

phase frequently passes unnoticed since the initial damage is often prevented by the innate immune response.

**Immunity** Cell-mediated immunity plays an important role in the pathogenesis of viral myocarditis. T lymphocytes are mainly caused by the effect of myocardial cell injury immune cells. T responses in the pathogenesis of myocarditis has included T helper (Th) 1 [7], Th17 [8] and Th22 response [9]. Recent data indicate that elevated Th2 and Th17 responses during acute CVB3 myocarditis are critical for the progression from myocarditis to DCM and heart failure because of their ability to induce cardiac remodeling.

**Dilated cardiomyopathy** Part of the viral myocarditis (VMC) delayed healing eventually develop dilated cardiomyopathy (DCM), which is a kind of composite cardiomyopathy etiology, left ventricular and right ventricular or double heart enlargement, cause cardiac dysfunction such as characteristic. The results showed that the B virus (CVB) and DCM were most closely related to viral infection, especially Coxsackie virus [10].

**Conclusion** In summary, viral myocarditis is a complex process of interaction virus direct injury, immune response and so on. It is can control the occurrence and development of viral myocarditis through study the pathogenesis and mechanism of viral myocarditis. With the continuous development of modern immunology and molecular biology, for the study of the pathogenesis of VMC provides an important method. The study of the immune mechanism inhibits viral invasion of myocardium and its immune responses will for the therapy of myocarditis open a new way.

#### References

1. Cooper LT Jr. Myocarditis. *N Engl J Med.* 2009 360:1526–1538.
2. Esfandiarei M, McManus BM. Molecular biology and pathogenesis of viral myocarditis. *Annu Rev Pathol.* 2008;3:127–155.
3. Badorff C, Lee GH, Lamphear BJ, Martone ME, Campbell KP, Rhoads RE, Knowlton KU. Enteroviral protease 2A cleaves dystrophin: evidence of cytoskeletal disruption in an acquired cardiomyopathy. *Nat Med* 1999;5:320–326.
4. Baboonian C, Davies MJ, Booth JC, McKenna WJ. Coxsackie B viruses and human heart disease. *Curr Top Microbiol Immunol.* 1997;223:31–52.
5. Martin, A. B., S. Webber, F. J. Fricker, R. Jaffe, G. Demmler, D. Kearney, Y. H. Zhang, J. Bodurtha, B. Gelb, J. Ni, et al. Acute myocarditis. Rapid diagnosis by PCR in children. *Circulation.* 1994 Jul;90(1):330–9.
6. Zack, F., K. Klingel, R. Kandolf, and R. Wegener. Sudden cardiac death in a 5-year-old girl associated with parvovirus B19 infection. *Forensic Sci Int.* 2005 Dec 1;155(1):13–7.
7. Noutsias M, Rohde M, Göldner K, Block A, Blunert K, Hemaidan L. Expression of functional T-cell markers and T-cell receptor Vbeta repertoire in endomyocardial biopsies from patients presenting with acute myocarditis and dilated cardiomyopathy. *Eur J Heart Fail.* 2011;13:611–8.
8. Yang F, Wu WF, Yan YL, Pang Y, Kong Q, Huang YL. Expression of IL-23/Th17 pathway in a murine model of Coxsackie virus B3-induced viral myocarditis. *Virol J.* 2011;8:301.
9. Kong Q, Wu W, Yang F, Liu Y, Xue Y, Gao M, et al. Increased Expressions of IL-22 and Th22 cells in the coxsackievirus B3-Induced mice acute viral myocarditis. *Virol J.* 2012;9:232.
10. Yue-Chun L, Guang-Yi C, Li-Sha G, Chao X, Xinqiao T, Cong L, Xiao-Ya D, Xiangjun Y. The Protective Effects of Ivabradine in Preventing Progression from Viral Myocarditis to Dilated Cardiomyopathy. *Front Pharmacol.* 2016 Nov 1;7:408.

### STUDY ON THE MODEL OF COMMONLY USED RAT FEVER

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**Abstract** Objective: To explore the process and characteristics of fever induced by dry yeast, 2,4-dinitrophenol, lipopolysaccharide (LPS) in SD rats, and to compare the influence of different types of exogenous pyrogens on the fever process.

**Methods:** To establish rat fever models induced by ten percent of dry yeast (10ml/kg), and 2,4-dinitrophenol (20mg/kg), LPS (20µg/kg), record the fever values at different time points, and compare their fever characteristics.

**Results:** In the febrile rats induced by subcutaneous injection of dry yeast suspension, first the temperature to drop, temperature began to rise after 2 hour to 3 hour, reached to the peak value after 5 hour to 7 hour, and lasted for 21 hour. In the febrile rats induced by subcutaneous injection of 2,4-dinitrophenol solution, the temperature began to rise after 20min, reached to the peak value after 1-1.5 hour, and lasted for 4 hour to 5 hour. In the febrile rats induced by intraperitoneal injection of LPS, temperature began to rise after 0.5 hour, then the fever curves were biphasic or triphasic, and lasted for 6 hour to 8 hour.

