

Lecture datafile
Medical faculty 3rd year
Winter semester

GENERAL MEDICINE
DENTISTRY

FEVER - Basics

R.Beňačka, MD, PhD

Department of Pathophysiology
Medical faculty, P.J.Šafarik University
Košice, Slovakia

Termoregulation, terminology

- **Thermoregulation** = active maintenance of body core temperature at relatively stable level irrespective of outer temperature (homoeothermic) as adapted to body needs (important part of homeostasis)
- **Homoeothermic** (mammals) vs poikilothermic (amphibians); **endothermic** vs. exothermic
- Mechanisms of maintenance: **physiological** (thermogenesis, vasoconstriction, shivering; **behavioral** (clothing, sheltering, avoiding of thermally non-habitable zones)
- Heat production: liver (increases ~10-times during catabolism), muscles (during activity (30-40x), brain, heart, brown adipose,
- Heat dissipation: vasodilation, sweating, breathing, conduction, cold water bath
- **Normal body temperature (T_t)**: As measured in **axilla** T_t varies in a range of **36-37 °C**; average in adults (18-40 y.) = **36,4 ± 0,4 °C**; in **rectum** + **0,5 °C** (36,5 - 37,5 °C), in **oral cavity** + **0,3°C** (36,3 - 37,3°C).
- **Daily temperaire fluctuations** T_t varies mostly within ± 1°C; Slightly larger deviations are in young. The lowest temperature T_{min} is acxhived in the early morning in bed rest (2-6 h), highest (T_{max}) between 16-18 h

Termoregulatory zones

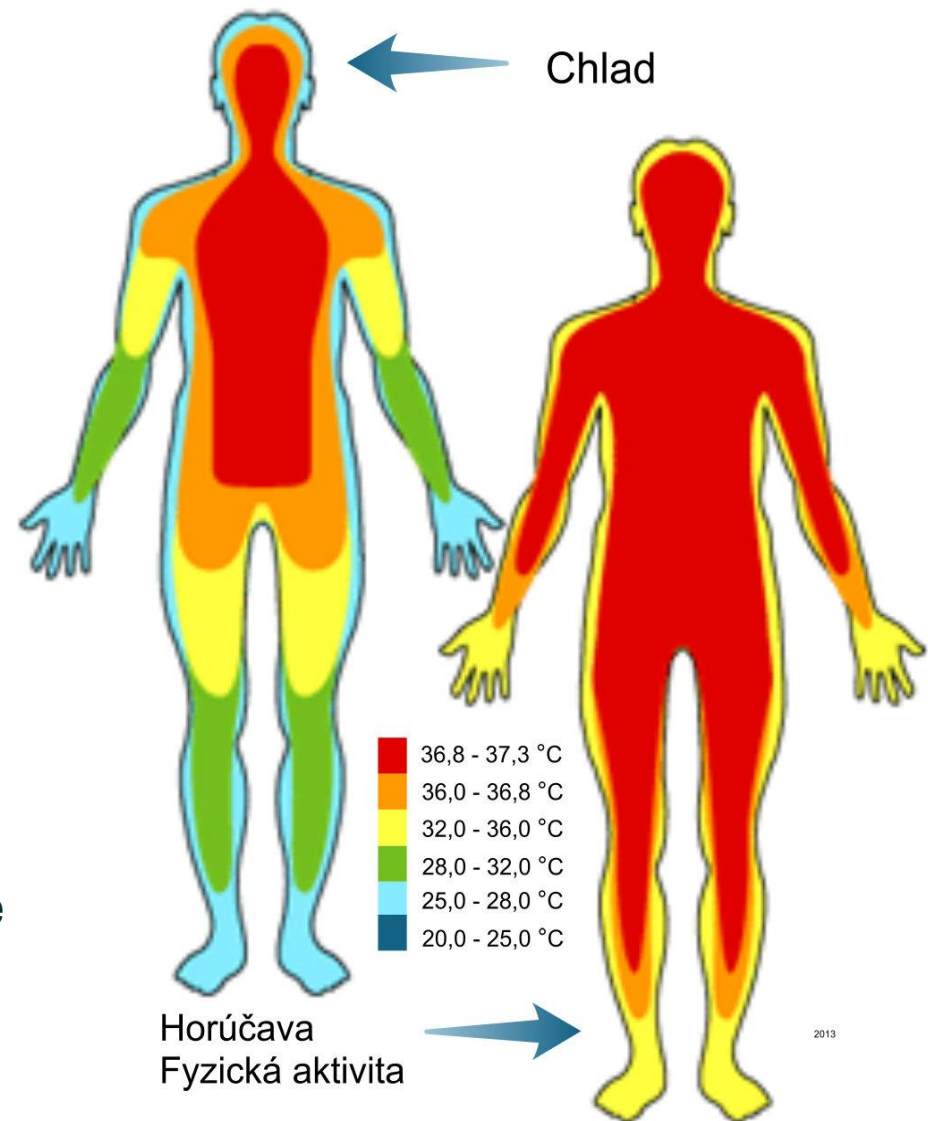
Body areas according to the thermal stability:

(a) Inner core (supercore) = temperature change does not exceed 1 °C; kept at 37 °C; does not change with outdoor temperature (-20 °C or + 40 °C); mediastinum, aorta/ large blood vessels, lungs-small circulation, heart, liver, brain, spinal cord, epi/mezogastrium, periaortal (stomach, pancreas, spleen, intestines)

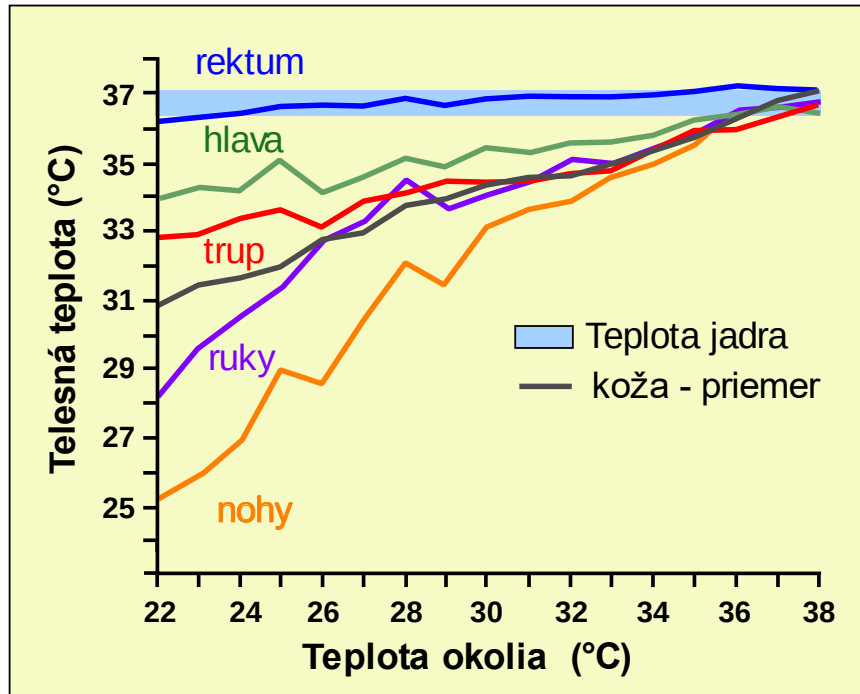
(b) Body core (body core) = temperature changes should not exceed 1-2 °C; The range of the area varies with external changes = whole abdomen (intestine, colon, uterus, bladder, kidney; muscles, tissues around the vessels on the limbs- axilla, inguines, neck

