PYREXIA

- *pyrogen* : any substance that causes fever.
- *Exogenous* pyrogens :
    - outside the patient;
    - most are microbial products, microbial toxins, or whole microorganisms.
    - E.g., the lipopolysaccharide endotoxin produced by all gram-negative bacteria.
    - Endotoxins (highly pyrogenic)
    - enterotoxins of *Staphylococcus aureus*
    - *Superantigens (*streptococcal toxins*)*

PYROGENIC CYTOKINES

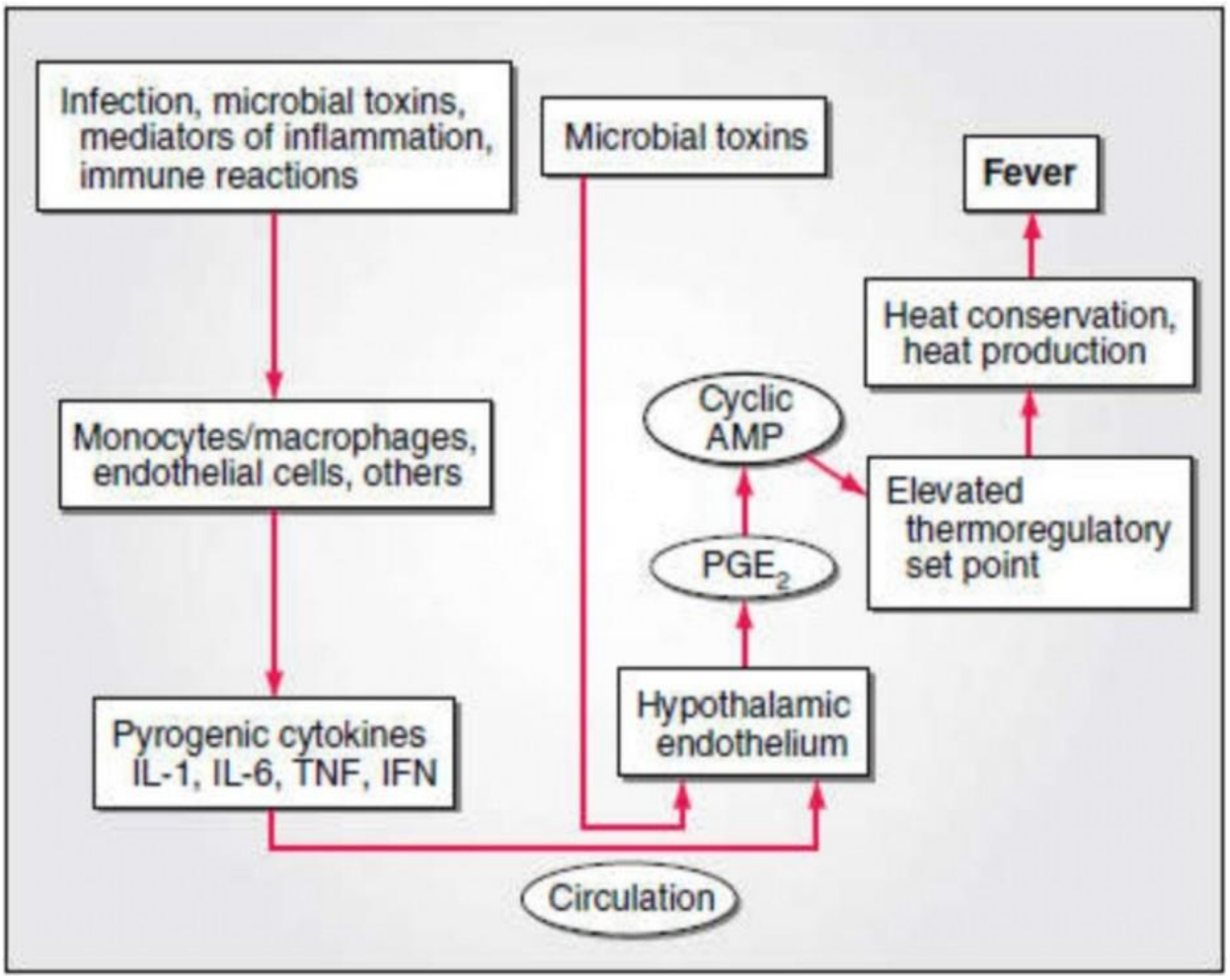
- Cytokines
    - small proteins
    - regulate immune, inflammatory, and hematopoietic processes.
- Some cytokines cause fever and hence are called
    - called *endogenous pyrogens*.
    - include IL-1, IL-6, tumor necrosis factor (TNF), ciliary neurotropic factor (CNTF), and interferon (IFN) alpha.

