

**CESAREAN SECTION VERSUS VAGINAL DELIVERY: EARLY
MICROBIOME SEEDING AND LATER HYGIENE-RELATED DISEASE
RISK — A NARRATIVE REVIEW**

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Abstract

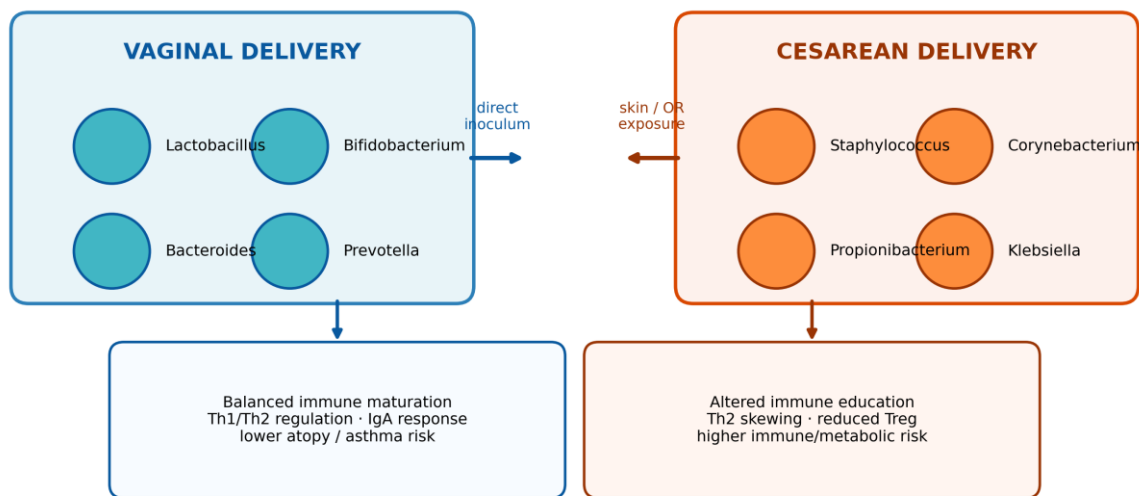
Birth is the first and arguably the most consequential microbial exposure of a human life. During vaginal delivery, the newborn passes through the birth canal and is inoculated with maternal vaginal and perineal microbiota dominated by *Lactobacillus*, *Prevotella*, and *Bacteroides* species; infants born by cesarean section (C-section) bypass this inoculum and are instead colonized mainly by skin and operating-room-associated organisms such as *Staphylococcus* and *Corynebacterium*. This early divergence, occurring within a narrow developmental window of immune education, has been proposed as one mechanistic bridge linking the modern rise in C-section rates to the parallel rise in allergic, autoimmune, and metabolic conditions predicted by the hygiene hypothesis. This narrative review synthesizes current evidence on: (i) how delivery mode alters the composition and maturation trajectory of the infant gut microbiome; (ii) epidemiological associations between C-section and asthma, atopy, food allergy, obesity, type 1 diabetes, and celiac disease; (iii) proposed mechanisms involving T-helper imbalance, regulatory T-cell function, and short-chain fatty acid signaling; and (iv) the emerging intervention of vaginal seeding, its evidentiary support, safety concerns, and regulatory status. We conclude that while the association between C-section and hygiene-related disease is consistent across many cohorts, causality remains incompletely established, confounding factors such as peripartum antibiotics, labor status, and breastfeeding must be carefully parsed, and large randomized trials of microbiome restoration are needed before clinical implementation. Birth mode should be viewed not as a deterministic risk factor but as one modifiable exposure within a wider ecosystem of early-life microbial influences.

1. Introduction: Birth as the First Microbial Event

Human beings carry more microbial cells than human cells, and the assembly of this community begins not in the cradle but in the delivery room. Until recently, it was assumed that the fetal gut was essentially sterile and that microbial colonization began after birth with whatever organisms happened to be nearby. Landmark work by Dominguez-Bello and colleagues overturned this assumption in 2010, showing that the mode of delivery predictably determines the founding populations of the infant microbiome. Vaginally delivered infants acquire bacterial communities that resemble their mother's vaginal and perineal flora, whereas infants delivered by C-section are first colonized by microbes resembling the mother's skin and the ambient environment of the operating room.