(c) Inner casing (inner bodyshell) = temperature changes in the range 5-10 °C (muscles covering the torso, back, limbs, bones, tendons, scrotum

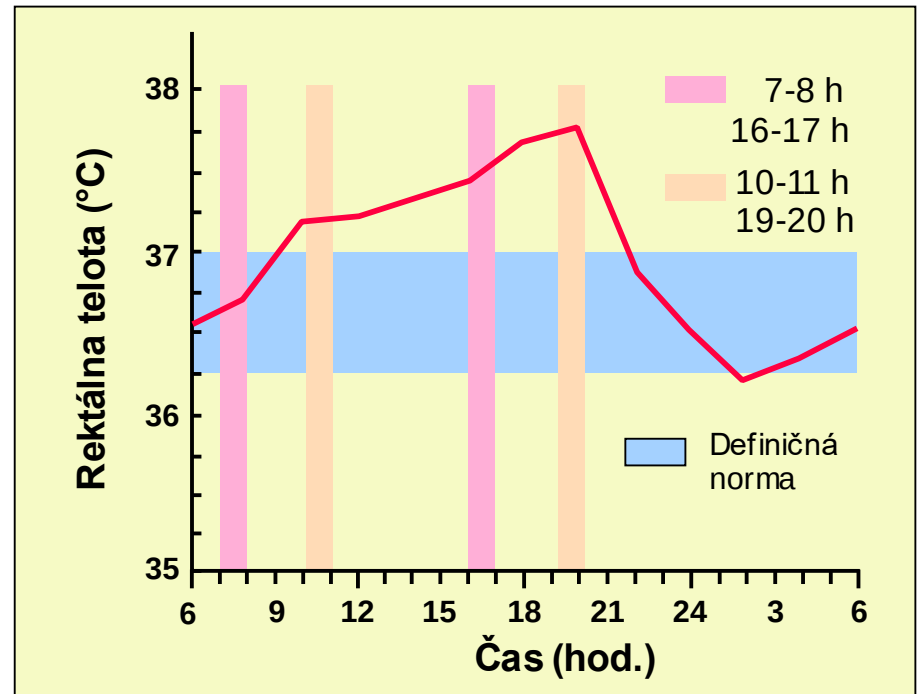
(d) outer sheath (bodyshell) = changes of up to 15-20 °C; depending on the external temperature (skin, subcutaneous tissue).



Changes of the body temperature during the day



Changes of the surface temperature on various body parts as dependent on environmental temperature. (C)
Blue is the range defined as normal body core temperature.



Normal diurnal variations of the temperature.

Usual 2-time or 4-times scheme of temperature measurement. Blue = norm. Temperature is lowest early in the morning and rises up during the day, achieving a maxima in the evening.

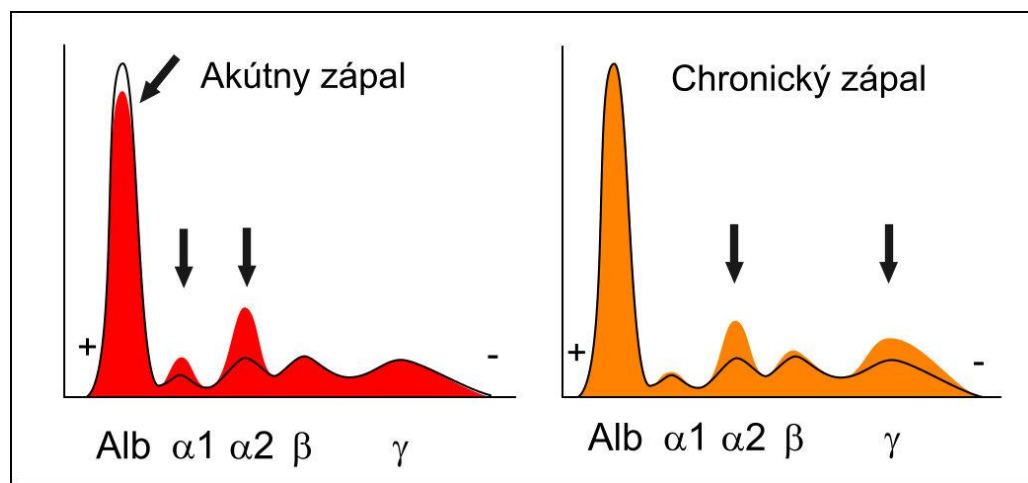
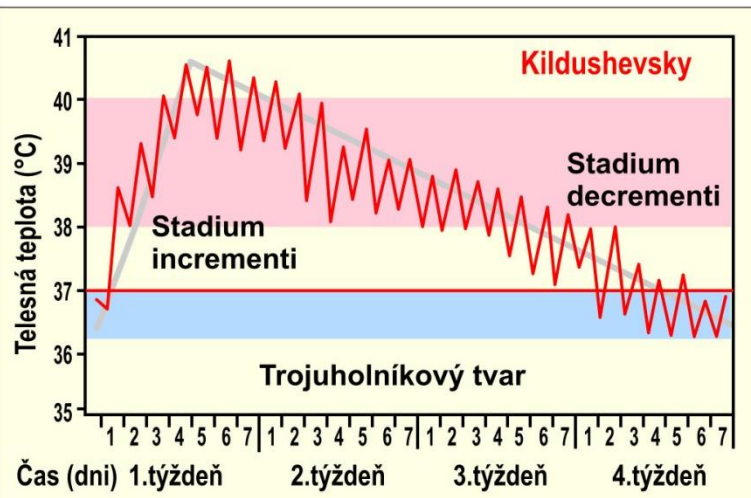
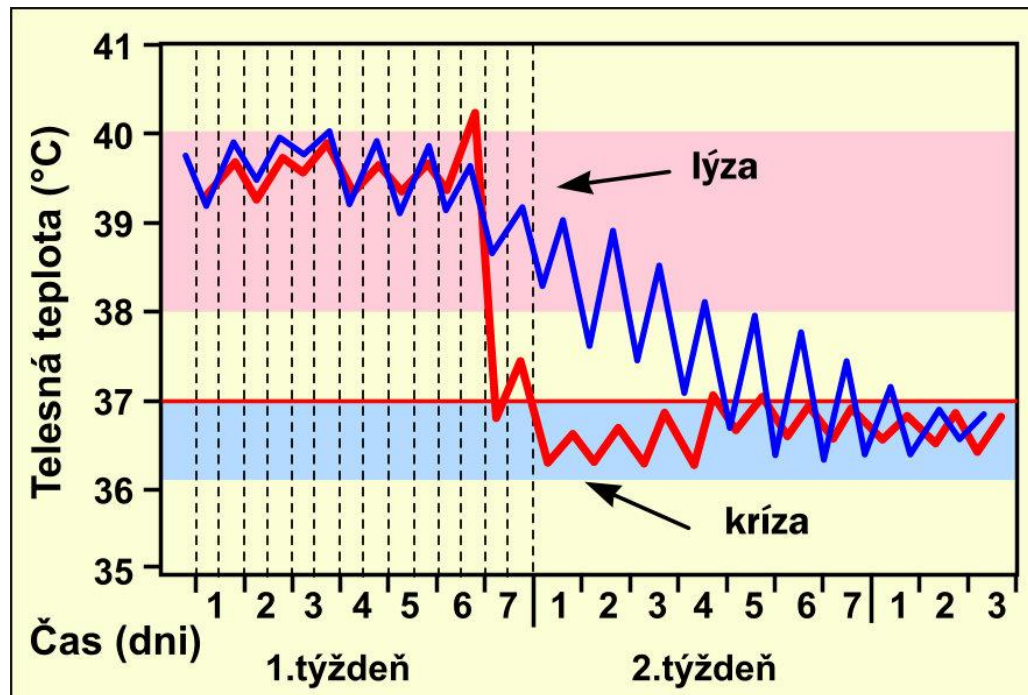
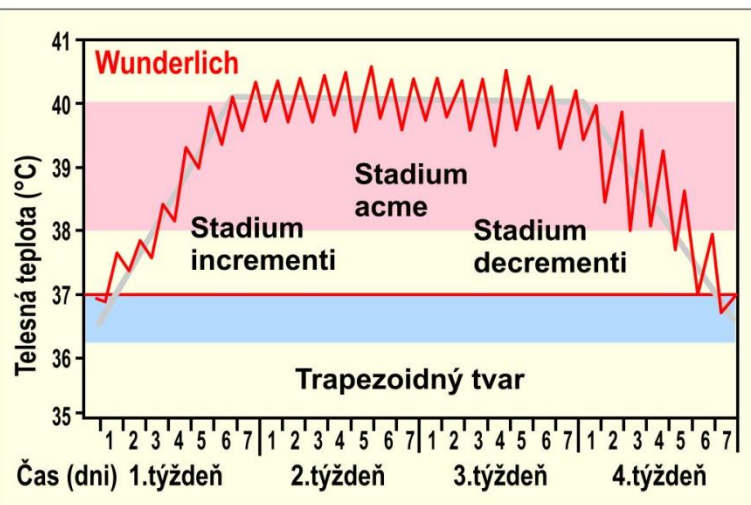
Fever

