KINETICS AND MECHANISMS OF THE INDUCTION OF AN INCREASE IN COMPLEMENT RECEPTOR POSITIVE (CR^+) MOUSE SPLEEN CELLS FOLLOWING A SINGLE EXPOSURE TO 2450 MHz MICROWAVES

[redacted]

We have previously shown that exposure of mice for 30 minutes to 2450 MHz microwaves induced a marked increase in the level of CR^+ lymphoid cells in the spleen. A series of experiments were conducted to examine the kinetics of this inductive event. It was determined that a minimum of a single 15-minute exposure induced a significant increase, and a maximal increase was noted after a 45-minute exposure. The orientation of the mice in the waveguide during exposure did not alter the results.

The mechanisms for the induction of the increase of CR^+ cells were reasoned to be: a. due to maturation of CR^- to CR^+ cells; b. due to their effect on T cells, which subsequently produced factors affecting B-cell receptors; c. due to the increased permeability of the gut lining, which allowed molecules like lipopolysaccharide (LPS) from the gut flora to cause B-cell activation; and d. it could be due to a genetic susceptibility for this specific inductive event. Experiments performed with the use of athymic nu/nu mice showed data which suggested that this increase in CR^+ cells was not due to the presence of mature T cells. Secondly, mice less than 6- to 8-weeks old, which normally possess few CR^+ cells, failed to show an increase 3 to 6 days following microwave exposure. This suggests that if microwaves are inducing the maturation of CR^- to CR^+ cells, the CR^- cells must first undergo a certain level <u>in situ</u> maturation before being converted to CR^+ cells by microwaves. Thirdly, intraperitoneal injection of several strains of mice with LPS resembled the effect of microwaves by inducing an increase in CR^+ cells. However, two strains of mice that showed a marked increase in CR^+ cells following exposure to microwaves (C3H/HeJ and CBA/N) failed to show a similar increase after LPS injection, suggesting perhaps that other mechanisms were involved. Finally, using various genetically defined mice, it was determined that mice bearing the major histocompatibility ($H\text{-}2^k$) haplotype showed marked increases, whereas mice bearing the $H\text{-}2^b$ and $H\text{-}2^d$ haplotypes were refractory.

We conclude that susceptibility to the inductive events may be under H-2 control. The inductive effects of microwaves are not mediated by LPS, nor by T-cell factors that affect B-cell surface receptors. The evidence suggests that microwaves are inducing the maturation of relatively mature CR^- to CR^+ B cells. We cannot exclude the possibility that microwaves are increasing the density of CR on the B-cell surface.

SUMMARY

We have previously shown that a near-field exposure of mice to 2450 MHz microwaves (amplitude-modulated 12Hz) at a forward power of 0.6 watts induced a marked increase in the level of lymphoid cells in the spleen bearing a receptor for the third component of complement (CR^+). A series of experiments were conducted in an environmentally controlled waveguide facility to examine the kinetics of this inductive event. The absorbed dose rate was computer-calculated from measurements of forward, transmitted, and reflected power and was in the range of 12 to 15 mW/g body weight for each exposure. The proportion of CR^+ spleen cells was determined on days 3 and 6 following microwave exposure. Sham-exposed mice served as controls.

It was determined that a minimum of a single 15-minute exposure induced a significant increase on day 3, which peaked on day 6, and that a maximal increase was noted after a 45-minute exposure. The orientation of the mice in the waveguide (head-to-tail, tail-to-head, left-to-right, or right-to-left to the power source) during exposure did not alter the results.

The mechanisms for the induction of the increase of CR^+ cells were reasoned to be due to: a. the maturation of CR^- to CR^+ cells; b. their effect on T cells which subsequently produced factors that affected B-cell receptors; c. the increased permeability of the gut lining which would allow molecules like lipopolysaccharide (LPS) from the gut flora

to cause B-cell activation; and d. possibly to a genetic susceptibility for this specific inductive event. Experiments performed with athymic CBA/J nu/nu mice suggested that this increase in CR^+ cells was independent of the presence of mature T cells. Mice less than 6- to 8-weeks old, which normally possess few CR^+ cells, failed to show an increase 3 to 6 days following microwave exposure. This suggests that if microwaves are inducing the maturation of CR^- to CR^+ lymphoid cells, the CR^- cells must first undergo a certain level of in situ maturation before being converted to CR^+ cells by microwaves.

The intraperitoneal (i.p.) injection of CBA/J mice with 0.1 or 1.0 µg of LPS resembled the effect of microwaves by inducing an increase in CR^+ cells. Two strains of mice that showed a marked increase in CR^+ cells following exposure to microwaves (C3H/HeJ and male CBA/N which are genetic nonresponders to LPS) failed to show a similar increase in CR^+ cells after LPS injection. This suggests that other mechanisms are involved in the inductive effects of microwaves.

Not all strains of mice tested responded to microwave exposure with an increase in CR^+ spleen cells. Using various genetically defined mice, it was determined that mice bearing the major histocompatibility ($H\text{-}2^k$) haplotype showed marked increases, whereas mice bearing the $H\text{-}2^b$ and $H\text{-}2^d$ haplotypes were refractory. The susceptibility to the inductive events may be under H-2 control. The mechanism(s) of this control remains unknown. The prerequisite for in situ maturity suggests that if microwaves are inducing maturation of B cells, they are interacting with a more mature B cell rather than stem cells. An interesting speculation

is that the target cell is the Ig^+, Ia^+, CR^- B cell which reaches adult levels at 6 to 8 weeks of age. Microwaves would then be inducing the maturation of Ig^+, Ia^+, CR^- B cells to Ig^+, Ia^+, CR^+ B cells. We cannot exclude the possibility that microwaves are increasing the density of CR on the B-cell surface. In this scenario, weakly CR^+ B cells which could not be detected as CR^+ in our assay system would become strongly CR^+ B cells that are readily detectable.