2843. Maternal Fecal Transplantation to Infants Born by Cesarean Section: Safety and Feasibility

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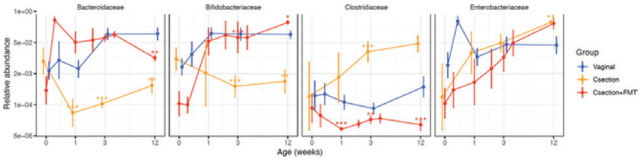
Background. A complication of cesarean section delivery is its interference with the normal intestinal colonization of the infant, affecting the development of immune system in early life—a process that has been associated with long-term morbidity, such as allergy and diabetes. We evaluated, in CS-delivered infants, whether the normal intestinal microbiome and its early life development could be restored by immediate postnatal transfer of maternal fecal microbiota to the newborn.

Methods. Seventeen healthy mothers with planned elective CS were recruited and screened thoroughly for infections, after which 7 mothers were included in the study. A fecal sample was processed according to a transplantation protocol and an aliquot (3–7 mg) was orally administered in breast-milk to the newborn during the first feeding. The infants were followed and fecal samples were gathered during the first 12 weeks of age and subsequently at the age of 8–18 months.

Results. The bacterial communities in the fecal samples of the mothers and their offspring were analyzed by sequencing of 16S rRNA amplicons from isolated fecal DNA and compared with that of 11 nontreated CS-delivered infants and 34 vaginally delivered infants. The fecal microbiota at 3 and 12 weeks was similar between treated CS and vaginally delivered infants, in contrast to that of the untreated CS-delivered infants both in overall composition ($P = 0.001$, Figure) and development of early-life signature bacteria, i.e., bacteroides and bifidobacteria and clostridia ($P < 0.0001$).

Conclusion. The seeding of maternal fecal microbes to the newborn intestine can be safely and successfully mimicked in elective CS by transferring a small amount of maternal fecal microbiome orally to the newborn infant. In these infants, this process results in a microbial development that is highly similar to that of the vaginally born infants, and provides support for the hypothesis that microbial colonization in early life results from a maternal fecal transfer.



Disclosures. **All Authors:** No reported Disclosures.

2844. Butyrogenic Bacteria After Acute Graft vs. Host Disease Associate with the Development of Steroid Refractory GVHD

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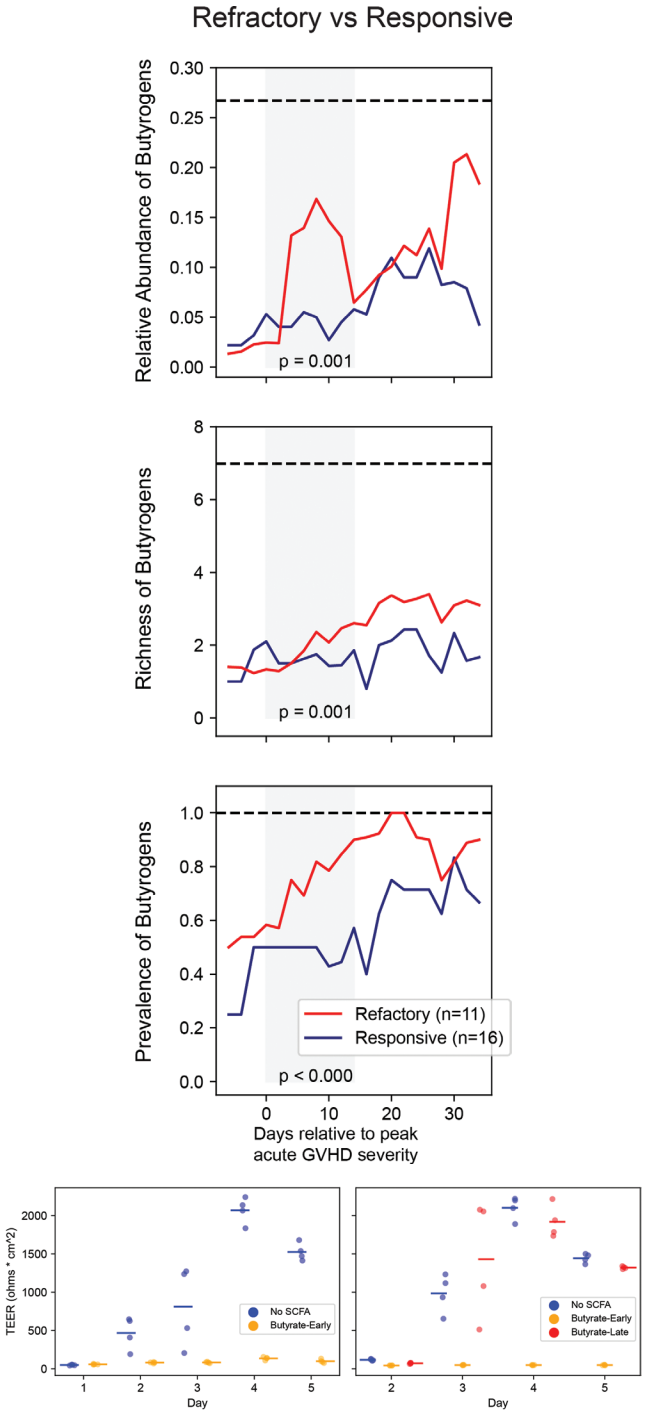
Background. Steroid refractory acute graft- vs. -host-disease (GVHD) after hematopoietic cell transplantation (HCT) is highly morbid with limited treatment options. Murine studies show protection from GVHD with butyrate exposure but direct exposure of stem/progenitor cells to butyrate inhibits colonic stem cell proliferation.