- **Def.:** Fever = pathological finding (sign) of elevated body temperature (over $> 38^{\circ}\text{C}$ measured in axilla in infants and adults) due to active body thermogenesis (liver, muscle, fatty tissue) caused by resetting of the normal temperature setpoint in hypothalamus thermoregulatory center to higher level by pyrogens.
- Various sources? $37.8\text{-}38.3^{\circ}\text{C}$ (in adults below, in small children higher values).
- **Forms:** Light fever: $38\text{-}38.5^{\circ}\text{C}$, Moderate fever: $> 38.5\text{-}39^{\circ}\text{C}$; Severe fever: $> 39.5^{\circ}\text{C}$; Hyperpyrexia: $> 41.0^{\circ}\text{C}$;
- **Subfebrility** = permanent/ periodical increases in Tt above the norm ($T_{\text{max}} = 37\text{-}37.5^{\circ}$ in axilla in the morning and 37.8°C at the evening)
- **Status febrilis (SF)** = persistent febrile state lasting over several few weeks ($\sim 38.5^{\circ}\text{C}$).
- **Febrile state with elevated sedimentation rate (FW):** chronic inflammation (TB, tuberculosis, syphilis, Q fever, chronic hepatitis, chronic polyarthritis, latent or masked infections (, focal infect deposits - chronic tonsillitis, dental granulomas, cholecystitis, appendicitis, cystopyelitis, phlebitis; malignant tumors (in humans > 60 years of age.)
- **Febrile state with normal sedimentation rate (FW):** neurovegetative hyperthermia, premenstrual hyperthermia, postinfective convalescence, allergies. etc.



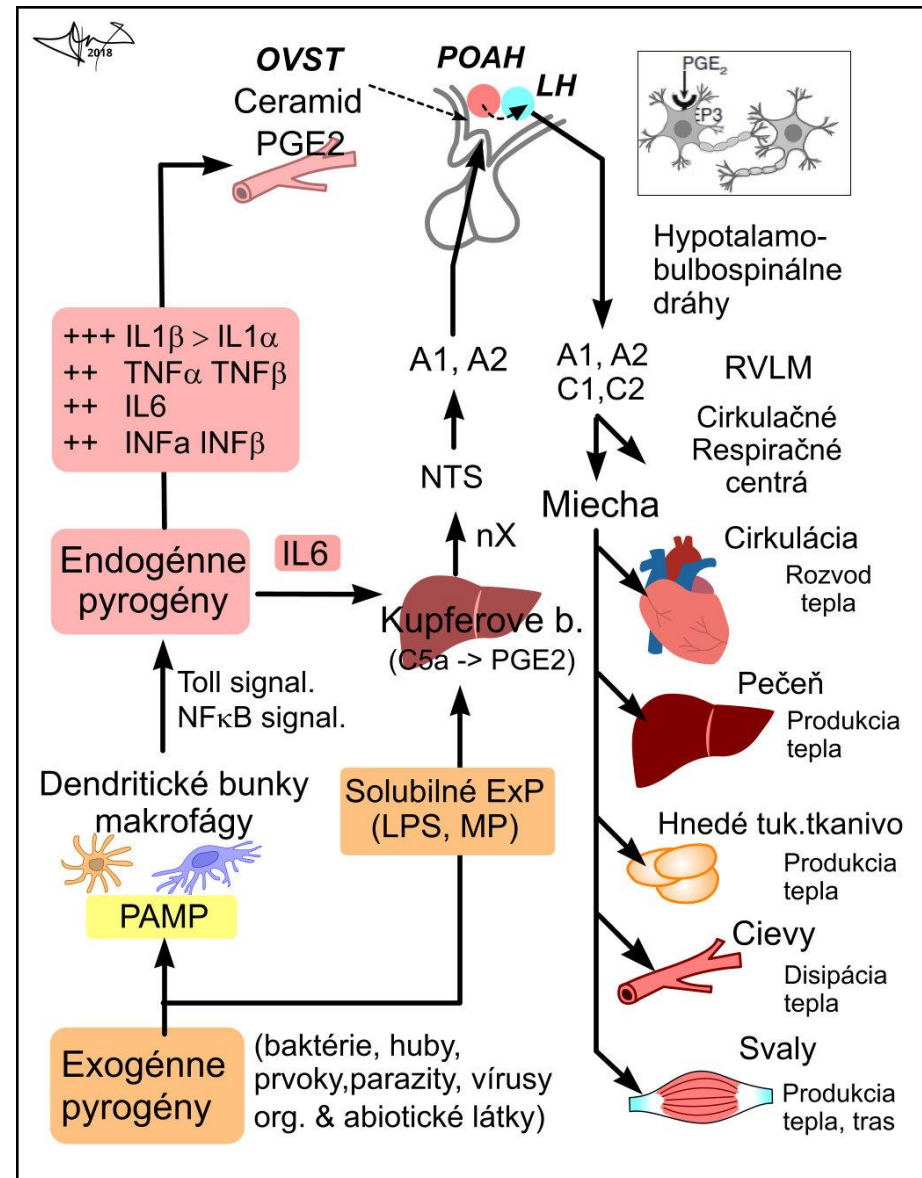
Carl Reinhold August Wunderlich
(1815-1877) - nemecký lekár, univerzitný profesor v Lipsku, psychiater. Určil priemernú teplotu zdravého ľudského tela 37°C (dnes $36,8^{\circ}\text{C}$; $98,2^{\circ}\text{F}$), zaviedol systematický záznam teplotnej krivky v nemocniciach, definoval horúčku ako symptóm a nie chorobu.

