

PATHOGENICITY

DEVELOPMENT OF ANIMAL MODELS FOR *LISTERIA MONOCYTOGENES* (N. Mytle, D. Williams, E.A. Irvin, G. A. Anderson, and M. A. Smith)

Many foodborne illnesses are more serious for certain segments of the population such as immunocompromised individuals. At-risk populations include people taking immunosuppressive drugs or people who have illnesses that suppress the immune system. The very young and very old are also more susceptible to certain foodborne pathogens although the mechanisms of their decreased ability to respond to pathogens are poorly understood. *Listeria monocytogenes* is a foodborne pathogen that has serious and oftentimes fatal effects in at-risk populations. Using *L. monocytogenes* as an example, animal models are being examined for their similarities and differences in susceptibility to listeriosis.

Listeriosis during pregnancy frequently results in stillbirths or neonatal illness and death. Using pregnant rhesus monkeys, pregnant guinea pigs or adult mice, dose response information was collected for *L. monocytogenes* using endpoints of stillbirth and fecal shedding for primates and guinea pigs, and mortality for mice. Pregnant rhesus monkeys were sedated and administered *L. monocytogenes* by nasogastric intubation at doses ranging from 10^3 - 10^8 cfu at the beginning of the third trimester. Pregnancies were allowed to continue normally until parturition. Seven out of 33 animals had adverse pregnancy outcomes.

Experiments conducted in our lab using pregnant guinea pigs confirm they are susceptible to *Listeria*-induced stillbirths. Pregnant guinea pigs were fed orally with 10^7 cfu *L. monocytogenes* in whipping cream at about mid-gestation and sacrificed 21 days later. Twenty-eight percent of fecal samples collected from treated guinea pigs were positive for *L. monocytogenes* while samples from control animals were negative. In control animals, 95% of the fetuses were viable compared to 68.4% at 10^6 cfu and 25% in 10^7 cfu treated animals. In animals treated with 10^7 cfu *L. monocytogenes*, 75% of placentas and 67% fetal livers were positive for *L. monocytogenes*.

Normal or immunocompromised ICR female mice were administered *L. monocytogenes* by intraperitoneal injection. LD₅₀s were determined for 3-and 5-days post-treatment. The mouse LD₅₀ is 10^5 cfu. Preliminary results from guinea pigs indicate a fetal LD₅₀ at approximately 10^6 - 10^7 cfu. Dose response curves for nonhuman primates indicates 50% fetal mortality at a dose of approximately 10^7 cfu which is similar to FDA's estimated LD₅₀ from the human Mexican style cheese outbreak. Thus, when comparing the LD₅₀s of humans, primates and mice after exposure to *L. monocytogenes*, primates and guinea pigs more closely predict the human LD₅₀ than mice. Choosing an appropriate animal model is essential to understanding the biological basis for at-risk populations.