Methods. Stool samples were collected weekly in a cohort of HCT recipients (n = 210) undergoing allogeneic transplant, and underwent 16S rRNA sequencing to determine the number and relative abundance of butyrogens. Dissociated primary human colonoid cell aggregates (200,000 per well) were plated onto collagen IV-coated transwells (0.4 µm pore size, 0.33 cm^2, PET) in stem cell medium for 24 hours. From 24 hours onwards, the basal-lateral chamber was switched to differentiation medium; the apical chamber was Hanks Buffered Salt Solution (HBSS), HBSS with 10 mM butyrate sodium salt early (24 hours onwards) or late (72hours onwards). Trans-epithelial electrical resistance was measured daily.

Results. Retrospective chart review identified 27 recipients who developed acute GVHD of the gut, stratified to be either steroid refractory GVHD (failed to respond to 2 mg/kg of methylprednisolone) or responsive. The presence of butyrogens in the gut microbiome after the onset of severe acute GHVD of the gut associated with increased risk of steroid refractory GVHD (Figure 1; $P < 0.05$). Direct exposure of human colonic stem/progenitor cells to butyrate inhibits the development of trans-epithelial electrical resistance; exposure after differentiation had no inhibition of barrier formation (Figure 2; $P < 0.05$ by T-test).

Conclusion. Butyrogens may help prevent the development of acute GVHD of the gut, but once severe GVHD has developed may inhibit recovery due to the loss of crypt architecture exposing colonic stem cells to microbe-produced butyrate with impaired differentiation and cell replacement.



Disclosures. **All Authors:** No reported Disclosures.

2845. Oral Antibiotic Use and Risk of Colorectal Cancer in the UK, 1989–2012: A Matched Case–Control Study

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Background. Microbiome dysbiosis predisposes to colorectal cancer (CRC), but a population-based study of oral antibiotic exposure and CRC risk is lacking.

Methods. A matched case–control study (incident CRC cases and up to 5 matched controls) was conducted in the Clinical Practice Research Datalink (CPRD; 1989–2012). The CRPD is validated as 92% and 99% sensitive and specific for CRC detection (98% PPV). Antibiotic exposure [categorical and continuous terms (spline)] was investigated for risk pattern, stratified by tumor location, using conditional logistic regression and adjusting for known confounders.