Fever – part of APR



Fever – pathways

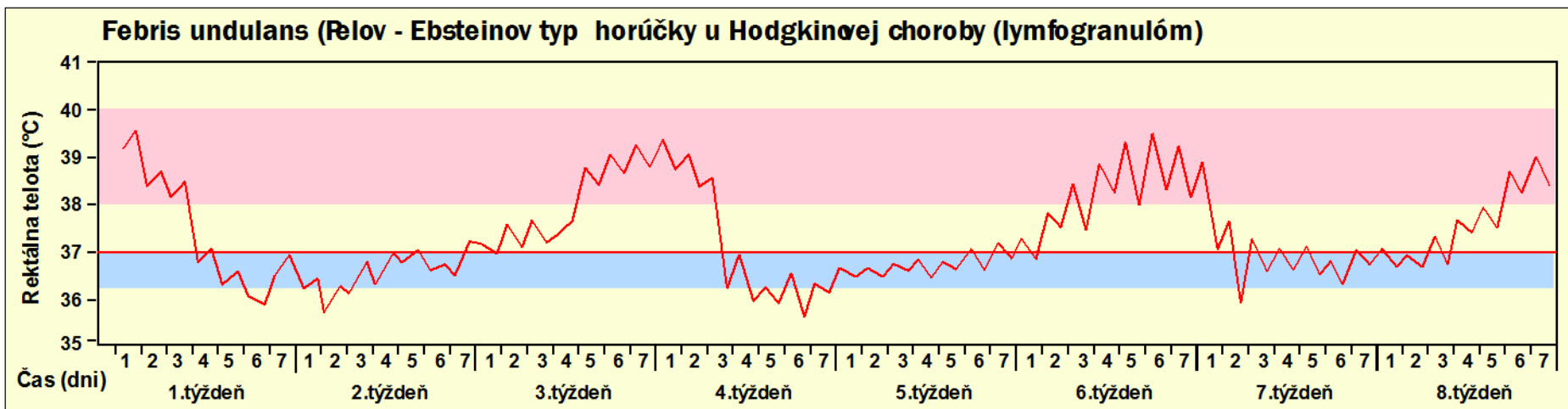
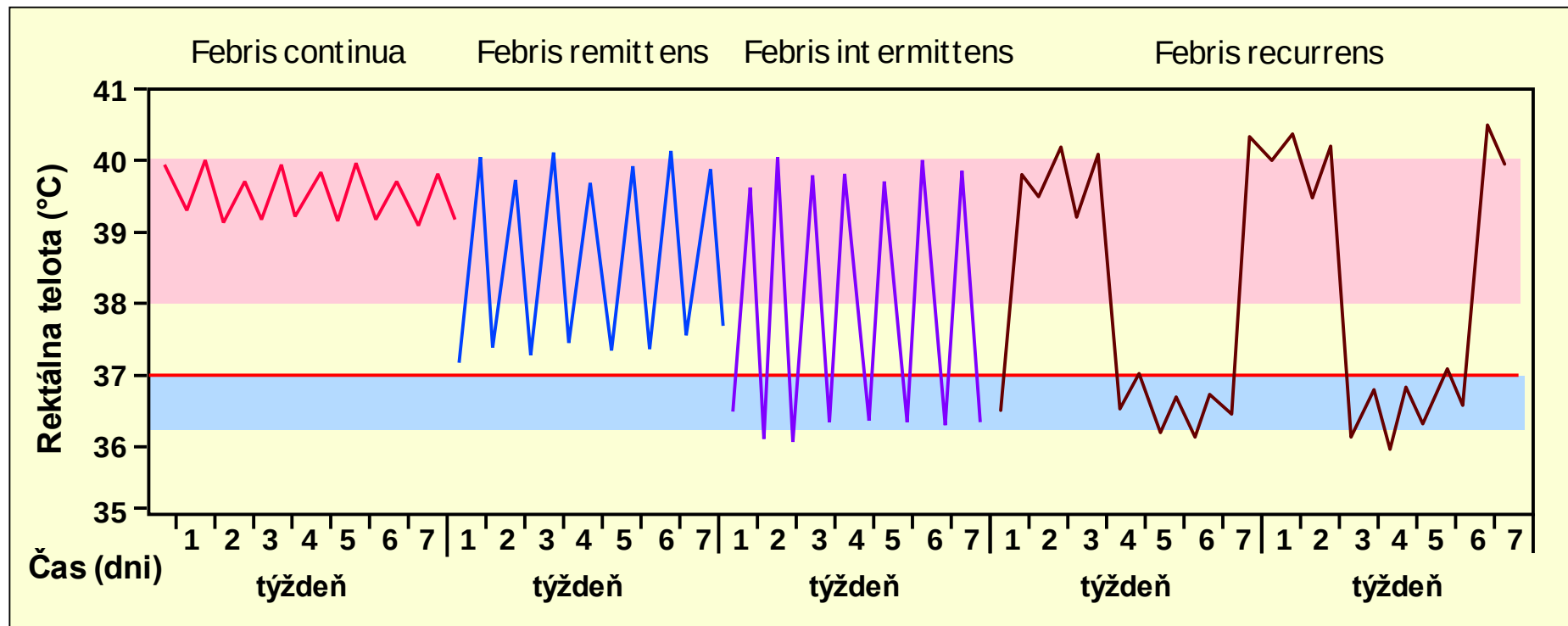
- **Pyrogens** = substances that act on the hypothalamic thermoregulatory center resetting its temperature threshold to higher levels. Vegetative hypothalamo - bulbar and bulbo-spinal pathways incite thermogenesis and febrile response.
- **Exogenous pyrogens** = *lipopolysaccharide (LPS)*, present in the cell wall of gram-negative bacteria, *bacterial endotoxins antigen-antibody complexes, viruses, synthetic polynucleotides, incompatible blood, androgen breakdown (etiocholanolone)*.
- **Endogenous pyrogens** = *interleukin-6, interleukin-1, tumour necrosis factor α , interferon- α , gp130 receptor ligands, etc.*
 - Production:
 - **immune cells** - phagocytes (monocytes-macrophages, neutrophils) and lymphocytes activated by infectious agents (e.g. bacteria, viruses, prions, viroids) and products
 - **other cells** (endothelium glial cells, mesangium, mesenchymal cells)



