Disrupting primary succession during childbirth: Is there a long-term consequence?

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Abstract

Background/Questions/Methods. Childbirth is a model system in which to study primary succession. Microbial colonization of a child starts as they move down the birth canal. Disruption of microbial colonization (i.e., primary succession) of the gut in newborns by antibiotics during this intrapartum period may have long term consequences on the development of a child's immune system, ultimately resulting in atopies (i.e., asthma, allergies, and eczema). Currently three possible explanations for the occurrence of such atopies exist, which include genetic inheritance, the hygiene hypothesis, and the microflora hypothesis. Based on the microflora hypothesis, which proposes atopies are a result of disrupted microbial colonization of the child, our goal was to determine if children exposed to intrapartum antibiotics were more likely to develop eczema than those who did not. A retrospective cohort study was conducted using survey data, medical records of women who gave birth vaginally with or without antibiotics during delivery, and pediatric records of the children.

Results/Conclusions. A total of 436 women enrolled in the study (22.4% response rate). Because some women had multiple children who met our study criteria, the data include 490 mother-child pairs. Preliminary analyses of the data suggest that no significant relationship exists between the use of intrapartum antibiotics and the development of eczema (RR 1.01, p=1.0000), allergies (RR 1.06 p=0.8059), or asthma (RR 0.88, p=0.6718). However, significant associations were found between asthma diagnoses in children and antibiotics administered by 1 month of age (RR 1.88, p<0.05) and male children (RR 1.55, p<0.05). Significant results were also found between eczema diagnoses in children and birth order (RR 1.80, p<0.05). The human microbiome is thought to encode 100-fold more unique genes than our own genome, therefore understanding how processes like primary succession of the gut are affected may help us better understand human health.

Introduction

Primary succession is the colonization process of newly exposed environments. In utero a developing fetus typically exists in a sterile environment; it is not until a child begins the progression down the birth canal that microbial colonization occurs. Childbirth therefore may serve as an ideal model system in which to study primary succession and ultimately ecosystem function.

Microorganisms that colonize the human body are essential to human health. The microbiome has essential roles in metabolism, immune system development, and other processes (Fig. 1). Children delivered vaginally have different microbiota than those delivered by cesarean (1-2). Community differences in the microbiota may persist for years (1). Such disruption of primary succession results in lowered abundances of Lactobacillus and Bacteriodes species and greater Clostridial species, which may also alter ecosystem function (2-5). Negele et al. (2004) have shown children delivered by cesarean are at greater risk of atopies than children delivered vaginally.

Antibiotics kill potentially pathogenic microorganisms and during childbirth, the expectant mother may receive antibiotics for a number of reasons. Effective antibiotic treatment during the intrapartum period, however, disrupts primary succession of the neonate, which may ultimately affect ecosystem function. Here we explore early childhood **health consequences as a result of disrupting primary succession with antibiotic exposure during childbirth.** We are particularly interested in the development of atopies (i.e., asthma, allergies, eczema).

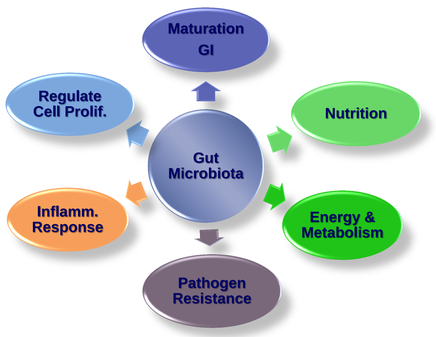


Fig. 1. The gut microbiota has an essential role in host processes.

Currently three possible explanations for the occurrence of atopies exist. Prevalence of asthma, allergies, and eczema may be explained by genetic inheritance, the hygiene hypothesis (i.e., lack of immune system challenge during development), or the microflora hypothesis (Fig. 2). The microflora hypothesis proposes atopies are a result of disrupted microbial colonization of the child. Using a retrospective study, we examine whether or not disruption of primary succession has long-term effects on the development of atopies.

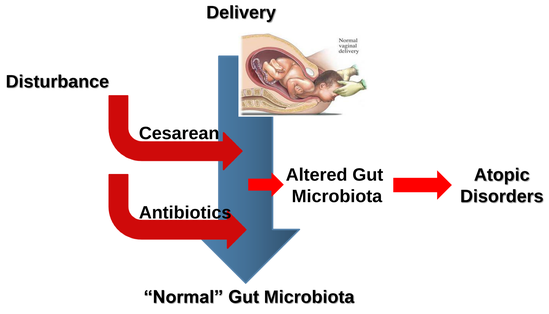
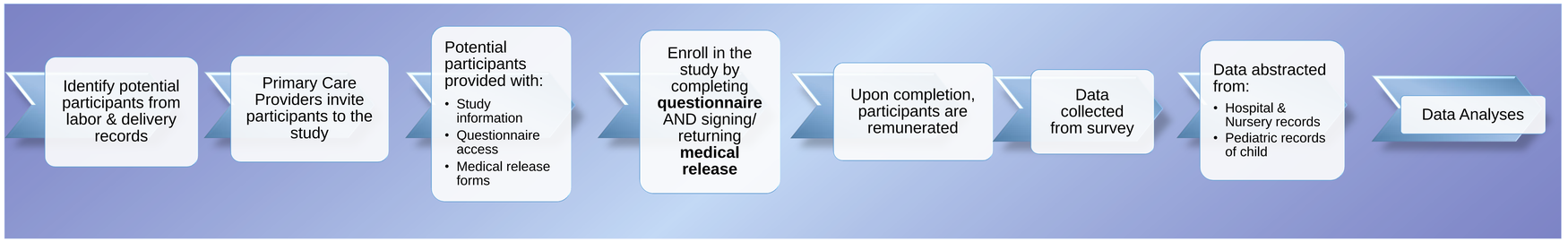


Fig. 2. The Microflora Hypothesis.

