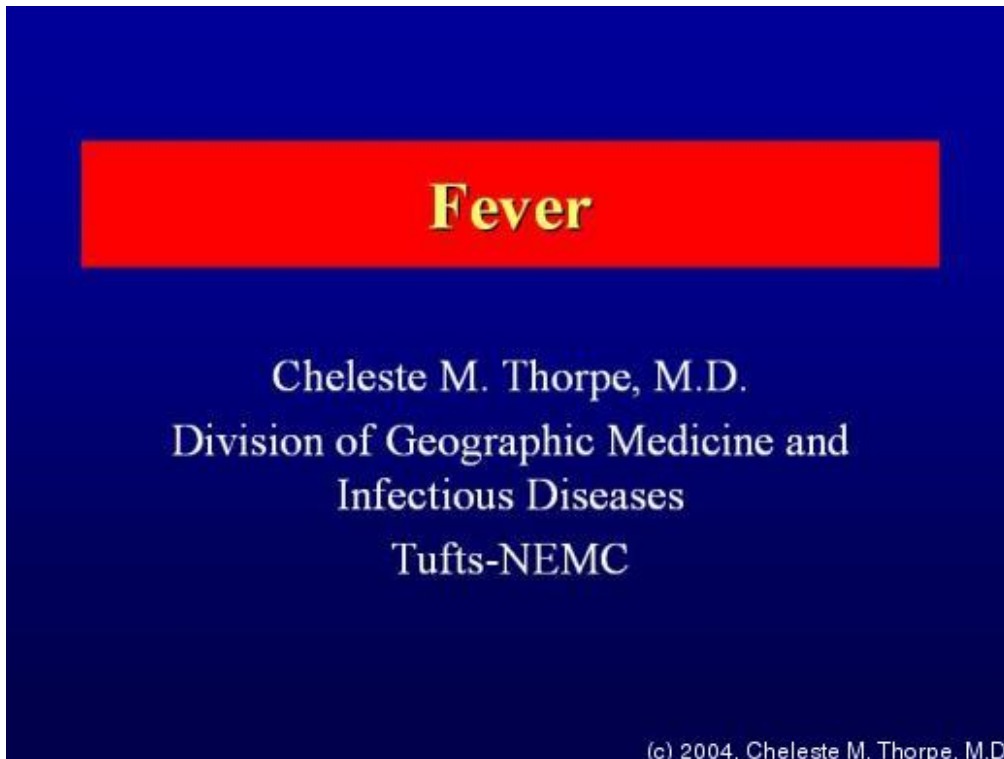


1.

Fever



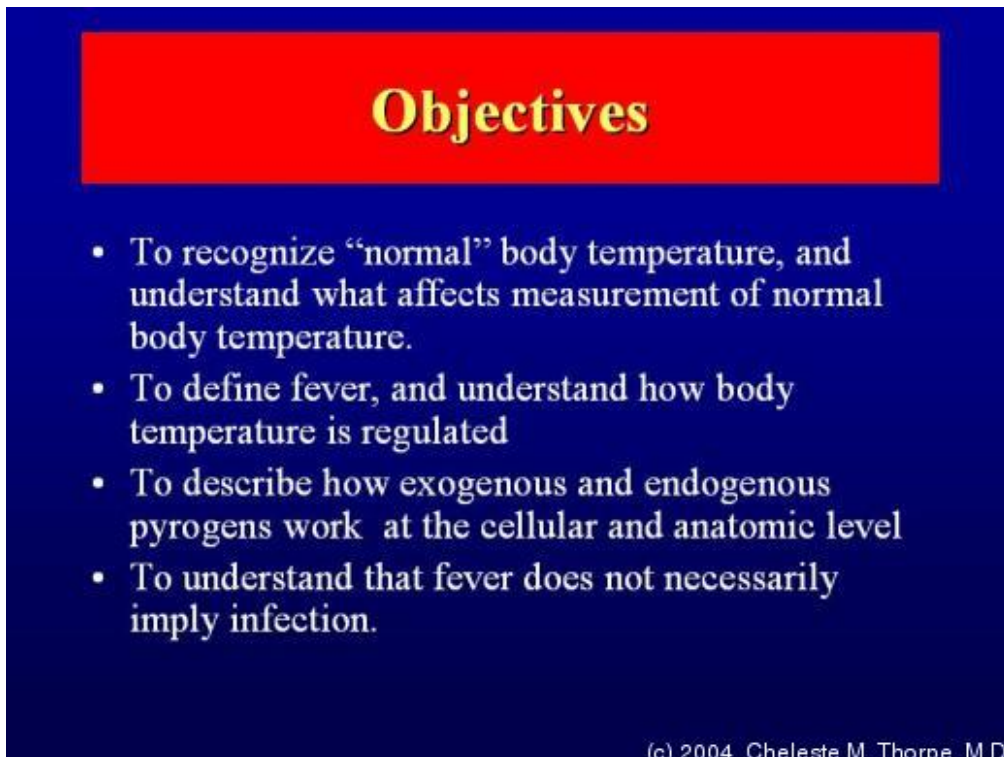
Fever

Cheleste M. Thorpe, M.D.
Division of Geographic Medicine and
Infectious Diseases
Tufts-NEMC

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2.