Causes of febrile states

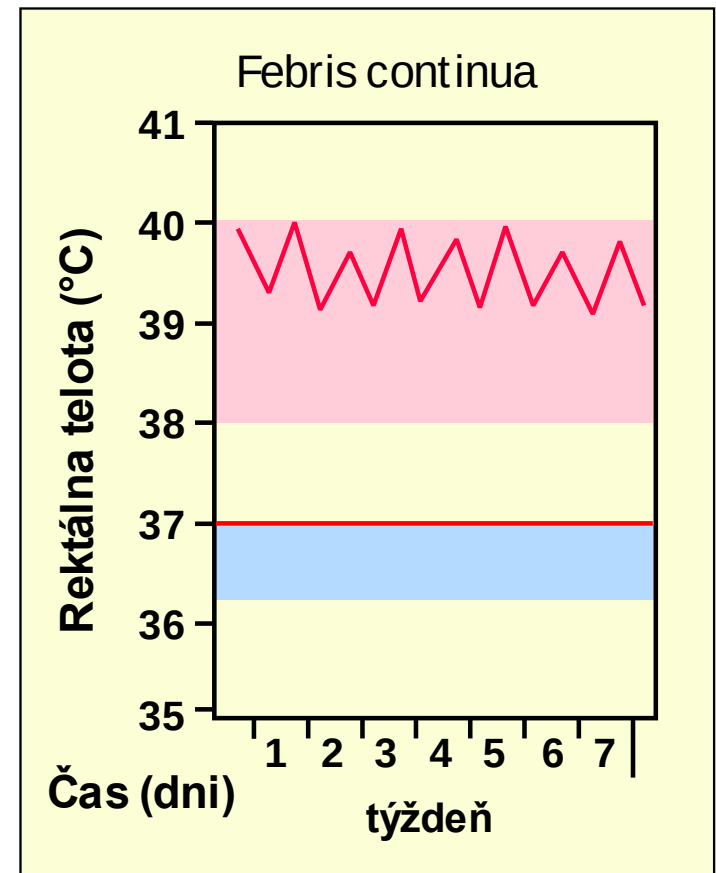
- **Infections:** **Focal** (abscess, pneumonia), **Generalized** (septicemia, typhoid fever), relapsing congenital, acquired immunodeficiency
- **Diseases of immunity** (immunodeficiencies, allergies, autoimmune disorders). Recurrent infections (congenital, acquired immunodeficiency), drug and drug allergic fever, Hashimoto's thyroiditis, Crohn's disease, ulcerative colitis primary active hepatitis, chronic active hepatitis, primary biliary cirrhosis, Subacute thyroiditis, acute sarcoidosis
- **Malignant tumors** : Lymphoma (Hodgkin's disease, Non-Hodgkinovské) malignancies of RES (Mononuclear phagocytes), Leucaemia, Myeloproliferative syndromes (osteomyelofibrosis, polycythemia vera, primary thrombocytemia), solid malignant tumours (kidney, liver, Intra-abdominal, myxoma of atria, etc.)
- **Endocrine & metabolic** : Thyrotoxic crisis (for subacute thyroiditis), Addison crisis, acute hyperparathyroidism (hypercalcaemia), pheochromocytoma (occasionally)
- **Other:** Pulmonary embolism, thrombophlebitis, non-infectious vasculitis, necrosis (infarctions), hematomas, hemolysis

Types of fever



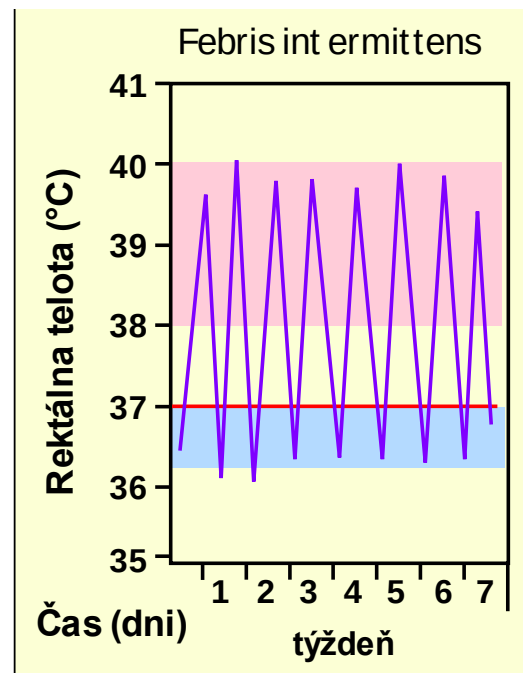
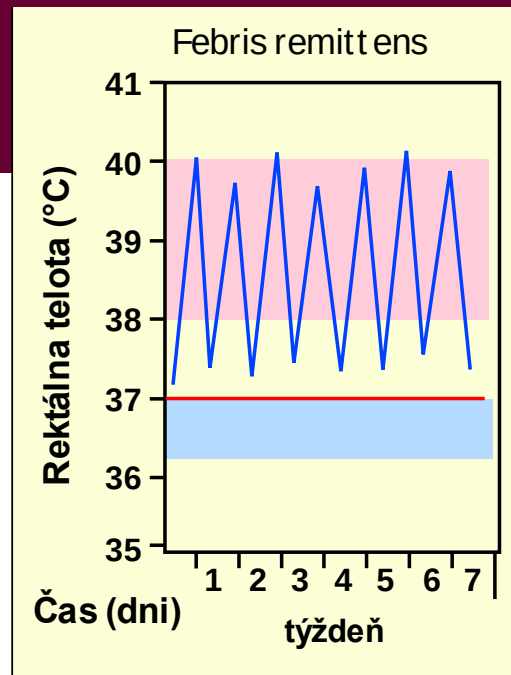
Types of fever

- **Continuous fever** – temperature remains above normal throughout the day and does not fluctuate more than 1 °C in 24 hours. Onset of the fever can be gradual (1-3 days), fast (hours) or very fast (30 min) (**stadium incrementi**). The temperature is plateauing (**fastigium**) then relieves (**stadium decrementi**) in fast (critical) or gradual (lytic) way
- The fever is usually high > 39 ° C, often with additional exacerbations (ie.crisis) with chills, redness, sweating, somnolence; lasts - few days to several weeks,
- **Causes: bacterial infections: typhoid, paratyphoid, brucellosis, erysipelas, lobar pneumonia (pneumococci), meningitis, urinary tract infection or viral infection, complications - sepsis**
- Typhoid fever may show a specific fever pattern (Wunderlich curve of typhoid fever)