Methods



Results

The primary care physicians invited a total of 1944 women to participate in the study. Of the invited women, 436 consented to participate through receipt of medical release forms for their child and completion of the on-line questionnaire (i.e., 22.4 % response rate). Each mother had 1-4 children enrolled; 490 mother-child pairs were analyzed that met our selection criteria.

Table 1. Descriptive variables of the study population.

Characteristic	Mean	
Gestational Age	39.4 weeks	
Birth Weight	3.52 kg 7 lbs, 12 oz	
	M	F
Children (n=490)	262	228
Eczema	76	56
Asthma	50	28
Allergies	67	46

Table 2. Relative Risk (RR) of having eczema, allergies, or asthma in children under 2 years of age based on gender, intrapartum or other antibiotics within the first 30 days of life, pets, or birth order. Asterisk (*) indicates significance (p<0.05).

		Eczema		Allergies		Asthma	
		n (%)	RR (p-value)	n (%)	RR (p-value)	n (%)	RR (p-value)
Gender	Male	76 (29.0)	1.18 (0.3015)	67 (25.6)	1.27 (0.1638)	50 (19.1)	**1.55*** (0.0474)
	Female	56 (24.6)		46 (20.2)		28 (12.3)	
Same Maternal Atopy	Yes	21 (31.8)	1.22 (0.3711)	83 (27.6)	**1.74*** (0.0029)	16 (23.9)	1.63 (0.0708)
	No	111 (26.2)		30 (15.9)		62 (14.7)	
Same Paternal Atopy	Yes	12 (41.4)	1.55 (0.1293)	58 (32.0)	**1.80*** (0.0004)	17 (41.5)	**2.93*** (0.0001)
	No	101 (26.6)		55 (17.8)		52 (14.2)	
Intrapartum Antibiotics	Yes	34 (27.2)	1.01 (1.0000)	30 (24.8)	1.06 0.8059	18 (14.4)	0.88 (0.6718)
	No	91 (72.8)		83 (22.7)		60 (16.4)	
Pediatric Antibiotics (≤30 days)	Yes	15 (27.3)	1.01 (1.0000)	12 (21.8)	0.94 (1.0000)	15 (27.3)	**1.88*** (0.0193)
	No	117 (26.9)		101 (23.2)		63 (14.5)	
Birth Order	First	78 (35.8)	**1.80*** (0.0001)	51 (23.4)	1.03 (0.9142)	33 (15.1)	0.91 (0.7105)
	Not first	140 (64.2)		62 (22.8)		45 (16.5)	
Pets	Yes	77 (27.9)	1.09 (0.6089)	69 (25.0)	1.22 (0.1638)	46 (16.7)	1.11 (0.6212)
	No	55 (25.9)		44 (20.6)		32 (15.0)	

Discussion

Study of primary succession leads to a better understanding of colonization dynamics and ultimately the link between communities and ecosystem function. Disrupting primary succession during childbirth by the introduction of antibiotics during delivery may have long-term consequences on ecosystem function leading to the presentation of atopies. We found disrupting primary succession during childbirth with antibiotics may have little to no long-term consequences in children under the age of two.

The microflora hypothesis proposes disruption of microbial colonization, thus altering the Th1 and Th2 balance of the baby leads to hypersensitivities. The calculated relative risk (RR) for these data indicated neither intrapartum antibiotics nor pediatric antibiotics before one month of age increased the likelihood of these children developing eczema or allergies (Table 1). Particularly for asthma, genetics may play an important role in atopies. Male children, as well as children with a father or mother having an atopy were at greater risk of having the same atopic outcome (Table 1). Siblings and pets may challenge the immune system through their introduction of additional microorganisms. In support of the Hygiene Hypothesis, first-born children have a greater risk of developing eczema than their counterparts (RR 1.80, p=0.0001). However, pets had no risk association with any atopy.

We can conclude from these findings that disruption of primary succession with antibiotics during delivery does not pose a risk for atopies. However, a more significant disruption of primary succession, such as cesarean delivery, or longer-term suppression of colonization by antibiotics or diet may have consequences on ecosystem function.

Literature Cited

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Acknowledgements

Many thanks to Katie Diamond, Stephanie Dougherty, Brittany Kuperavage, Muhammad Arslan Rashid, Liesl Sieber, and Kaitlyn Tyrie for all of your help with data abstraction and entry. We gratefully acknowledge support from the Biology Department of Elizabethtown College, Franklin and Marshall College's Center for Opinion Research, and Penn State University's Evaluation and Health Sciences. Funding provided by the National Institute of Health Award No. 1R15A1076933-01A1