This discovery arrived at a moment of epidemiological urgency. The global C-section rate has climbed from an estimated 7% of births in 1990 to roughly 21% today, exceeding 60% in some countries — far above the 10–15% that the World Health Organization considers medically necessary. Over the same decades, the burden of allergic rhinitis, asthma, atopic dermatitis, food allergy, obesity, and autoimmune conditions such as type 1 diabetes and celiac disease has risen sharply, particularly in industrialized and rapidly urbanizing societies. The hygiene hypothesis — first articulated by Strachan in 1989 and later refined into the 'old friends' and microbial-deprivation hypotheses — proposes that reduced exposure to diverse, immunomodulatory microorganisms early in life impairs immune calibration and increases susceptibility to these very conditions.

Birth mode sits precisely at the intersection of these two trends. It is the earliest environmental exposure that differs systematically between C-section and vaginally delivered infants, and it precedes the development of the diseases in question. This review examines the evidence connecting delivery mode, early microbiome seeding, and later hygiene-related disease risk; interrogates the strengths and weaknesses of that evidence; and evaluates vaginal seeding as a proposed remedy.



First microbial exposure at birth shapes the infant gut microbiome — and through it, immune development.

Figure 1. Conceptual schematic of first microbial exposure by delivery mode and its downstream immunological consequences.

2. What the Evidence Shows: Seeding of the Infant Microbiome

2.1 Founding populations differ by delivery mode

Cultivation-independent sequencing studies, beginning with Dominguez-Bello et al. (2010) and extended by large cohorts such as the Canadian CHILD study and the TEDDY consortium, have repeatedly confirmed a stereotyped pattern. Immediately after birth, the mouths, skin, and first stools of vaginally delivered infants are enriched in *Lactobacillus*, *Prevotella*, *Bacteroides*, and other taxa characteristic of the maternal vagina and perineum. C-section infants, by contrast, show enrichment of *Staphylococcus*, *Corynebacterium*, and *Propionibacterium* — organisms associated with skin — and, in their guts, delayed acquisition of *Bifidobacterium* species transferred from the maternal fecal reservoir.

The functional consequences of this different starting material extend beyond simple taxonomy. Gut bacteriophage communities also differ by delivery mode during the first months of life. C-section infants show reduced maternal-to-infant transmission rates overall, a higher early alpha diversity (paradoxically reflecting a more 'adult-like' but less specialized community), and increased carriage of potential opportunists such as *Klebsiella* and *Enterobacteriaceae*.

2.2 Divergence is strongest in a critical window, then partial convergence

The differences are most pronounced during roughly the first six months of life. Over the first weeks, vaginally delivered infants develop higher levels of Bifidobacterium and Bacteroides — the primary degraders of human milk oligosaccharides — while C-section infants lag in these beneficial taxa. After weaning and the introduction of solid foods, the microbiomes of the two groups begin to converge, and by school age most broad compositional differences disappear. Yet animal experiments warn against complacency: transient disruptions confined to the neonatal window can produce durable changes in immune phenotype, indicating that the timing of exposure matters as much as its duration.

An important nuance is that 'C-section' is not a single exposure. Infants delivered by C-section after the onset of labor and rupture of membranes share more maternal vaginal microbes than those delivered before labor, and routine peripartum antibiotics — administered in a large fraction of C-sections — independently suppress Bacteroides and other anaerobes, complicating attribution. Breastfeeding powerfully shapes the infant gut and can substantially narrow the gap between delivery-mode groups.

Table 1. Comparison of early microbiome seeding by delivery mode.

Feature	Vaginal delivery	Cesarean delivery
Primary inoculum	Maternal vaginal & perineal microbiota	Maternal skin & operating-room environment
Dominant early taxa	Lactobacillus, Prevotella, Bacteroides	Staphylococcus, Corynebacterium, Propionibacterium
Maternal gut transmission (Bifidobacterium)	High, rapid	Reduced, delayed
Early gut alpha diversity	Lower early, rising over weeks	Higher at birth ("premature" diversity)
Opportunist carriage (Klebsiella, Enterobacteriaceae)	Lower	Higher

Window of maximal divergence	First ~6 months; converges after weaning	First ~6 months; converges after weaning
Key confounders	Peripartum antibiotics; labor status; feeding mode	Peripartum antibiotics (routine); labor status; feeding mode