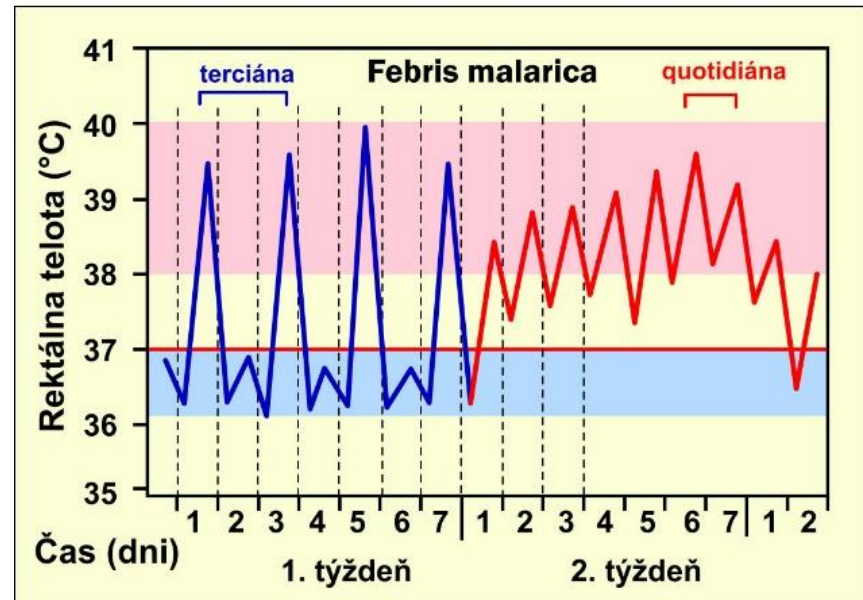
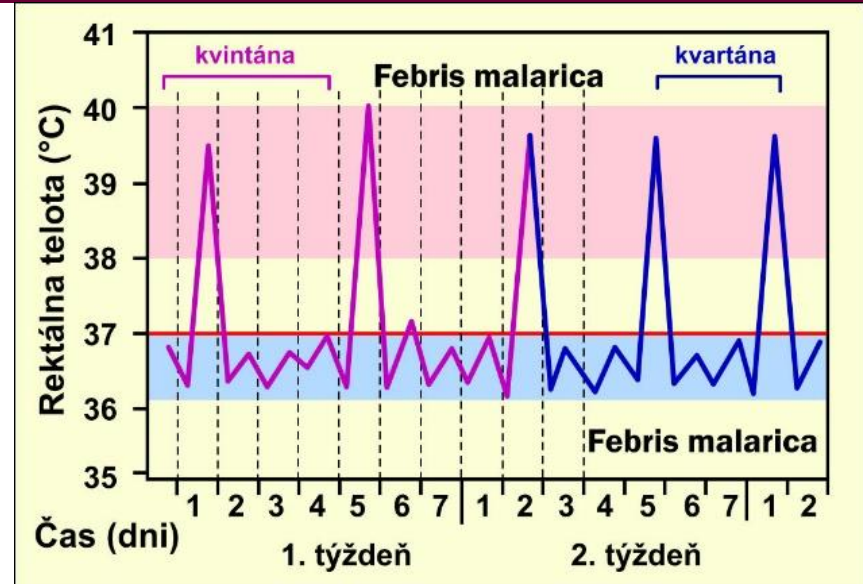
Types of fever

- **Remittent fever** – daily fluctuations within 2-4 °C; the temperature does not drop < 37 °C; morning subfebrility within afternoon fever $T_t > 39$ °C; febrile shivering.
- Causes: *tuberculosis, tuberculous peritonitis, abscesses, brochopneumonia, virus infections, rheumatic fever, sepsis*
- **Intermittent fever** – daily or day to day fluctuations are > 3-4°C, T_t returns to norm (< 37°C) (mostly in the morning; fever comes during the night (39-40°C). Similar fluctuations may occur in-between days (e.g. 1-2 days with fever, 1 day without fever).
- Príčiny: *acute pyelonephritis, pleuritis, sepsis, malaria*



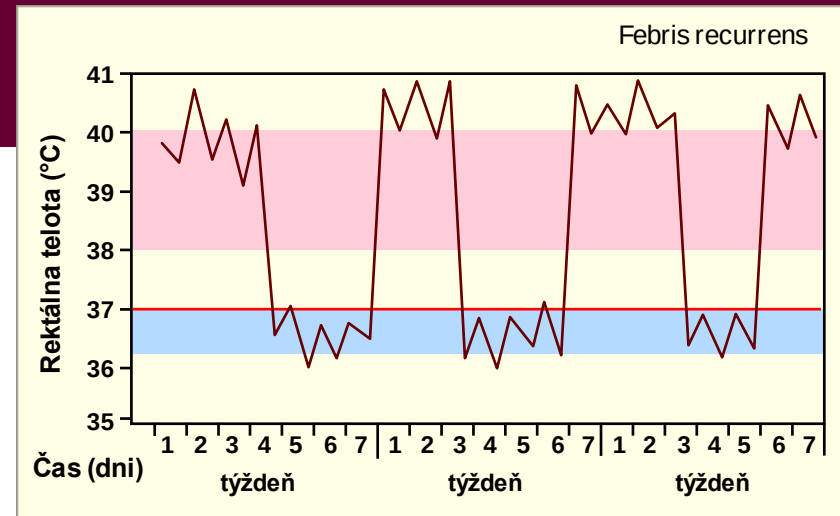
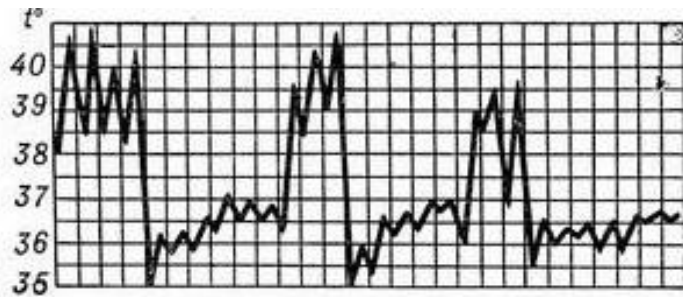
Types of fever

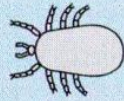
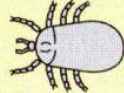
- **Malaric fever (febris malarica):** days of relieve are followed with attack of hyperpyrexia
 quitiana (1 fever : 4 relieve), qartana (1:3),
 terciana (1:2) a quotidiana (1:1) = intermitent
- **Recurrent fever :** periodic fever returning after several days; episodes without fever (nomal Tt) are followed with days with high fever (> 39°C), shivering, malaise Causes: **Volyn fever, sodoku, cholangitis**



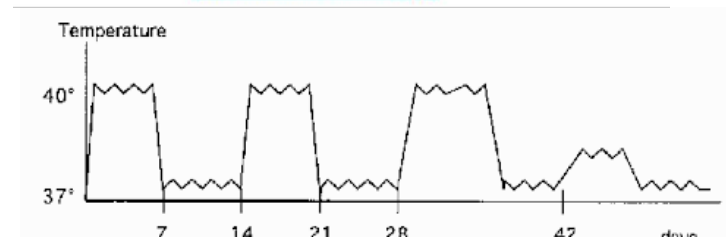
Types of fever

- **Recurrent fever (relapsing fever, tick fever, famine fever, Rückfallfieber)** : periodic fever returning after several days; episodes without fever (normal Tt) are followed with days with high fever ($> 39^{\circ}\text{C}$), shivering, malaise
- **Causes:** 1. Infections: **borreliosis, volynic fever, soda, malaria, cholangitis, recurrent viruses, Volyn fever, sodoku,**
- 2. Non.infective: **Monogenic autoinflammatory diseases, cholangitis**
- **Sy. of periodic fever:** aphthous stomatitis, pharyngitis and adenitis (PFAPA), the most common periodic fever in childhood.