Objectives

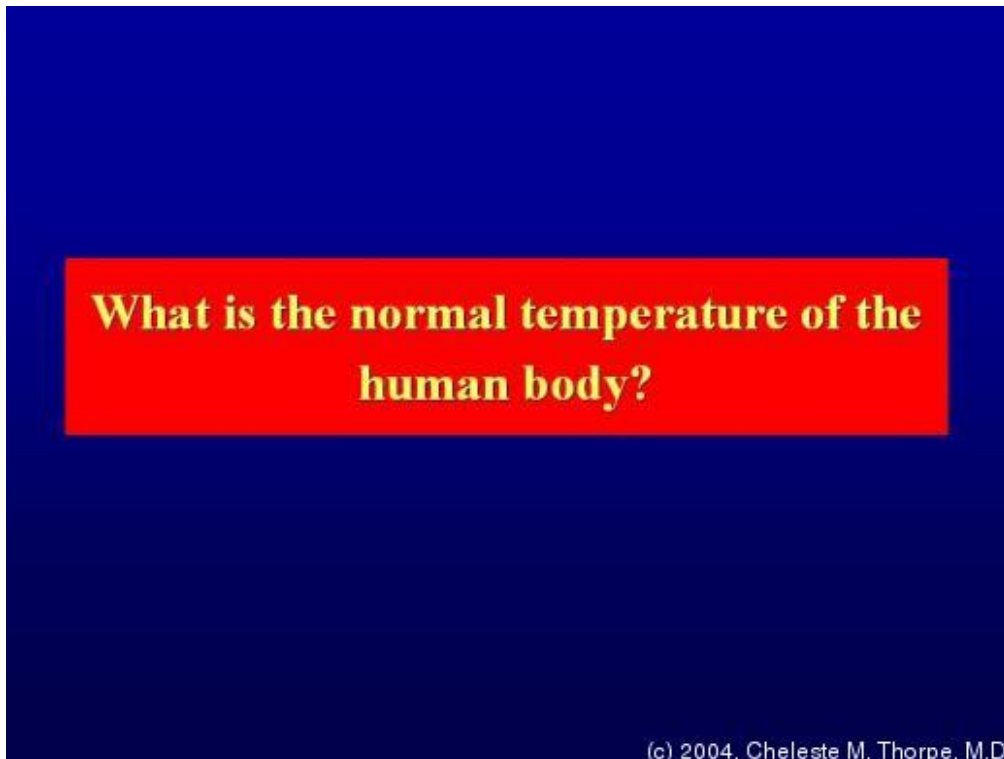


Objectives

- To recognize “normal” body temperature, and understand what affects measurement of normal body temperature.
- To define fever, and understand how body temperature is regulated
- To describe how exogenous and endogenous pyrogens work at the cellular and anatomic level
- To understand that fever does not necessarily imply infection.

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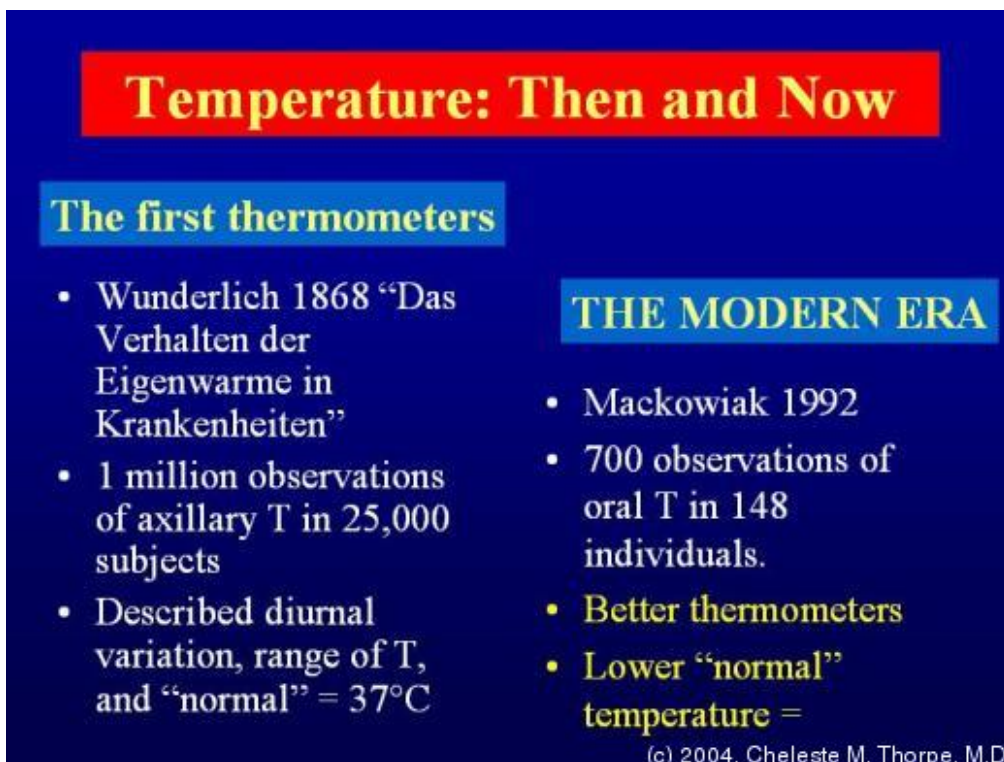
3. What is the normal temperature of the human body?



