Fever and Febrile syndromes

TOPICS of the lecture

- Thermoregulation
- Pathogenesis of fever
- Fever only
- Fever and Rush
- Fever and Lymphadenopathy

Fever of unknown origin (FUO)

- Definition
  - Classic
  - New
- Causes
- Diagnostic strategy
• In a healthy individual, body temperature is kept constant in a very small range despite of big differences in temperature of the surroundings and also those in physical activity.

• Very perfect regulation of body temperature, necessary for optimal progress of enzymatic reactions, is developed in all homoiothermic animals.

**Mechanisms of Heat Regulation**

<table>
<thead>
<tr>
<th>To raise Body Temperature</th>
<th>To lower Body Temperature</th>
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<tbody>
<tr>
<td><strong>Heat generation</strong></td>
<td><strong>Heat loss</strong></td>
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<tr>
<td>Obligate heat production</td>
<td>Obligate heat loss</td>
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<tr>
<td>Muscular work</td>
<td>Vasodilatation</td>
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<tr>
<td>Shivering</td>
<td>Sweating</td>
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<td><strong>Heat conservation</strong></td>
<td>Cold preference</td>
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<tr>
<td>Vasoconstruction</td>
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MAJOR THERMOREGULATORY PATHWAYS I

**Skin** temperature → **Core** temperature

- Peripheral thermoreceptors (in skin)
- Central thermoreceptors (in hypothalamus, other areas of CNS and abdominal organs)

**Hypothalamic thermoregulatory integrating center**

(temperatures depicted: 20°C ← Lufttemperatur → 30°C)
Fever

>37.8 °C (100.2°)

Elevated body temperature mediated by an increase in the hypothalamic heat-regulating set point

Hyperthermia

Increase in body temp. (>41°) that overrides or bypasses the normal homeostatic mechanisms
Causes of FEVER

1. **infections** caused by bacteria, rickettsia, chlamydia, viruses, and parasites
2. **immune reactions**, including the defects in collagen, immunological abnormalities and acquired immunodeficiency
3. **destruction of tissues**, such as trauma, local necrosis (infarction), and inflammatory reaction in tissues and vessels (flebitis, arteritis), pulmonary infarction, cerebral and myocardial infarction, and rhabdomyolysis
4. **specific inflammations** (sarcoidosis, granulomatous hepatitis)
5. **inflammation** of intestine and intraabdominal inflammatory processes
6. **neoplastic processes** with the participation of lymphoendothelial system and hemopoietic system, solid tumours (Grawitz tumour of the kidney, carcinoma of the pancreas, pulmonary and skeletal tumours, hepatoma) Fever is present in complications of solid tumours, usually in metastases that are associated with necrosis of the tumour, obstruction of ducts, or with infection
7. **acute metabolic failures** such as arthritis urica, porphyria, Addison's crisis, thyreotoxic crisis, and feochromocytoma
8. **administration of some drugs**
9. **dehydration or administration of salts**.
10. **administration of foreign proteins** (e.g. globulinum antitetanicium-antitoxic fraction of horse serum)
11. **Factitious of self-induced fever**
TYPES OF FEVER

1. *febris continua* is fever in which the temperature changes are less than 1 °C in 24 hours

2. *febris septica-hectica* is fever in which the swings are 3 °C

3. *febris remittens* is fever with big temperature swings

4. *febris intermittens* is fever characterized by several hours lasting apyretic periods

5. *febris recurrens* is fever that reoccurs after several days

6. *febris inversa* means that fever is higher in the morning than in the evening. This is typical for patients suffering from tuberculosis.
In fever, important changes occur in the function of organism

- tachycardia, extrasystoles
- Blood pressure increases than decreases \rightarrow \text{bradycardia}
- Oliguria caused by evaporation and sweating
- defect in secretion of digestive juices is observed associated with motor disorder
- Hyperglycemia
- Metabolic acidosis
- Changes in mental conditions
- Herpes
Utility of fever

• increases immune reactions, increases chemotactic, phagocytic, and bactericidal activity of polymorphonuclear leucocytes, stimulates the processes of antibody production.