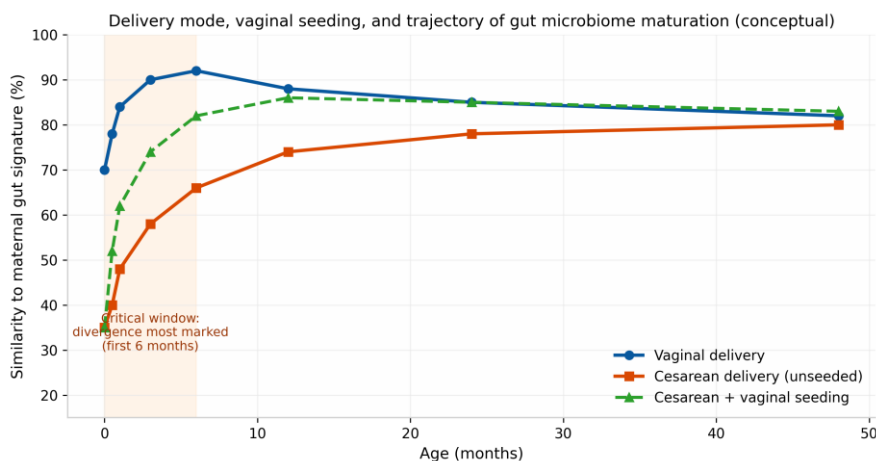


Figure 2. Conceptual trajectory of gut microbiome maturation after vaginal delivery, unseeded C-section, and C-section with vaginal seeding. The critical window of divergence lies within the first six months.

3. Mechanisms Linking Birth Mode to Immune Education

How could a difference in founding bacteria influence disease risk years later? The leading mechanistic framework has several layers. First, commensal organisms educate the developing immune system through pattern-recognition receptors: lipopolysaccharide from *Bacteroides* and *Escherichia* activates Toll-like receptor 4 signaling, while flagellin and other ligands engage additional receptors, jointly promoting proper maturation of gut-associated lymphoid tissue. Second, microbial fermentation of dietary fiber produces short-chain fatty acids (acetate, propionate, butyrate) that induce regulatory T cells, modulate histone deacetylases, and calibrate inflammatory tone. Third, specific taxa influence the Th1/Th2/Th17/regulatory balance; early colonization studies found lower serum IgG, IL-12p70, and IFN- γ -to-IL-4 ratios in C-section infants, consistent with a Th2-skewed phenotype that characterizes allergic disease.

Clinical observations lend biological plausibility. Vaginally delivered infants mount stronger antibody responses to pneumococcal and meningococcal vaccines, correlating with early-life *Bifidobacterium* and *E. coli* abundance. In the CHILD cohort, children

whose gut microbiome at one year retained a 'C-section-like' signature — low *Bacteroides*, *Faecalibacterium*, *Roseburia*, and *Akkermansia* with high *Enterobacteriaceae* and *Veillonella* — had substantially higher asthma rates by age six than C-section children whose microbiomes had normalized, and than vaginally delivered children. This is a crucial finding: it is not the surgery per se, but the persistence of a disrupted microbial trajectory, that tracks risk.

The hygiene-related diseases linked to C-section are precisely those characterized by immune dysregulation — excessive Th2 responses in allergy, failed tolerance in food allergy and celiac disease, loss of self-tolerance in type 1 diabetes, and low-grade systemic inflammation in obesity. This coherence across mechanistic, immunological, and epidemiological levels is what makes the birth-mode hypothesis compelling, even as individual studies disagree.

4. Epidemiological Associations with Hygiene-Related Disease

Two decades of observational research, culminating in meta-analyses and registry studies of hundreds of thousands of children, have associated C-section delivery with a modestly increased risk of a broad set of immune and metabolic conditions. Effect sizes are typically small-to-modest (odds ratios of roughly 1.2–1.5), but the exposure is common, so the population-attributable burden is meaningful.

Table 2. Cesarean delivery and later hygiene-related disease: summary of epidemiological associations (approximate pooled effect sizes; for orientation — consult primary meta-analyses for precise estimates).

Outcome	Approx. OR (95% CI)	Selected evidence	Strength of evidence
Asthma / wheeze	1.21 (1.11–1.32)	Meta-analyses; CHILD cohort microbial-score analysis; risk concentrated in children with sustained microbiome disruption	Moderate–strong
Atopy / allergic rhinitis	1.46 (pooled across cohorts)	Large observational	Moderate

		studies and meta-analyses; associations strongest for intrapartum antibiotic-exposed and non-labor C-section	
Food allergy / sensitization	1.3–1.5 range in recent cohorts	High-risk cohort analyses; 2026 ACTIVATE trial data on sensitization after seeding	Emerging
Childhood overweight/obesity	1.33 (1.20–1.47)	Meta-analyses; partially attenuated after adjustment for maternal BMI; murine transplant models transmit the obese phenotype	Moderate
Type 1 diabetes	~1.19 (1.05–1.36)	Registry-based studies; consistent but modest; antibiotic exposure a key confounder	Moderate
Celiac disease	~1.26 (1.10–1.44)	Swedish registry data; association with elective more than emergency C-section	Moderate