What is the normal temperature of the human body?

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4. Temperature: Then and Now



Temperature: Then and Now

The first thermometers

- Wunderlich 1868 “Das Verhalten der Eigenwärme in Krankheiten”
- 1 million observations of axillary T in 25,000 subjects
- Described diurnal variation, range of T, and “normal” = 37°C

THE MODERN ERA

- Mackowiak 1992
- 700 observations of oral T in 148 individuals.
- Better thermometers
- Lower “normal” temperature =

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5. Things that affect T measurements

Things that affect T measurements

- Drinking ice water: transient drop (less than 10 minutes, avg 0.5°F).
- Chewing gum: sustained elevation (approx. 20 minutes, avg 0.3 ° F).
- Cigarette smoking: sustained elevation (more than 30 minutes, avg 0.2 ° F).
- Exercise

– from Rabinowitz et al 1996

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6. Key points (1)

Key points

- **“Normal” temperature is a range**, with typical variation of 36.3-37.5°C, or 97.3-99.5 F orally, and a diurnal variation (higher in afternoon)
- **Body T depends on site of measurement**—rectal T usually about 1° F higher than oral T

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7. Key points (2)

Key points

- For practical purposes, 99.4 oral and 100.4 rectal generally considered “abnormal” in normal, healthy, immunocompetent adults
- Modest, transient increases in T can occur with normal daily activities

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8. Regulation of body T (1)

Regulation of body T

- Occurs through both **voluntary and involuntary** mechanisms
- Consists of both T **generating** and T **dissipating** mechanisms

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9.

Regulation of body T (2)

Regulation of body T

<p>Heat-generating:</p> <ul style="list-style-type: none">• Peripheral vasoconstriction to prevent heat loss (α-adrenergic)• Involuntary skeletal muscle contraction (shivering)• Increased catabolism	<p>Heat-dissipating:</p> <ul style="list-style-type: none">• Vasodilation to promote heat loss (β-adrenergic)• Sweating (cholinergic)
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10.

Case I (1)

Case I

- A 63 year old woman who has a history of agoraphobia, mild hypertension, and recurrent UTI's is brought to the ER by EMT's when a worried neighbor called and said she hadn't been seen for over a week. She's had dysuria for a week, and some mid back pain for 2 days, and admits she has been a little confused and "feels very hot at night." She's also been "shivering a lot".

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11.

Case I (2)

Case I

On exam, her T is 104 F, and her skin is warm. In the middle of the exam, she begins to have shaking chills. Her lungs are clear, her cardiac exam is unremarkable, she has significant tenderness over her costo-vertebral angle R>L, and some suprapubic tenderness. Urine is loaded with white blood cells with some wbc casts and many bacteria. Blood cultures obtained at the time of the ER visit grow *Escherichia coli*, as does her urine culture.

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12.