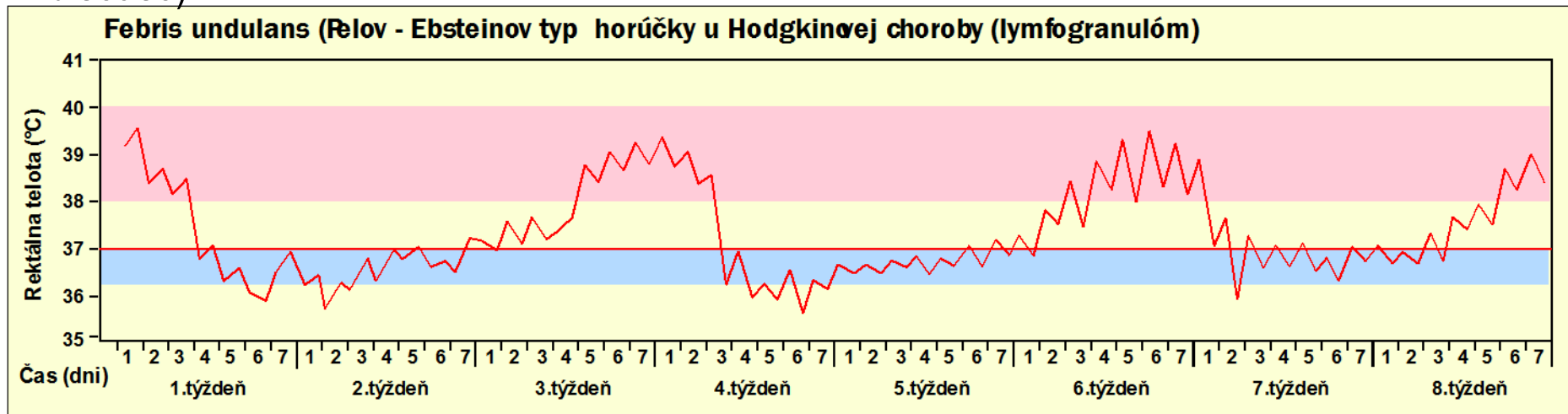
Infection	Reservoir	Vector
Relapsing fever Epidemic (louse-borne) <i>B. recurrentis</i>	Humans	Body louse 
Relapsing fever Endemic (tick-borne) Many <i>Borrelia</i> species	Rodents, soft-shelled ticks	Soft-shelled tick 
Lyme disease <i>B. burgdorferi</i>	Rodents, deer, domestic pets, hard-shelled ticks	Hard-shelled tick 

Relapsing fever is either louse-borne or tick-borne.
- Tick borne is more common in U.S.

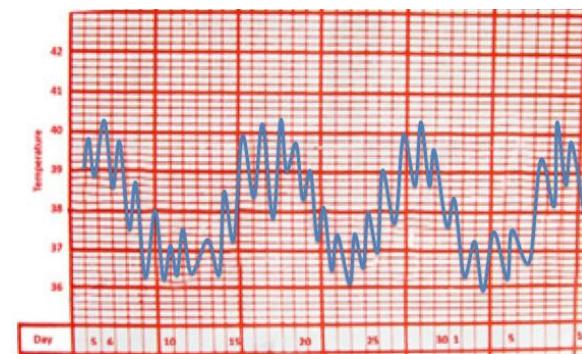


Types of fever

- **Undulant fever** - fever comes in irregular waves (1-3 weeks) alternated with periods without fever (normal Tt or subfebrility).
- Causes: ***M. Bang (pathognomonic), brucellosis, reticulosis, malignancies***
- Special forms of undulant fever is Pel-Ebstein fever in **lymfogranuloma** (Hodgkin's disease)



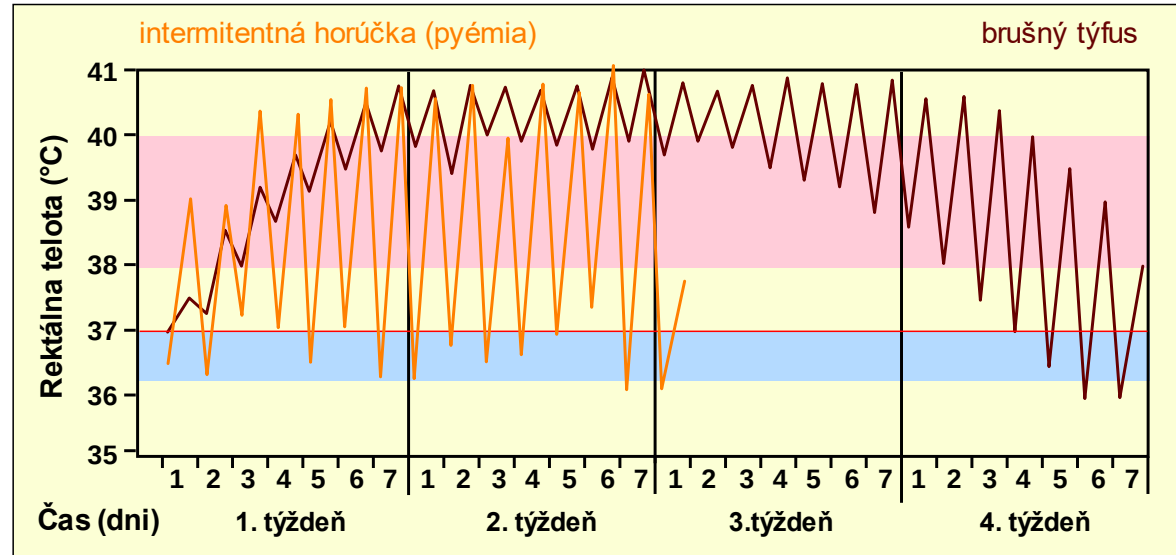
- **Brucellosis (*Brucella abortus*)** - undulating fever, weakness, arthralgia, severe fatigue, hepato-splenomegaly, mild anemia, increase in ALP, biliary obstruction



