

PATHOGENICITY

RISK ASSESSMENT FOR *LISTERIA MONOCYTOGENES*-INDUCED STILLBIRTHS BASED ON DOSE RESPONSE IN PREGNANT GUINEA PIGS AND NONHUMAN PRIMATES

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Pregnancy-related listeriosis accounts for one-third of the total number of annual cases of listeriosis. Ingestion of *Listeria monocytogenes* by a pregnant woman can lead to undesirable fetal effects including septicemia, meningitis, encephalitis and even death. In joint efforts to reduce the amount of foodborne listeriosis, the FDA/USDA/CDC and the FAO/WHO developed risk assessments of *L. monocytogenes* in various ready-to-eat foods. Both risk assessments relied on dose response data gathered from studies conducted in mice. Recent animal studies using nonhuman primates and guinea pigs have both estimated LD₅₀s of approximately 10⁷ *L. monocytogenes* CFU. The FAO/WHO estimated a human LD₅₀ of 1.9 x 10⁶ CFU based on an outbreak of listeriosis in pregnant women who had consumed contaminated soft cheese. We re-evaluated risk based on dose response curves from pregnant rhesus monkeys and guinea pigs. Using standard risk assessment methodology including hazard identification, exposure assessment, hazard characterization and risk characterization, risk was calculated based on the new dose response information. To compare models, we looked at mortality rate per serving at doses ranging from 10⁴-10¹² *L. monocytogenes* CFU. Based on a serving of 10⁶ *L. monocytogenes* CFU, the primate model predicts a death rate of 5.9 x 10⁻¹ compared to the FDA/USDA/CDC predicted rate of 1.3 x 10⁻⁷. Based on the guinea pig and primate dose response models, the mortality rate calculated by the FDA/USDA/CDC may underestimate the risk for this susceptible population.

ENTEROBACTER SAKAZAKII SUSCEPTIBILITY CHANGES WITH INCREASING AGE IN NEONATAL CD-1 MICE

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Enterobacter sakazakii has been associated with outbreaks of infection in neonatal intensive care units (NICUs), primarily affecting premature or very-low-birth-weight infants orally fed unintentionally contaminated reconstituted powdered infant formula. These infants may develop infections resulting in severe outcomes such as septicemia, necrotizing enterocolitis, meningitis, or death. Infants who recover from infection may have morbidities such as hydrocephalus, mental retardation, or developmental delays. Although increasing age appears to reduce susceptibility, it is not known at what age these infants become less susceptible to *E. sakazakii* infection. Our objectives were to compare the susceptibilities of neonatal mice of different ages to *E. sakazakii* infection and to identify biomarkers of infection. Timed-pregnant CD-1 mice were obtained and allowed to give birth naturally. Neonatal mice were orally gavaged at postnatal day (PND) 1.5, 5.5, and 9.5 with a single dose of vehicle or 10⁴, 10⁸, or 10¹¹ CFU *E. sakazakii* strain MNW2/ml reconstituted powdered infant formula. On post-treatment day 7, surviving pups were sacrificed and brains, livers, and ceca were excised and analyzed for the presence of *E. sakazakii* invasion. *E. sakazakii* was isolated from brains, livers, and ceca of neonatal mice treated at PND 1.5 and 5.5 but not from those of pups treated at PND 9.5. *E. sakazakii* was more invasive in brains than in livers and ceca with total isolations of 25.3%, 21.2%, and 19.7%, respectively. Mortality was observed in neonates treated at the older ages. Like human infants, neonatal mice show a time-dependent susceptibility to *E. sakazakii* infection with resistance increasing with increasing age. Future work will further characterize the infection and provide a model to develop treatments and therapies for *E. sakazakii* infection in human infants.