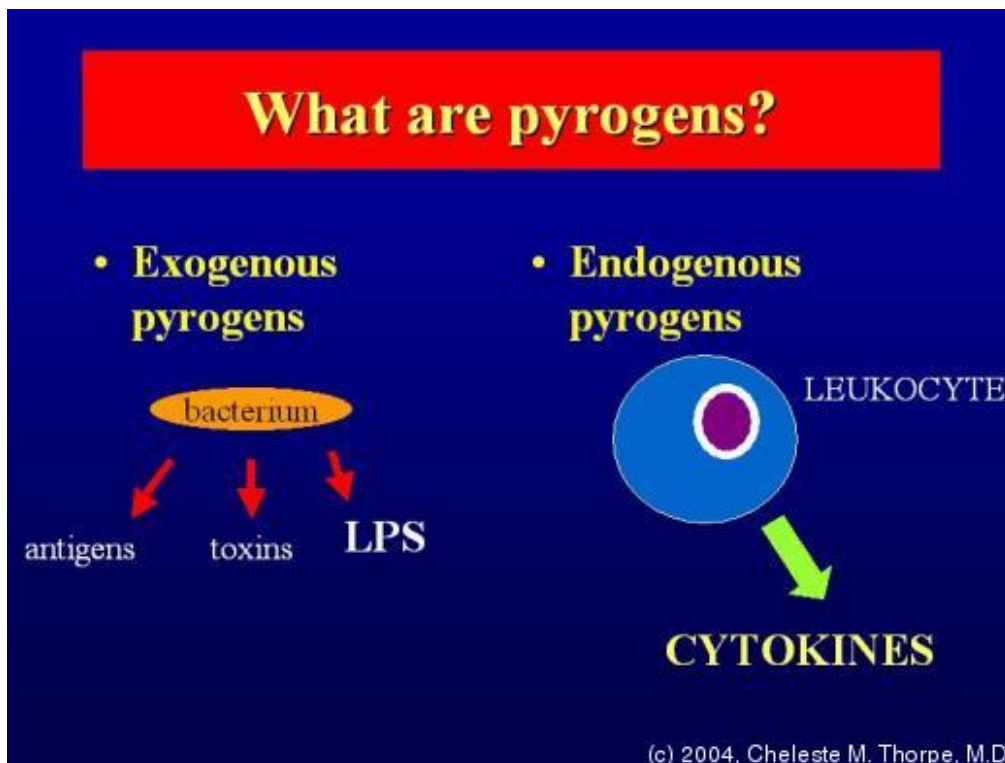
What is fever? (1)

What is fever?

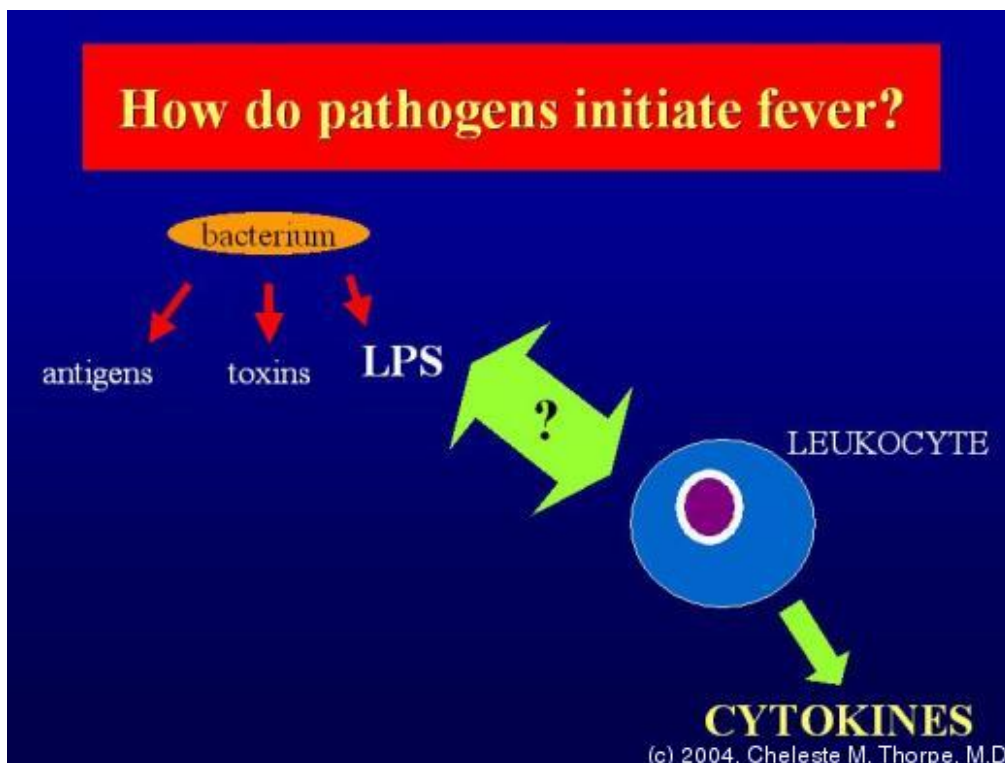
- Fever is “**a state of elevated core temperature, which is often, but not necessarily, part of the defensive responses of multicellular organisms (host) to the invasion of live (microorganisms) or inanimate matter recognized as pathogenic or alien by its host.**” - International Union of Physiological Sciences Thermal Commission, 1987.