IBD, juvenile arthritis, other autoimmune	Variable, 1.1–1.4	Mixed; several meta-analyses report small but significant associations	Weak–moderate
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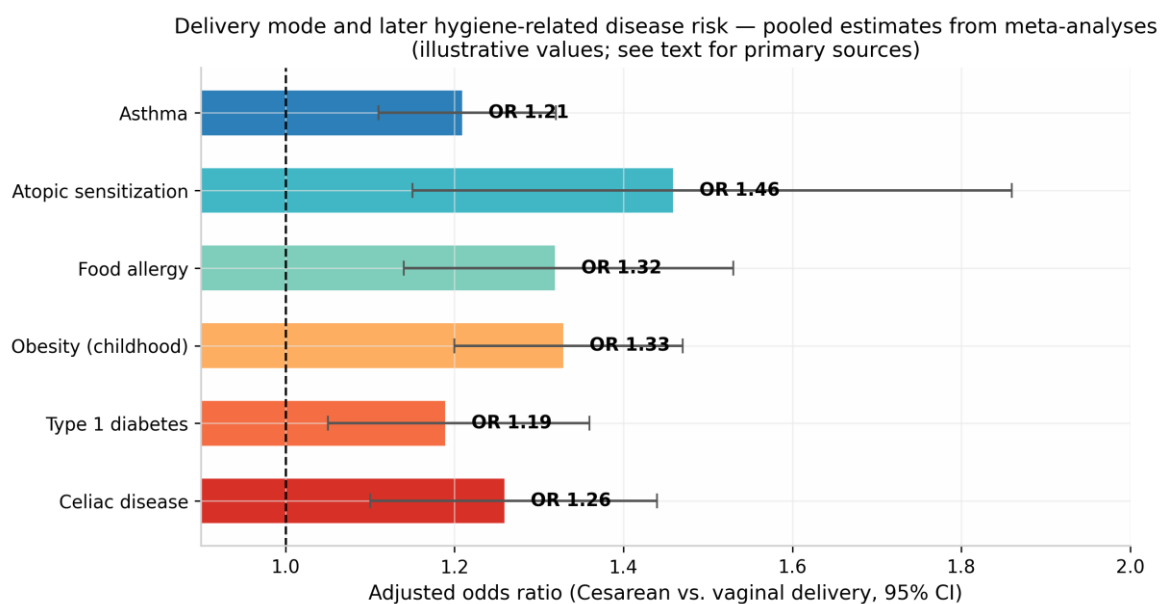


Figure 3. Illustrative pooled odds ratios (95% CI) for hygiene-related diseases comparing C-section to vaginal delivery, compiled from published meta-analyses and large cohorts.

Three caveats temper these associations. First, residual confounding is substantial: women delivering by C-section differ from those delivering vaginally in maternal obesity, age, indication for surgery, antibiotic exposure, and breastfeeding initiation, each of which independently affects both microbiome and disease risk. Some studies that adjust aggressively for these factors see the obesity and asthma associations shrink. Second, heterogeneity matters: elective pre-labor C-section generally carries higher risk associations than intrapartum C-section, underscoring the role of labor-related microbial exposure. Third, effect sizes are small — the large majority of C-section children never develop any of these conditions — so birth mode is best understood as one probabilistic tile in a larger mosaic that includes diet, antibiotics, siblings, pets, and environment.

5. Vaginal Seeding: Can the Inoculum Be Restored?

If disrupted seeding is part of the problem, restoring it might be part of the solution. Vaginal seeding — inserting a sterile gauze into the mother's vagina before C-section, then swabbing the newborn's mouth, face, and skin with it — was pioneered in a small 2016 pilot study that showed partial normalization of the seeded infants' microbiomes within the first month. Subsequent randomized trials have refined the picture:

Table 3. Key studies of vaginal seeding and related microbial restoration interventions in C-section infants.