• body defends itself against microbes but also against replication of viruses

Harmful effects of fever

• Increased basal metabolism, minute heart volume, and water and salt loses may complicate other basic illnesses.

• Very high temperature suppress immune mechanisms.

• Longlasting fever causes dysfunctions of parenchymal organs. It is so in malignant (extreme) fever, febrile spasms, epilepsy, cardiac problems, and the disease of the central nervous system.
Infections producing Fever and Rush

Maculopapular Erythematous
- Enterovirus
- EBV, CMV, Toxoplasma gondii
- HIV
- Colorado tick fever
- Salmonella thyphi
- Leptospira interrogans
- Measles virus
- Rubella virus
- Hepatitis B virus
- Treponema pallidum
- Parvovirus B19
- Human herpesvirus 6

Cutaneous petechiae
- Neisseria gonorrhoea
- N. meningitidis
- Rickettsia rickettsii (RMSF)
- Ehrlichia chaffeensis
- Echoviruses
- Viridans-streptococci (endocarditis)

Diffuse erythroderma
- Group A streptococci (scarlet fever, toxic shock syndr.)
- Staphylococcus aureus (toxic shock syndr.)

Vesicular
- Varicella-zoster
- Herpes simplex virus
- Coxackie A virus
- Vibrio vulnificus

Mucous membrane lesions
- Vesicular pharyngitis – Coxackie A virus
- Palatal petechiae – rubella, EBV, Scarlet fever

Distinctive rush
- Ecthymia gangrenosum –
- Pseudomonas aeruginosa
- Erythema chronicum migrans – Lyme disease
- Erythema – toxic shock syndr.
- Oral ulceronodular lesion –

Histoplasma capsulatum
- Koplik’s spots – measles virus
### Infections with Fever and Lymphadenomegaly

**(generalized)**

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<tr>
<th>Viral</th>
<th>Bacterial</th>
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<tr>
<td>Measles</td>
<td>Scarlet fever</td>
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<tr>
<td>Rubeola</td>
<td>Brucellosis</td>
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<tr>
<td>Hepatitis B</td>
<td>Leptospirosis</td>
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<td></td>
<td>Tuberculosis</td>
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<td>Syphilis</td>
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<td>Lyme disease</td>
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### Infections with Fever and Lymphadenomegaly

**(regional)**

| Pyogenic infection     | Staphylococcus aureus, Streptococcus                  |
| Tuberculosis           | Scrofula (tbc. Cervical adenitis)                     |
| Cat-scratch disease    | Bartonella                                           |
| Ulceroglandular fever  | Tularemia                                            |
| Oculoglandular fever   | Tularemia, sporotrichosis, etc.                      |
| Inguinal lymphadenopathy| Syphilis, herpes                                     |
| Plague                 | Yersinia pestis                                      |
DIAGNOSTIC EVALUATION

Comprehensive history
- Illness, medical intervention, medication
- Journey
- Profession
- Age
- Animal contact
- Season
- Contact infection

Physical examinations
- Skin and bellies
- Lymphnodes
- Respiration
- Splenomegala
- Rectal digital exam.
- Sore when touched muscles, bones and articulations
- Muscles, bones and articulations
- Nervous system

LABOR
- X-Ray, CT, MRI, PET, ultrasonic exam.
FUO

Definition changed

1961 Petersdorf RB et al.
1991 Durack DT et al.

More than 200 diseases
Major diagnostic challenge

1. Fever $\geq 38.3^\circ$C ($>101^\circ$F) on several occasions

2. Duration $\geq 3$ weeks

3. Failure to reach a diagnosis despite
   1 week appropriate in-hospital investigation
   or 3 outpatient visits

Classical FUO
Nosocomial FUO
Neutropenic FUO
HIV-associated FUO
Algorithm for the Diagnosis of FUO

Complete history and physical assessment

Positive findings

Order appropriate and specific diagnostic testing

blood culture, urinalysis, urine culture, PPD skin test, chest radiograph

Positive results

Order appropriate follow-up diagnostic testing

No

CT of abdomen / pelvis with contrast

Assign most likely category

Infection Malignancies Autoimmune
THANK YOU FOR YOUR ATTENTION!