

Title: CHANGES IN POLYMORPHONUCLEAR LEUKOCYTE FUNCTION IN VIVO AND IN VITRO WITH ANESTHESIA AND HYPOTHERMIA

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**Introduction.** Environmental temperature can influence the incidence and severity of infections in man and experimental animals. The sensitivity of different components of host defenses to changes in temperature is not clearly defined for man. Hypothermia can prolong antigen elimination and influence the kinetics of antibody production (1). We have observed neutropenia and frequent life threatening bacterial infections in children subjected to controlled hypothermia as part of their management for increased intracranial pressure. Because of this neutropenia and the importance of polymorphonuclear leukocytes (neutrophils) for defenses against bacterial infections, we examined the effects of hypothermia (29°C) and anesthesia on neutrophil function *in vivo* and *in vitro*.

**Methods.** The effects of anesthesia and hypothermia on neutrophil function *in vivo* were studied in 4 to 6 week old pigs (10-15kg), anesthetized with oxygen and 1.5-2.0 percent halothane. Ventilation was controlled to maintain normocarbida. Esophageal temperature was reduced to 29°C with surface cooling over a period of 90 mins. For *in vitro* studies, neutrophil-rich plasma was obtained by sedimentation of heparinized blood in a solution of 6 percent dextran in saline (4ml dextran and 100 units of heparin/20ml of blood). Neutrophils were sedimented by centrifugation from the neutrophil-rich plasma, washed and resuspended in Krebs-Ringer phosphate medium, pH 7.4. The effect of hypothermia (29°C) on hexose monophosphate pathway activity, oxygen consumption and bacterial phagocytosis and killing by neutrophils was examined (2).

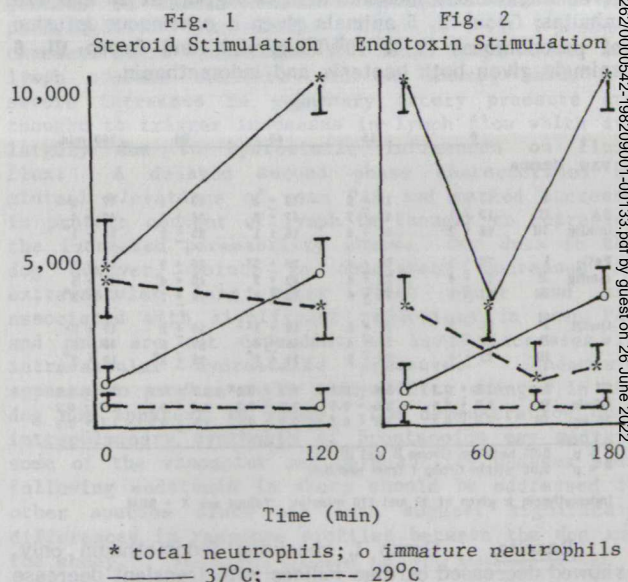
**Results.** No significant change in the number of circulating neutrophils was observed for periods up to 5 hours at 37°C under anesthesia. At 29°C, the number of circulating neutrophils in 13 pigs had fallen by  $2,330 \pm 268$  (cells/cu mm) or 35 $\pm$ 2.8 percent. The effect of hypothermia on the ability of neutrophils to shift from the marginating blood pool to the circulating blood pool was examined by the intravenous administration of catecholamines. Following catecholamine administration at either 37°C or 29°C, there was a brisk and transient increase in the number of circulating neutrophils. The effect of hypothermia on the release of mature and immature neutrophils from the bone marrow was examined by the intravenous (IV) administration of 100mg hydrocortisone sodium succinate (HC) (Fig. 1) or endotoxin (*E. coli*, 0111: B4, Difco Laboratories, Detroit, Michigan), (Fig. 2) both of which are known to stimulate neutrophil release from bone marrow. Following endotoxin administration (1.4 $\mu$ g/kgm IV) at 37°C, there was a rapid fall in the number of circulating neutrophils (Fig. 2). This was followed by an early rise in the number of mature and immature neutrophils. The number of circulating immature neutrophils following endotoxin was approximately equal to the number of mature cells.

At 29°C, endotoxin induced a neutropenia, however the subsequent release of mature and immature neutrophils was minimal.

Neutrophil function was assessed *in vitro* at 37°C and 29°C. Phagocytosis and killing of *Staphylococcus aureus* 502A was reduced at 29°C. Neutrophil metabolism, thought important for bacterial killing, including hexose monophosphate pathway activity and oxygen consumption, were reduced at 29°C.

**Discussion.** Our study demonstrates that halothane anesthesia without nitrous oxide does not depress the number of circulating neutrophils over periods of 2-5 hours. Our finding is supported by the report that halothane did not affect neutrophil function *in vitro* (3).

Hypothermia is accompanied by a fall in neutrophils that may be due, in part, to increased margination. Margination is partially reversible with catecholamines. The release of mature and immature neutrophils from the marrow following HC and endotoxin administration is significantly reduced during hypothermia. Neutrophil metabolism and their interaction with bacteria *in vitro*, are reduced by hypothermia. Our findings may explain in part, the host's apparent susceptibility to bacterial infection during hypothermia.



**References.**  
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3. Nunn JF, Sturrock JE, Jones AJ, et al: Br J Anes 51:1101-1108, 1979.

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