- The synthesis and release of endogenous pyrogenic cytokines are induced by a wide spectrum of exogenous pyrogens,
    - most of which have recognizable bacterial, fungal or viral sources.
- They trigger the hypothalamus to raise the set point to febrile levels.

- The cellular sources of pyrogenic cytokines are primarily monocytes, neutrophils, and lymphocytes.

HYPOTHALAMIC SET POINT ELEVATION

- During fever, levels of PGE2 are elevated in hypothalamic tissue and the third cerebral ventricle; highest near the circumventricular vascular organs
- Destruction of these organs reduces the ability of pyrogens to produce fever.
- pyrogens (exogenous/endogenous) interact with the endothelium of these capillaries
- is the first step in initiating fever



PRODUCTION OF CYTOKINES IN CNS

- Glial and neuronal cells synthesize IL-1, TNF, and IL-6.
- CNS production of these cytokines: raise the hypothalamic set point
- CNS cytokines may account for the hyperpyrexia of CNS haemorrhage, trauma, or infection.
- Physical examination
- complete blood count;
- A differential count
- the smear examined for pathogens (febrile illness severe or prolonged)
- erythrocyte sedimentation rate.
- Urinalysis (urinary sediment)
- abnormal fluid accumulation (pleural, peritoneal, joint) testing (culture)
- Stool examination (occult blood; leukocytes, ova, or parasites).
- Electrolyte,
- blood glucose,
- blood urea nitrogen,
- creatinine levels.
- R/O organ involvement:
    - Liver function tests.
    - measurement of creatinine phosphokinase or
    - measurement of amylase.
    - CXR

- self-limited infections: use antipyretics.
- The routine use of antipyretics automatically to treat low-grade fevers unacceptable.
    - masks fever & important clinical indicators.
- Temperature-pulse **dissociation** (relative bradycardia) occurs in typhoid fever, brucellosis, leptospirosis, some drug-induced fevers, and factitious fever.
- fever may not be present despite infection, or core temperature may be hypothermic in:
    - new-borns,
    - the elderly,
    - patients with chronic renal failure,
    - patients taking glucocorticoids.
    - septic shock

Indications for the Treatment of Fever

- The objectives:
    - to reduce the elevated hypothalamic set point
    - to facilitate heat loss.
- Treatment of fever recommended for:

– pre-existing cardiac, cerebrovascular, or pulmonary insufficiency.

– organic brain disease

– Children

Regimens for the Treatment of Fever

- Antipyretics also reduce systemic symptoms of

headache, myalgias, and arthralgias.

- **Acetaminophen** (**Paracetamol**)is preferred to all of these agents as an antipyretic.

- Oral aspirin and NSAIDs effectively reduce fever but can adversely affect platelets and the GIT.
- In children, acetaminophen must be used because aspirin increases the risk of Reye's syndrome.

Regimens for the Treatment of Fever

- Patient cannot take oral antipyretics use:
  - parenteral preparations
  - rectal suppository preparations of antipyretics.
- In hyperpyrexia, the use of cooling blankets facilitates the reduction of temperature;
  - cooling blankets should not be used without oral antipyretics.
- In hyper pyretic patients with CNS disease or trauma, reducing core temperature mitigates the ill effects of high temperature on the brain.
- A high core temperature in a patient
- with an appropriate history
  - (e.g., environmental heat exposure or treatment with anticholinergic or neuroleptic drugs, tricyclic antidepressants, succinylcholine, or halothane)
- along with appropriate clinical findings
  - (dry skin, hallucinations, delirium, pupil dilation, muscle rigidity, and/ or elevated levels of creatine phosphokinase).
- normal hypothalamic set point
- Physical (external)cooling: initiated immediately.
  - with sponging, fans, cooling blankets, and even ice baths
- in conjunction with the administration of IVF and appropriate pharmacologic agents.
- Internal cooling: gastric or peritoneal lavage with iced saline.
- In extreme circumstances,

    - haemodialysis or
    - even cardiopulmonary bypass with cooling of blood.

Malignant hyperthermia

- should be treated immediately
- cessation of anaesthesia
- intravenous administration of dantrolene sodium.
- The recommended dose of dantrolene is 1 to 2.5 mg/kg of body weight given intravenously every 6 h for at least 24 to 48 h—until oral dantrolene can be administered, if needed.
- Procainamide should also be administered to patients with malignant hyperthermia because of the likelihood of ventricular fibrillation in this syndrome.
- Dantrolene at similar doses is indicated in
    - Neuroleptic Malignant Syndrome
    - drug-induced hyperthermia
    - hyperthermia of the serotonin syndrome and
    - thyrotoxicosis.
- Tricyclic antidepressant overdose may be treated with physostigmine.
- NMS may also be treated with
    - bromocriptine,
    - levodopa,
    - amantadine, or
    - nifedipine or
    - by induction of muscle paralysis with curare and pancuronium.