Types of fever

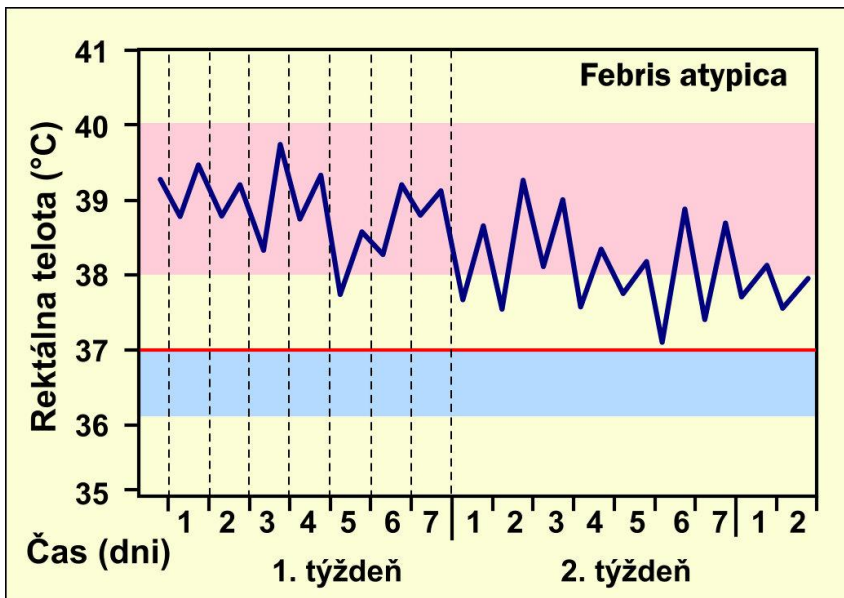
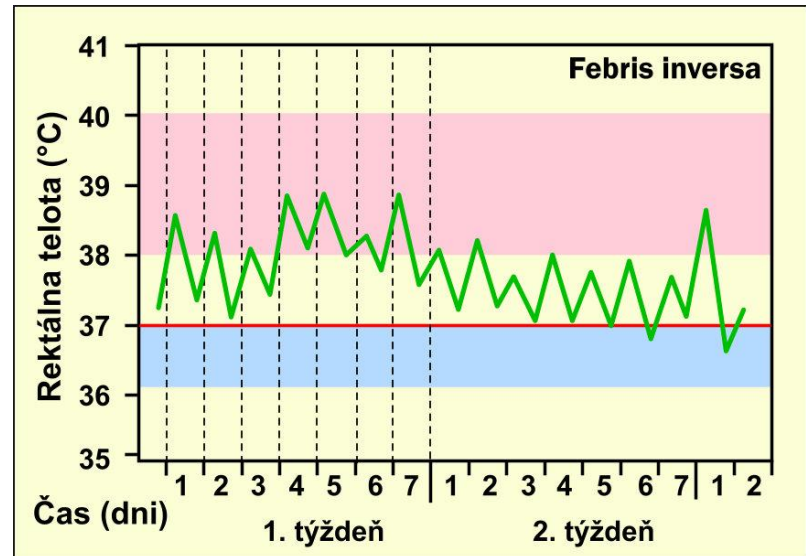
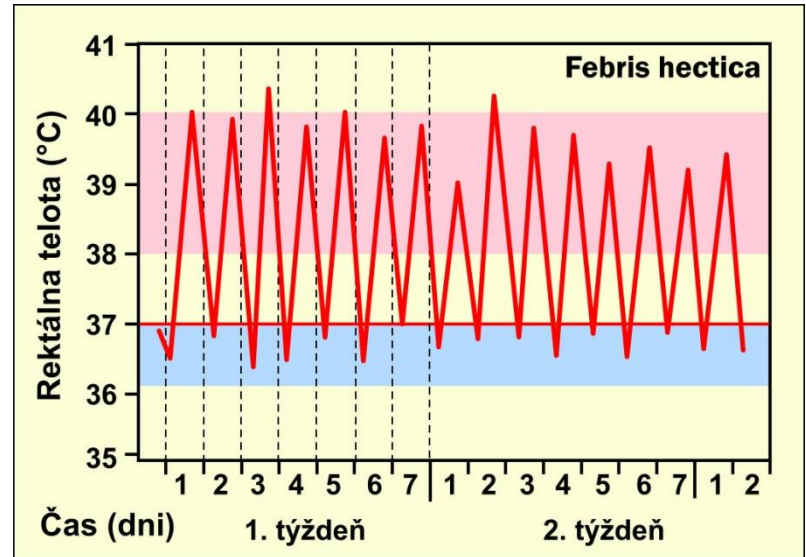
- **Febris ephemerica** – obviously sudden onset and very short duration (1-2 days) febrile state with rapid decline Causes: poisoning, inhalatory toxins

- **Febris hectica (septica)** high fluctuations from subfebrility to hyperpyrexia ($> 2-4^{\circ}\text{C}$)



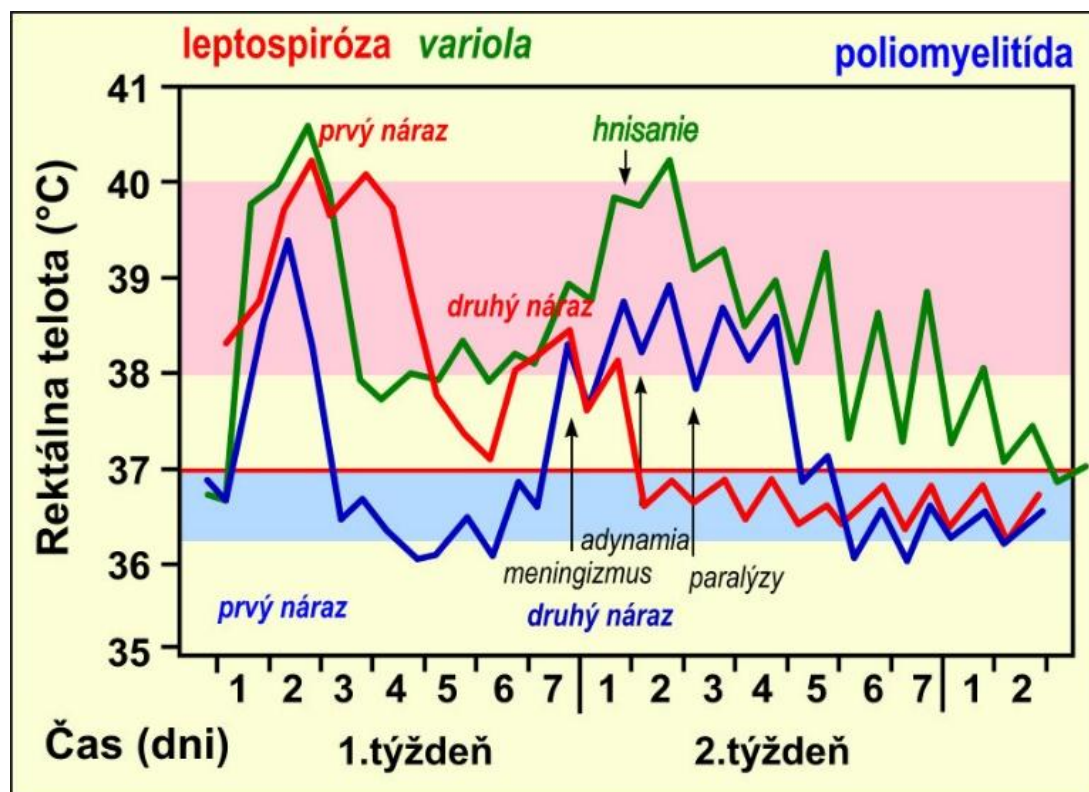
- **Febris periodica.** Periodically recurring fever with irregular intervals of fever and normal Tt ; Causes:
 - complications of the underlying disease = e.g. staphylococcal or streptococcal infection superimpose on viral disease (influenza); dissemination of the disease to other organs or complications (emphysema → pneumonia, pericarditis → myocardial abscess)
 - relapses (e.g. antimicrobials - temporary silencing of infection)
 - progressive generalization of diseases;

- **Febris inversa** - morninf Tt is higher than evening Tt ; Causes: tuberculosis
- **Febris hectica (septica)** high fluctuations from subfebrility to hyperpyrexia ($> 2-4^{\circ}\text{C}$)



Biphasic fever

- **Biphasic fever** – second rise of fever after transient decline or normalization Causes: poliomyelitis, measles, smallpox, leptospirosis, myalgia epidemica etc.



Febris biphasica (dromedaria)

2 waves of fever

Measles – second fever attack on 4.th day

Variola – second fever attack occurs after break of pustules

Poliomyelitis – second fever attack on 8.-10.d

Leptospirosis -second fever attack on 6.-7. d

- In certain infective diseases the onset of fever is synchronized (preceding, delayed etc.) with outbreak of skin manifestations (e.g. measles, pox, scarlet fever); with purulent wounds again in relation to the filling / evacuation of abscess

Fever in various disorders

