

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

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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 $\sim 2 \times 10^{12}$ colony-forming units [CFU] per kg of enteroinvasive *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 \pm SEM, * $P < .05$, ANOVA & post-hoc Scheffe test).

Experimental Groups	NaCl + <i>E. coli</i>	Li_2CO_3 + <i>E. coli</i>	Dithizone + <i>E. coli</i>
Jejunal Homogenate (CFU)	$1.2 \times 10^6 \pm 0.5 \times 10^6$	$1.6 \times 10^6 \pm 0.9 \times 10^6$	$19.0 \times 10^6 \pm 4.5 \times 10^6$ *
Ileal Homogenate (CFU)	$6.8 \times 10^6 \pm 3.5 \times 10^6$	$8.2 \times 10^6 \pm 2.2 \times 10^6$	$10.8 \times 10^6 \pm 3.9 \times 10^6$
Jejunal Lavage (CFU)	$0.7 \times 10^6 \pm 0.2 \times 10^6$	$1.2 \times 10^6 \pm 0.6 \times 10^6$	$46.7 \times 10^6 \pm 15.5 \times 10^6$ *
Ileal Lavage (CFU)	$1.6 \times 10^6 \pm 0.6 \times 10^6$	$5.3 \times 10^6 \pm 1.4 \times 10^6$	$68.8 \times 10^6 \pm 8.6 \times 10^6$ *
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.