Study (year)	Design / population	Microbiome effect	Clinical outcome
Dominguez-Bello et al. (2016)	Pilot, 4 seeded vs 7 unseeded C-section, 7 vaginal	Seeded infants resembled vaginally delivered infants, esp. week 1	Not assessed
Song et al. / Zhou et al. (2023), Cell Host & Microbe	Blinded RCT, China, ~86 infants	Engraftment of maternal bacteria; reduced pathobionts (Enterobacteriaceae)	Improved neurodevelopment scores at 6 months (early signal)
Liu et al. (2023), AJOG MFM	RCT, China, 120 infants, follow-up to 24 months	No significant compositional differences; trend to more Lactobacillus/Bacteroides	No effect on BMI or allergy risk to 2 years
ACTIVATE (2026, reported)	Double-blind RCT, high-allergy-risk infants, 113 total	Confirmed maternal microbial transfer; Lactobacillus enriched in stool	Differences in food sensitization at 12 months under analysis
Korpela et al. (2020, proof of concept)	Maternal fecal transplant to 7 C-section infants	Increased Bacteroides to 21 days; reduced pathobionts	Not assessed

The evidence is therefore mixed: seeding measurably transfers maternal microbes and shifts early composition toward a vaginally delivered pattern in most trials, but effects on hard clinical endpoints remain unproven, and one adequately powered trial found no durable compositional or clinical benefit. Safety is the central concern. Maternal vaginal fluid can harbor group B Streptococcus, herpes simplex virus (often asymptomatic at delivery), HIV, hepatitis, chlamydia, gonorrhea, and E. coli K1, any of which could cause devastating neonatal infection when deliberately inoculated. Consequently, the American College of Obstetricians and Gynecologists does not recommend vaginal seeding outside institutional review board-approved research, and trial protocols impose rigorous screening — STI panels, group B strep testing, and vaginal pH ≤ 4.5 to confirm a Lactobacillus-dominated, non-dysbiotic flora — plus exclusion of any woman with signs of infection.

Researchers are also exploring alternatives and complements: maternal fecal microbiota transfer administered with the first feed (which more directly restores gut Bacteroides), probiotic supplementation, and — most pragmatically — supporting immediate breastfeeding and skin-to-skin contact after C-section, both of which demonstrably narrow the microbiome gap.

6. Discussion and Future Directions

The birth-mode hypothesis has matured from a striking observation into a research program with real mechanistic depth, but it has not yet earned deterministic status. The most defensible reading of current evidence is threefold. First, C-section reproducibly alters early microbial colonization, and these alterations plausibly contribute to immune and metabolic phenotypes. Second, epidemiological associations with asthma, atopy, obesity, and autoimmunity are consistent in direction and coherent with mechanism, but modest in size and vulnerable to confounding — particularly by peripartum antibiotics, which are inextricably entangled with surgical delivery. Third, the clinical translation of microbiome restoration remains experimental; vaginal seeding is biologically rational and microbiologically effective, but not yet proven to improve health outcomes, and it carries real infectious risk without stringent screening.

Several research priorities follow. Large, factorial randomized trials that disentangle delivery mode from antibiotic exposure, labor status, and feeding are needed. Trials of seeding should be powered for clinical endpoints — asthma, obesity, food allergy — rather than surrogate compositional outcomes, and should prespecify analysis of which maternal microbial features predict benefit. Longitudinal multi-omics tracking from

birth through school age, with immune phenotyping, would help identify which transient microbial signals cast the longest shadows. Finally, a systems view is warranted: birth mode is one node in a network of early-life exposures, and the most realistic near-term strategy for C-section families is likely a bundle of breastfeeding support, judicious antibiotic stewardship, and avoidance of unnecessary surgical deliveries.

For clinicians counseling expectant parents, the practical message is balanced. C-section, when medically indicated, remains safe and often lifesaving; the absolute increase in any single later disease from an individual C-section is small. At the same time, elective C-section without medical indication — and elective antibiotic use in labor — deserves renewed scrutiny as modifiable exposures. Vaginal seeding should be neither marketed nor performed outside approved trials.

7. Conclusion

Vaginal delivery provides the newborn's first microbial inoculum, and C-section departs from this ancestral pattern in a consistent, measurable way. The resulting divergence in early gut ecology coincides with — and in animal and human mechanistic studies plausibly contributes to — the heightened risk of allergic, autoimmune, and metabolic diseases that define the hygiene hypothesis era. Yet correlation is not destiny: the microbiome differences are largest in the first six months, converge with maturation, and are buffered by breastfeeding and labor exposure, while disease associations are modest and confounded. Vaginal seeding offers a tantalizing proof of concept that the trajectory can be shifted, but evidence of clinical benefit is not yet sufficient, and safety demands respect. The coming decade of adequately powered randomized trials will determine whether restoring the microbial handshake of birth can translate into preventing disease — and, in the meantime, supports a simple clinical posture: protect vaginal birth where safe, support early feeding, and use antibiotics and surgery judiciously.

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