PANETH CELLS DEFEND NEONATAL SMALL BOWEL AGAINST INVASIVE *ESCHERICHIA COLI.*

Michael P. Sherman, Stephen H. Bennett, and Freda Y. Hwang. University of California, Davis, CA 95616.

Background and Aims. In adults, small bowel crypts have special epithelia called Paneth cells (PCs). These epithelia contain and secrete many anti-bacterial proteins that are believed to protect crypt stem cells from bacterial invasion. Though changes in PC-related morphology have been identified in preterm infants with necrotizing enterocolitis, the role of PCs in anti-bacterial defense of neonatal small bowel is undefined. We theorized that destruction of PCs followed by gut infection with *E. coli* would result in high numbers of planktonic and epithelia-adherent *E. coli*, a finding associated with an increased mortality rate. Methods. Dithizone, a zinc binding dye, was used to rapidly deplete PCs from the intestine of 4-d-old rats. Dithizone [75 mg/kg] was suspended in saturated Li_2CO_3 and given by intraperitoneal injection 6 h before rat litters were infected with an intra-gastric dose of ~2 x 10^{12} colony-forming units [CFU] per kg of entero-invasive *E. coli*. Control litters were given either Li_2CO_3 or NaCl i.p. followed by gut infection with *E. coli*. Survival was determined 18 h later. Small bowel lavage (planktonic or luminal growth) and small bowel homogenates (epithelial gut-related growth) were quantitatively cultured for *E. coli.* Treated and control pups had jejunum and ileum examined microscopically for PCs [hematoxylin & eosin stained, 1000x]. Results. The Table shows the growth of *E. coli* in small bowel fluid & gut wall and the mortality rate; all were significantly higher in dithizone v. controls (mean ± SEM, **P*<.05, ANOVA & post-hoc Scheffe test).

Experimental Groups	NaCl + *E. coli*	Li_2CO_3 + *E. coli*	Dithizone + *E. coli*
Jejunal Homogenate (CFU)	1.2 x 10^6 ± 0.5 x10^6	1.6 x 10^6 ± 0.9 x10^6	19.0 x 10^6 ± 4.5 x10^6*****
Ileal Homogenate (CFU)	6.8 x 10^6 ± 3.5 x10^6	8.2 x 10^6 ± 2.2 x10^6	10.8 x 10^6 ± 3.9 x10^6
Jejunal Lavage (CFU)	0.7 x 10^6 ± 0.2 x10^6	1.2 x 10^6 ± 0.6 x10^6	46.7 x 10^6 ± 15.5 x10^6*****
Ileal Lavage (CFU)	1.6 x 10^6 ± 0.6 x10^6	5.3 x 10^6 ± 1.4 x10^6	68.8 x 10^6 ± 8.6 x10^6*****
Deaths/# of pups [%]	2/24 [8.3 %]	2/24 [8.3 %]	12/32 [37.5 %]***** (χ^2)

Conclusions. Histologic studies showed dithizone kills PCs. There were no deaths after dithizone therapy without infection [n = 24]. This study shows for the 1st time the role of PCs in newborn gut host defense.