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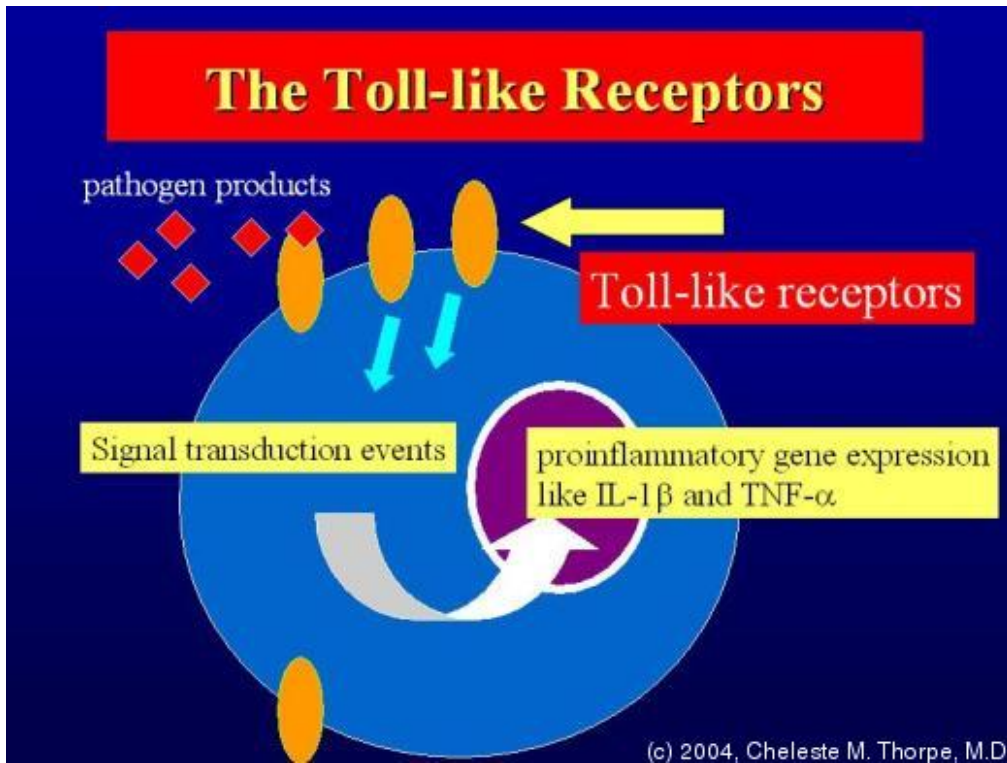
13. What are pyrogens?



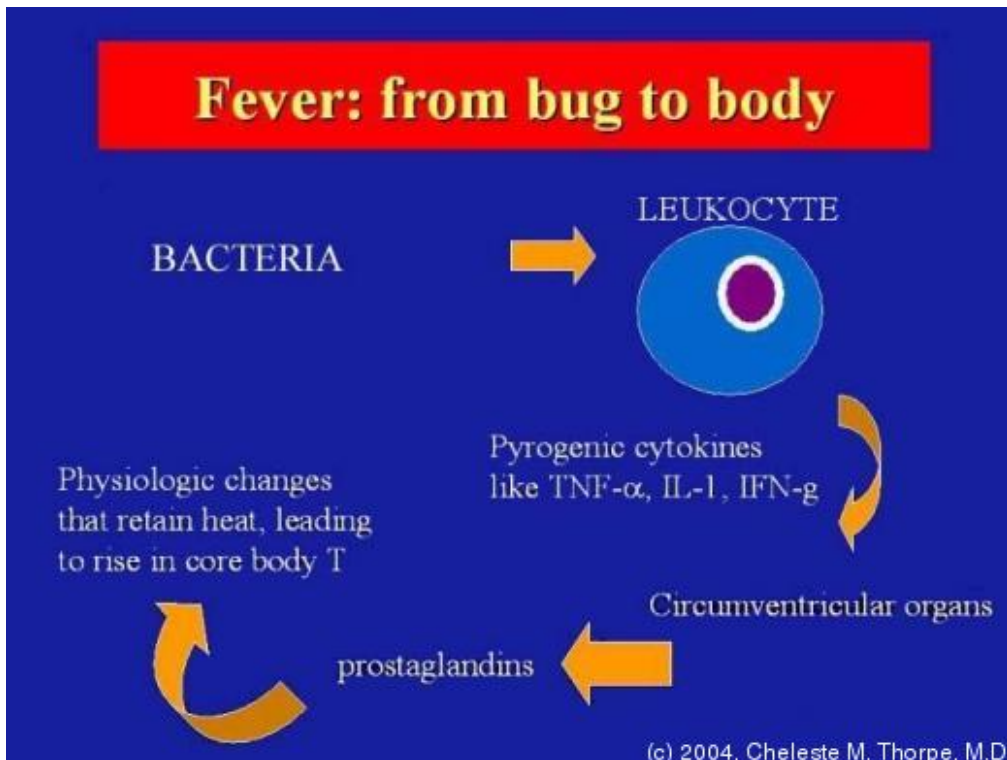
14. How do pathogens initiate fever?