**Conclusions:** Different exogenous pyrogens at different concentrations cause different fever process and characteristics in SD rats. In antipyretic experiments, suitable fever models should be appropriately selected based on the nature of the tested drug and according to the types of fever process and characteristics of the used animal models.

**Key words:** Febrile rats model; Fever process; Fever characteristics; Drug research

#### 1. Materials and methods

##### 1.1 Materials

1.1.1 Experimental animals: SD rats , License number: SCXK (Beijing) 2006-0009. Purchased from Beijing Weitong Lihua Experimental Animal Technology Co. Ltd.

1.1.2 Experimental reagents: Sodium chloride injection, batch number: 170109D1, Harbin Sanlian pharmaceutical Limited by Share Ltd; High active dry yeast powder, batch number: 20110104W, Angel yeast Limited by Share Ltd; DNP, batch number: 981, China Pharmaceutical and Biological Products Institute; Lipopolysaccharide (LPS), batch number: L2880, Sigma.

1.1.3 Laboratory apparatus: PB602-N electronic balance (METTLER TOLEDO Instruments (Shanghai) Co., Ltd.); MC-106B OMRON electronic thermometer (Dalian OMRON Co., Ltd.).

## 1.2 Experimental method

1.2.1 Administration and grouping: The blank group was subcutaneously injected with 0.9% Sodium Chloride Injection 10ml /kg . Dry yeast group: 10% yeast suspension was injected subcutaneously (10ml /kg). 2, 4- dinitrophenol group: subcutaneous injection of 2, 4- dinitrophenol 20 mg /kg. Intraperitoneal injection of LPS 20 µg / kg.

## 2. Results

2.1 In the febrile SD rats induced by subcutaneous injection of dry yeast suspension, their body temperature to decrease in the first hour. After 2 hour, the body temperature rose rapidly, reached to the peak value after 5 hour to 7 hour. After that, the heating curve is at the peak plateau stage and can maintain 7 hour. After 12 hour, the rats temperature began to decrease. Up to 24 hour, the heating value falls below 1 degrees Celsius.

2.2 In the fibrilerats induced by subcutaneous injection of 2,4 -dinitrophenol solution, the temperature immediately increased rapidly, reached to the peak value after 1 hour to 1.5 hour. The peak value is 3.5 degree Celsius. After that, the body temperature began to recover gradually, and lasted for 4-5 hour.

2.3 After intraperitoneal injection of LPS 30 min, the body temperature increased significantly in rats. There were two peaks at about 2 hour and 4 hour. The maximum peak is 2.3 degrees Celsius. At 6 hour after injection, the body temperature was reduced to below 0.6 degrees Celsius.

3.1 Fever caused by dry yeast is a severe inflammatory reaction caused by local ulceration at the injection site. It is the most common febrile model in rats. [1] The experimental results showed that the dry yeast fever model rats after a short time after cooling temperature increases rapidly, and can maintain a peak plateau in the peak, after injection of 24 hour is observed in local injection has obvious symptoms of inflammation. The heating effect of dry yeast caused fever in rats was stable and lasting.

3.2 2,4-dinitrophenol is a strong metabolic stimulator, which can stimulate the animals to produce aseptic inflammation after subcutaneous injection, is a non infectious fever model. The role of rapid transient heating, high amplitude, not suitable for study on the role of slow, lasting antipyretic antipyretic effect, and is suitable for quick effect, obvious curative effect, used to study the antipyretic drugs in the treatment of non infective fever.

3.3 Lipopolysaccharide (LPS) is an active component of endotoxin (ET) in gram negative bacteria. The heating peak produced by 20µg /kg dose in rats 0.5 hour may be stress induced fever, so it is not considered as the first phase heat, that is, 20µg /kg can cause biphasic fever in rats.

The results showed that the heating time, peak time and maintenance time were different in fever models caused by different exogenous pyrogen.

## References

[1] Gu Xuehong, Ren Ainong, Peng Yunru, et al. J the antipyretic effect of qingqiliangying injection. Chinese medicine, 2010, 32 (2): 200.

## THE INFLUENCE OF IL-17、MMP-7 of GA RATS TREATED BY TKED METHOD

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**Abstract** According to the study of the effect of tonifying kidney and excreting dampness method on gouty arthritis (GA) rats, 84 SD rats were randomly divided into 7 groups, 12 rats in each group, using the model of uric acid sodium combined with oxonic acid potassium, induced acute GA. Using ELISA method to detect the level of IL-17 and MMP-7 of the serum. As a result of this study, the prescription of tonifying kidney and excreting dampness method (TKED method) can reduce the level of IL-17 and MMP-7 significantly, which has a certain effect on the prevention and treatment of GA.

**Key words:** IL-17, MMP-7, Tonifying kidney and excreting dampness method (TKED method)