Results. In total, 28,980 CRC cases and 137,077 controls were identified. Oral antibiotic use increased risk of colon cancer in a dose-dependent fashion (P_{trend} < 0.001), but effects differed by anatomic location. Colon cancer risk was greatest in the proximal colon and with antibiotics with anti-anaerobic activity (Figure 1). In contrast, an inverse association was detected between antibiotic use and rectal cancers (P_{trend} = 0.003), particularly with length of antibiotic exposure >60 days (adjusted odds ratio [AOR], 0.85, 95% CI 0.79–0.93) when compared with no antibiotic exposure. Nonlinearity models showed significantly increased colon cancer risk after minimal antibiotic use, but decreased rectum cancer risk with cumulative use of over 30 days (Figure 2). Penicillins, particularly ampicillin/amoxicillin, increased risk of colon cancer (AOR,1.09, [1.05–1.13]) whereas tetracyclines reduced risk for rectal cancer (AOR, 0.90, [0.84–0.97]). Significant interactions were detected between antibiotic use and tumor location (colon vs. rectum, $P_{interaction}$ < 0.001). The antibiotic-cancer association was found for antibiotic exposure occurring >10 years before diagnosis (AOR, 1.17, [1.06–1.31]).

Conclusion. We conclude that oral antibiotic use associates with increased colon cancer risk, particularly in the right colon, but a reduced risk for rectal cancer. This effect heterogeneity suggests unabsorbed antibiotics impact gut microbiota in the right colon to enhance carcinogenesis whereas antibiotic anti-inflammatory or anti-proliferative actions may yield an inverse effect on carcinogenesis in the rectum.

Figure 1. Association between antibiotic use (categorical) and CRC risk

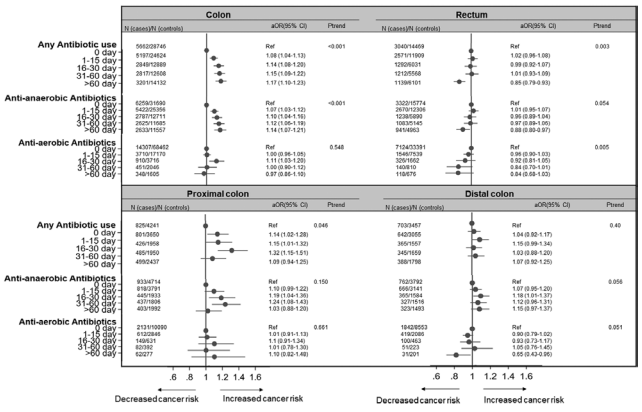
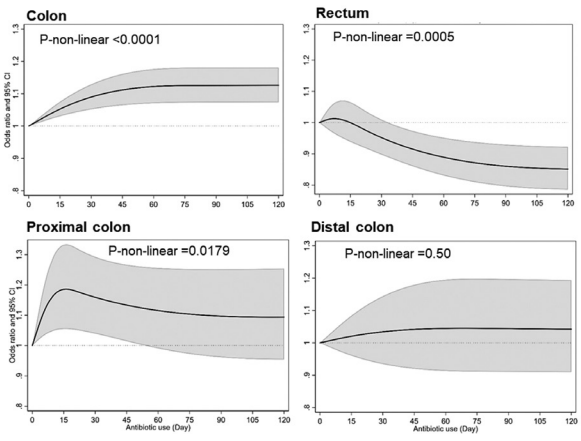


Figure 2. Non-linearity modeling of association between antibiotic use and CRC



Disclosures. Sara E. Cosgrove, MD, MS, Basilea: Consultant; Theravance: Consultant.

2846. Perirectal Samples for Analysis of the Gut Microbiota as a Predictive Tool for Multi-drug-Resistant Organism (MDRO) Acquisition in Nursing Facility (NF) Patients

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Background. Most research examining the association between gut microbiota disruption and MDRO acquisition has been done in acute care settings. Obtaining stool samples in older NF adults is challenging. We hypothesized that perirectal samples can be used as a proxy of the gut microbiota. This prospective cohort study investigated the association between perirectal swab-derived gut microbiota features in newly admitted NF patients and the acquisition of vancomycin-resistant Enterococcus and/or resistant Gram-negative bacteria (rGNB) within 14 days.

