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### The Mechanism of Fever and its Clinical Management

Yan Wang MD, PhD

Doctor and Director in Shanghai Hngci Children's Hospital, University of Pennsylvania School of Medicine, USA

**\*Corresponding author:** Yan Wang MD, PhD, The membership in the American Physiology Society, Doctor and Director in Shanghai Hngci Children's Hospital, University of Pennsylvania School of Medicine, USA, Tel: 001-9293545218; Email: drwangi@hotmail.com

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Fever is the most common symptom in clinical patients, and the pattern and time period of the fever can present the change of ill status, which could refer to its diagnosis, treatment and prognosis. In clinical, which is required to be treated not only by defining it on etiological, but also on symptomatic.

#### Fever Defining

Body temperature depends on equilibrium between thermogenesis and thermolysis which is under control of thermoregulatory center; Preoptic-antihypophysis (POAH) is the highest part of thermoregulatory center which has secondary parts of medulla, pons, middlebrain and spinal cord. The set point of body temperature is scale of central body temperature by POAH [1]. Usually, 0.5°C over normal temperature is called fever, and most pathological etiology agent such as pyrogen and virals could raise the set point and cause fever.

#### Mechanism of Fever

The mechanism of fever can be summarized as following:

##### Effect of thermogenesis activators [2,3]

Exogenous pyrogen can stimulate production of endogenous pyrogen in body as activator, the activators include of endotoxin, exotoxin, bacteria or virus, and as well as inflammatory protein, lymphokine, antigen or antibody, all those can subsequently activate endogenous pyrogen (EP) cells to produce and release endogenous pyrogen.

EP has also named leukocytic pyrogen (LP), which is mostly produced and released by neutrophilic granulocyte, mononuclear cell, tissue macrophage or tumor cell. It is widely acknowledged that LP is interleukin firstly, then at lately time, more interferon, tumor necrosis factor and inflammatory protein have been found out to be in EP group. EP can take effect on macrophage cell in vascular area and following on inducing it to release fever activators by taking effect on POAH to thermogenesis response.

##### Central Mechanism

So far, it is difficult to define the activated locus of EP, then most scientists think that EP is impossible to pass through blood-brain barrier, but it may ascend up the set point of body temperature by through central mediums in hypothalamus by PGE [4].

#### Response to thermoregulatory on ascending up of the set point

When the central body temperature is lower than the new level of the set point, the thermoregulatory will give order out to those thermogenesis and thermolysis organs, which will lead to fever by increasing thermogenesis and decreasing thermolysis.

#### Clinical Presentation of Fever

Fever usually is caused by acute inflammation reaction by various etiology, the clinical presentations of it can be divided into three phases:

##### Ascending phase of body temperature

The central body temperature begins to rise rapidly or gradually as well; the faster process may reach the top temperature in several hours; and the slower one needs several days. In this ascend-up phase, patients may feel chilly or frigoris or skin pallescence. Children may lack of typical manifestation due to rapid ascension of their body temperature, but they usually present as lassitude, anorexia and dysphoria.

##### Peak time

Corresponding to the rising level of the set point of body temperature, the body temperature will fluctuate at where it reaches; the balance of thermogenesis and thermolysis is kept at this time.

##### Later time

At this phase, thermogenesis activators are controlled and EP might be cleared away; meanwhile, the ascended set point of body temperature is back to the normal level, patients would present as exhausted with dehydration and circulation failure once seriously [5].

#### Physiological Metabolism During Fever

1. Oxygen consumption is increasing with metabolism rate rising; protein decomposition is strengthening, which may lead to negative nitrogen balance.
2. Gluco-metabolism is intensifying, decomposition of hepatic and muscle glycogen is also strengthening, thus blood sugar is increasing and reserve of glycogen is decreasing.

Decomposition of fat is enhancing significantly and intaking is relatively decreased during fever. Patients may lose their weight because of high consumption. Some even may occur ketonemia and ketonuria due to intensify decomposition of fat.

3. For water-salt metabolism: urine volume is decreasing during fever,  $\text{Na}^+$  and  $\text{Cl}^-$  is retained in the body, all these might lead to dehydration and exacerbation of fever.
4. For changes of physiological function: heart and breath rate is rising, heart load is increasing, and also with anorexia and hypotyalism if they are severe enough, and children will occur convulsion.

### Antipyretics in application

The common tipyretics drugs are applied in clinic are acetylsalicylic acid, acetaminophen, phenacetin, aminopyrin and ibuprofen [6-8]

#### Ibuprofen

Its antipyretic action is significant, but with those side effect manifested as granulocytopenia, thermocytopenic purpura or aplastic anemia under long term of administration.

#### Aspirin

Its antipyretic and analgesic action are defined, and its anti-inflammatory and anti-rheumatism action are stronger. It has been granted as excellent medicine for many years. Absorption of Aspirin by oral administration is rapid and the plasma concentration can reach to the peak after 2-3 hours. Though it is used widely in clinic, then, its toxic side effect is also extended, which mainly presents in gastrointestinal reaction, platelet aggregation, Reiter's Syndrome, allergic reaction or renal papillae necrosis [9].

#### Acetaminophen

It has rapid absorption through oral administration, and the plasma concentration will be up to the peak after 2-3 hours after administration and subsequently maintains for 4-6 hours, thus it is suitable for clinical administration every 4-6 hours interval, meanwhile it has broad safety tolerance range on its therapeutic dosage, and acetaminophen is not easy to cause intoxication, therefore it is safer for children.

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