15. The Toll-like Receptors



16. Fever: From Bug to Body



17.

Key points

Key points

- Know the definition of fever.
- Understand that certain exogenous pyrogens from microorganisms can act via Toll-like receptors to stimulate endogenous pyrogens.
- Recognize that TNF- α and IL-1 β are the main endogenous pyrogens.
- Know that fever is regulated via the effects of these cytokines on the circumventricular organ in the hypothalamus.

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18.


The Acute Phase Response

The Acute Phase Response

- Somnolence, lethargy, anorexia
- changes in plasma protein synthesis like increased C-reactive protein, ferritin, and decreased albumin
- changes in hormone synthesis
- inhibition of bone formation
- negative nitrogen balance, changes in lipid metabolism
- decreased serum iron, Zn
- elevated white blood cells and platelets, decreased synthesis of red blood cells

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19. What is fever? (2)

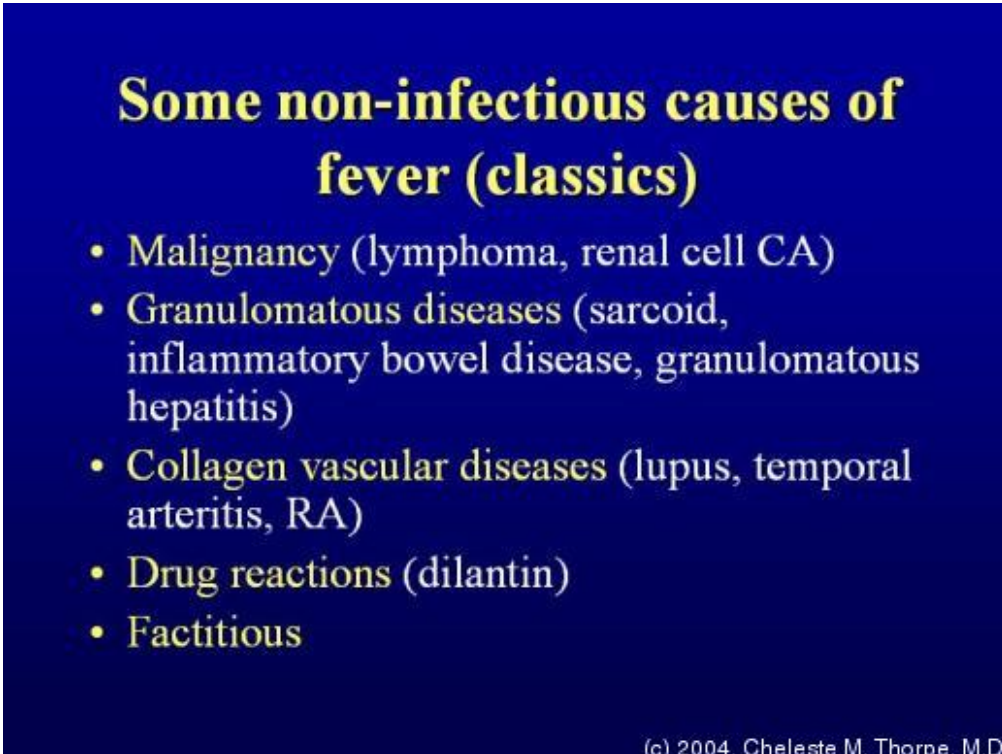


What is fever?

- Fever is “a state of elevated core temperature, which is often, **but not necessarily**, part of the defensive responses of multicellular organisms (host) to the invasion of live (microorganisms) or inanimate matter recognized as pathogenic or alien by its host.”- International Union of Physiological Sciences Thermal Commission, 1987.

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20. Some non-infectious causes of fever (classics)



Some non-infectious causes of fever (classics)

- Malignancy (lymphoma, renal cell CA)
- Granulomatous diseases (sarcoid, inflammatory bowel disease, granulomatous hepatitis)
- Collagen vascular diseases (lupus, temporal arteritis, RA)
- Drug reactions (dilantin)
- Factitious

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21. Fever of unknown origin (FUO)

Fever of unknown origin (FUO)

- T > 101 F or 38.3 C noted on multiple occasions over a 3 week period.
- Unknown cause after a reasonable intensive diagnostic evaluation over a period of approximately 1 week.
- Classic ID problem—must think of both infectious and non-infectious etiologies

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22. Explanations for Fever Throughout History