Methods. Patients were recruited at 6 MI NFs from September 2016 to October 2018 as part of a larger NIH-funded trial. Colonization status was determined by culture swabs collected from multiple body sites at enrollment, d7, and d14. Our analysis focused on patients with no MDRO at baseline, a perirectal swab collected at baseline, and at least one follow-up visit. The V4 region of the 16S rRNA gene was sequenced from samples and processed with the mothur bioinformatics pipeline. Sequences typically associated with the skin microbiota were removed. The primary outcome was any MDRO acquisition. Exposures of interest included patient and microbiota characteristics. The Microbiome Health Index (MHI) was used to assess microbiota health. An MHI of 0 indicates a balanced abundance between taxa associated with protection and dysbiosis; an MHI above/below 0 suggests better/poorer health, respectively (Figure 1).

Results. Among 60 eligible patients (Table 1), 18 (30%) acquired MDROs within 14 days of enrollment (3 VRE, 13 rGNB, 2 both). The baseline microbiota features differed significantly in those who acquired a new MDRO. Of the major 8 phyla found across samples, patients who acquired an MDRO were depleted in the number of phyla present (4.4 ± 1.1 vs. 5 ± 1.1; P = 0.08) (Figure 2). The log-transformed relative abundance of Enterococcus was enriched in patients who acquired an MDRO (−0.7 ± 3.41) compared with those who did not (−4.2 ± 4.8; P < 0.01) (Figure 3). An MHI below 0 was predictive of MDRO acquisition after adjusting for catheter use within 30 days before baseline (adjusted OR 4.9; 95% CI 1.1–21.1).

Conclusion. Microbiota metrics calculated from perirectal samples are predictive of MDRO acquisition. The clinical utility of perirectal samples warrants further assessment.

Table 1: Baseline characteristics and unadjusted analysis of patients who acquired versus who did not acquire an MDRO. Patient characteristics are shown in n (%) or mean ± standard deviation. Odds ratio of age is calculated using 10 years as a unit.

	Acquired (n = 18)	Did Not Acquire (n = 42)	Odds ratio (95% CI)	p
Age	74.5 (11.5)	71.14 (13.6)	1.24 (0.79 - 1.94)	0.36
Male sex	7 (38.9%)	15 (35.7%)	1.15 (0.37 - 3.58)	0.82
White race	10 (55.6%)	26 (61.9%)	1.3 (0.42 - 3.98)	0.65
Presence of urinary catheter within 30 days before baseline	4 (22.2%)	4 (9.5%)	2.85 (0.62 - 13.05)	0.18
Physical self-maintenance scale	11.44 (3.9)	11.54 (3)	0.99 (0.83 - 1.18)	0.92
Log Charlson's comorbidity score	1.16 (0.6)	1.09 (0.6)	1.21 (0.49 - 3)	0.69
BMI > 30	4 (22.2%)	17 (40.5%)	0.41 (0.11 - 1.52)	0.18
BMI < 20	3 (16.7%)	6 (14.3%)	0.86 (0.18 - 4.16)	0.85
Exposure to high-risk antibiotics	7 (38.9%)	6 (14.3%)	3.24 (0.86 - 12.26)	0.08
Exposure to low-risk antibiotics	2 (11.1%)	11 (26.2%)	0.51 (0.09 - 2.73)	0.43

Figure 1: Proportion of patients with different MHI categories (> 0, higher; < 0, lower). Higher MHI indicates higher abundance of bacterial classes associated with protection than those associated with disruption, and vice versa. Having an MHI < 0 was an independent predictor of MDRO acquisition after adjusting for urinary catheter use (adjusted odds ratio, 4.9; 95% confidence interval, 1.1 to 21.1; P = 0.03). RA = relative abundance.