ZYMOSAN-INDUCED FEVER: ROLE OF COMPLEMENT

J. Llanos-Q., S. Li, and C.M. Blatteis, Department of Physiology, The University of Tennessee Health Science Center, Memphis, TN

We have shown in previous studies that complement (C) is a necessary mediator of the febrile esponse of guinea pigs and mice to lipopolysaccharides (LPS), but not to muramyl dipeptide or poly I:C. However, these latter two exogenous pyrogens are weak stimulators of the C cascade. Zymosan (Zym), on the other hand, strongly activates C. It is also pyrogenic, probably, according to the available evidence, via induction of cytokines and prostaglandin E2, similarly to LPS. This study was undertaken, therefore, to determine whether C also is pivotal in the production of the fever evoked by this pyrogen. Zym injected intravenously (iv) at 0.5 mg/kg induced a monophasic, 1°C core temperature (Tc) rise, with latency of *ca*. 36 min, peak at 88 min, and recovery at 180 min. Zym at 25 mg/kg, on the other hand, produced a quick-onset, *ca*. 1.1°C Tc fall which reached its nadir at ˜66 min; recovery was completed by 180 min. A second iv injection of 25 mg Zym/kg at 210 min yielded a smaller and briefer fall in Tc, analogous to the effects of consecutive iv injections of 50 U of cobra venom factor (CVF (Sehic *et al.*, 1998), a prototypic activator of the C cascade. The smaller response to a second injection of CVF is attributed to the depletion of C. CVF pretreatment (100 U, iv; C!93%) 18 h before 25 mg Zym/kg converted this Tc fall into a 1.1°C rise that persisted at this level for 92 min, then gradually returned to control over the following 60 min. These results suggest that Zym is inherently pyrogenic, but that this effect is manifested only when the dose of Zym is too small to activate C (*e.g*., 0.5 mg/kg) or when C has been reduced by prior activation of the C cascade (*e.g*., Zym at 25 mg/kg, 100 U CVF). Hence, C would not seem to be a mediator of the febrile response to Zym, but rather to its cryogenic effect.

Sehic, E. *et al.* (1998) *Am. J. Physiol.* 274: R1594-R1603.

Supported in part by NIH grant NS 34857.

blatteis@physio1.utmem.edu