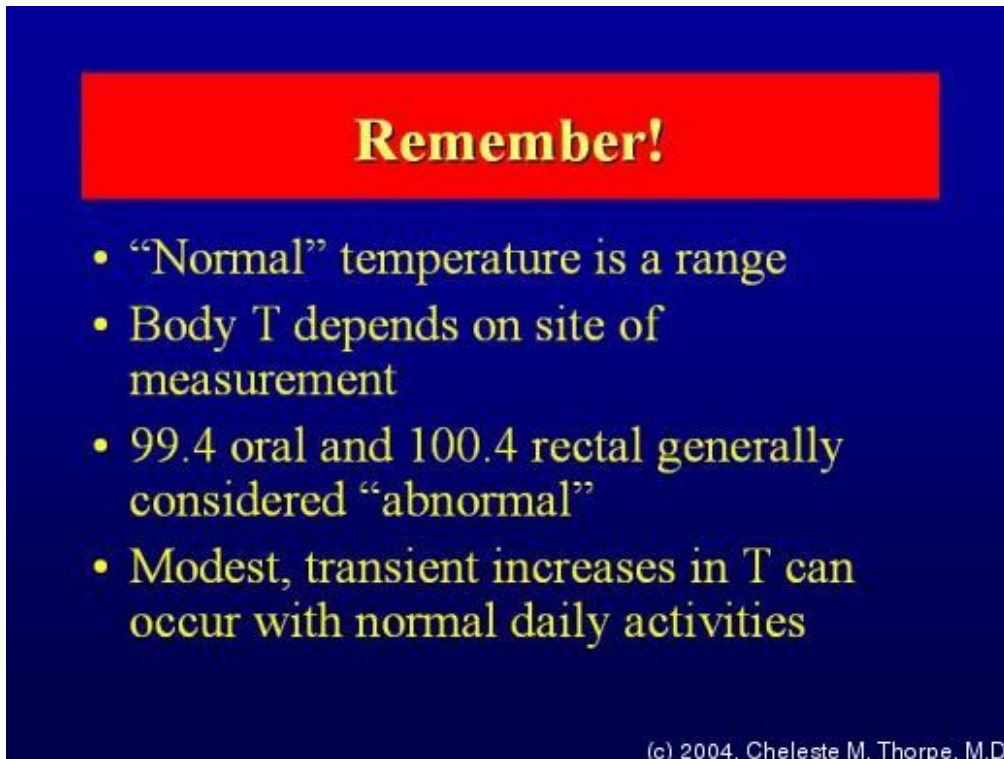
Explanations for Fever Throughout History

- “Too much yellow bile” -
Hippocrates
- “Demonic possession” -*Middle
Ages*
- “Friction of blood flow and gut
fermentation” -*18th century*

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23.

Remember! (1)

A blue rectangular slide with a red header box containing the word "Remember!" in yellow. Below the header, there is a bulleted list of four points in yellow text. At the bottom right, there is a small copyright notice in white text.

Remember!

- “Normal” temperature is a range
- Body T depends on site of measurement
- 99.4 oral and 100.4 rectal generally considered “abnormal”
- Modest, transient increases in T can occur with normal daily activities

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24.

Remember! (2)

A blue rectangular slide with a red header box containing the word "Remember!" in yellow. Below the header, the text "Involuntary heat-generating mechanisms include:" is written in yellow. This is followed by a bulleted list of three points in yellow text. At the bottom right, there is a small copyright notice in white text.

Remember!

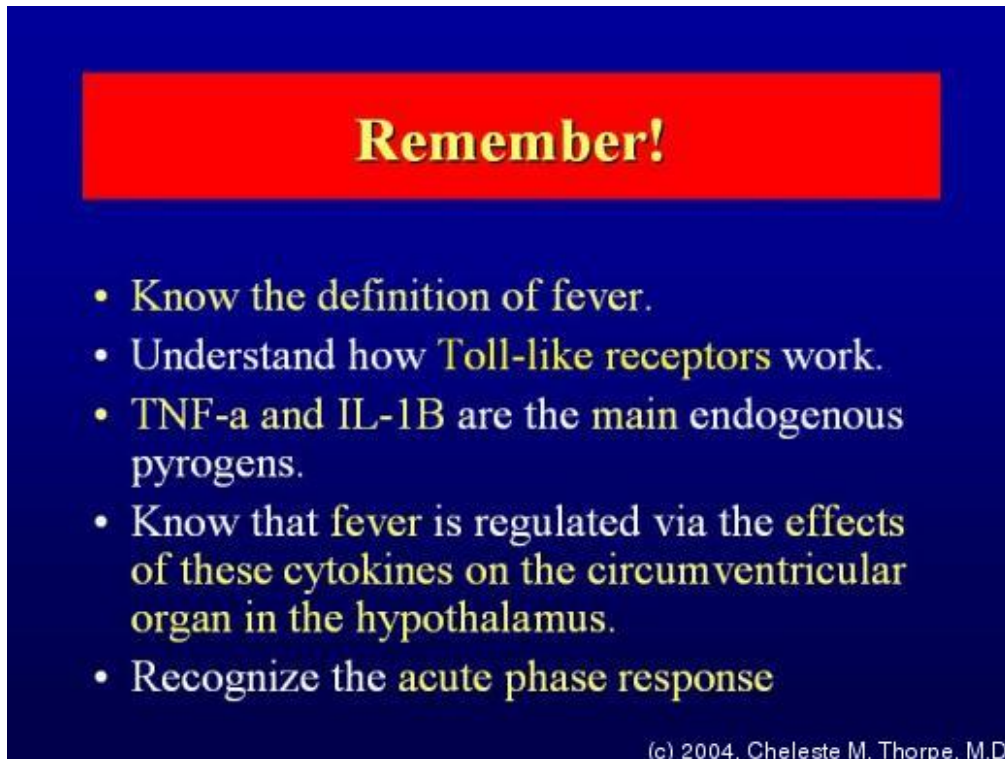
Involuntary heat-generating mechanisms include:

- **Increased catabolism**
- **Peripheral vasoconstriction**
- **Involuntary skeletal muscle contraction (shivers, rigors).**

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25.

Remember! (3)

A blue rectangular slide with a red horizontal bar at the top containing the word "Remember!" in yellow. Below the bar is a bulleted list of five items in yellow text. At the bottom right, there is a small copyright notice in white text.

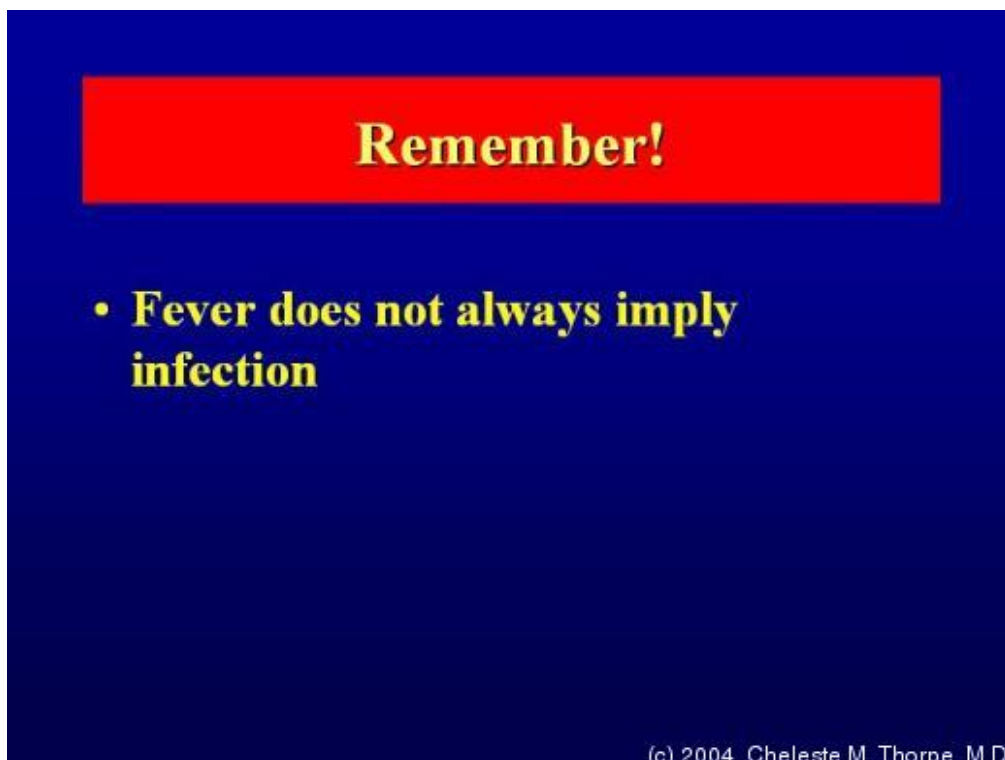
Remember!

- Know the definition of fever.
- Understand how Toll-like receptors work.
- TNF- α and IL-1 β are the main endogenous pyrogens.
- Know that fever is regulated via the effects of these cytokines on the circumventricular organ in the hypothalamus.
- Recognize the acute phase response

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26.

Remember! (4)

A blue rectangular slide with a red horizontal bar at the top containing the word "Remember!" in yellow. Below the bar is a single bullet point in yellow text. At the bottom right, there is a small copyright notice in white text.

Remember!

- **Fever does not always imply infection**

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