

**The immunological consequences of Caesarean sections
as associated with host susceptibility to
a human papillomavirus (HPV) infection**

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Excerpt

In 2010, the World Health Organization reviewed studies that assessed the association between national Caesarean section (CS) rates and mortality and morbidity outcomes in mothers and newborns, concluding that the upper limit recommendation for these rates should be 15% of a country's total number of births—this rate including both CSs considered necessary and those considered as excess [1]. However, despite this recommendation, approximately 6.2 million CSs in excess are performed every year, with China and Brazil's national rates accounting for almost half of the total number of unnecessary CSs worldwide. Studies have attributed these two countries' overwhelmingly high number of CSs to a number of social factors including cultural beliefs, women's fears of the physiological implications of the natural birthing process such as labor pain and impaired sexual performance post-delivery, patient concerns regarding quality of care, health insurance policies for mothers, and physicians' preference for the possibility of higher revenue and flexible working hours with CSs [2]. Furthermore, according to a case study in Rio de Janeiro, 70% of a study population of mothers initially did not prefer CSs; however, after consultations with their physicians, 90% of the study population elected for a CS as the mode of delivery, demonstrating the influence of interaction with health services [3].

Unfortunately, this transition toward a CS-centric childbirth care model in many developing countries has had a detrimental effect on the early immune development of offspring, resulting in increased susceptibility to immune disorders as well as to other acute and chronic diseases. Studies thus far have observed associations between CS and later risks of

developing asthma, neonatal lung disease, allergic rhinitis, childhood-onset type 1 diabetes, gastroenteritis, celiac disease, aseptic necrosis of the femoral head and cancer (leukemia, neuroblastoma, testicular cancer) in comparison with children born by vaginal delivery [4]. Most findings regarding the compromised immune health of CS offspring have been attributed to lower intestinal bacterial colonization (from bypassing delivery through the mother's birth canal and perianal region) [5], insufficient activation of the hypothalamic-pituitary-adrenal axis (as infants delivered by CS are deprived of the surge of stress hormones brought on by vaginal delivery) [6], and permanent epigenetic alterations that may affect the early gene methylation involved in regulating T-helper type 1 and 2 cells [7], which play integral roles in adaptive immunity. These considerations have suggested further study into the direct effects of Caesarean section—low birth weight [8], early treatment of antibiotics for the mother undergoing CS and her infant [9], delayed breastfeeding [10], decreased intestinal microflora population, and altered stress responses—on immune health and development in CS-offspring.

In light of the possible links between CS and compromised immune development in offspring, we will investigate the possibility of an association between the immunological consequences of Caesarean sections and increased host susceptibility to a human papillomavirus (HPV) infection. Human papillomavirus, a DNA virus transmitted through sexual contact via keratinocytes of the skin or mucous membranes, can cause genital warts and, if persistent or left untreated, can develop into precancerous intraepithelial lesions and invasive cancers, such as cervical cancer [11]. In developing countries, there is often a high prevalence of HPV and cervical cancer, as well as a high rate of pre-labor, elective CSs. For example, in Brazil, cervical cancer linked with positive HPV-16/18 results ranks as the second most common cancer among women between ages 15 and 44 [12] and CSs account for about three-quarters of births among private patients—one of the highest percent of cases in the world. Furthermore, many of these developing countries also suffer from high rates of HIV/AIDS within their populations. As primary HIV-1 infections and CSs have both been associated with abnormal CD4+ T lymphocyte

counts in the gastrointestinal tract [13], and HPV and HIV have been found to display complementary coinfection [14], there could be an indirect association between mode of delivery and offspring susceptibility to human papillomavirus infection.

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Author Commentary

Isabella Gomes

My fall semester junior paper focused on the effects of the immunology of Caesarean sections (CS) on newborns and the interaction (and similarities) of this biology with the infection pathways of human papillomavirus (HPV) later in life. I started the process by delving into the history of CS, choosing Brazil as a lens through which to study national rates of CS and the impact of the procedure on a population public health level.

In order to create a compelling motive, I followed a three-pronged approach: (1) I included findings from existing literature that created precedent for additional study on the matter, (2) I addressed gaps in the research that had overlooked or inadequately analyzed my specific topic, and (3) I described specifically why additional research was necessary and what further studies could do for the field, thereby appealing to a broad audience that included public health researchers as well as the general public. A guiding principle in good writing is “Why should this issue matter to people?” Great writing comes from making this explicitly clear throughout the piece.

Next, I dove into academic papers that discussed my topic both directly and tangentially, extracting and categorizing interesting, relevant key points that could be used to direct the creation of my thesis. Using the natural story arc that comes with the sequential processes within virus pathogenesis, I organized my thesis to target three points, each building on the previous point: (1) the pathways through which the mode of delivery could potentially affect HPV susceptibility such as the microenvironment created before infection, (2) the mechanism of infection and evasion of the immune response, and (3) the progression of the infection into cancer.

Through my writing seminar and the writing-oriented classes I had taken afterwards, I learned that organization and connectivity of body paragraphs should not be random—whether it’s a scientific paper or a humanities paper, the writer has an obligation to take the reader on a journey, and both the motive and the thesis help to set this up.

Instead of recapitulating my motive—or even my thesis—in my final paragraph, the conclusion, I emphasized why the research I had proposed within my three body paragraphs was specifically important on a public health level and suggested policy recommendations based on this research. From beginning to end, my piece was directed by a clear motive, because a motive should be just that—motivation that guides the structure of your piece and most importantly, motivation for the reader to turn the page and keep reading.

Editor Commentary

Aparna Raghu

Isabella’s Ecology and Evolutionary Biology junior paper explores how the effects of Caesarean sections on offspring immune systems may affect offspring susceptibility to HPV infection. In her introduction, Isabella first establishes the immunological consequences of excessive use of Caesarean sections, then transitions into a careful discussion of the potential effects of this compromised immunity on HPV susceptibility.

By the end of her first and second paragraphs, she has successfully introduced two key aspects of her motive—that Caesarean sections are harmful for immune development and that they are performed in excess in certain regions. These two key ideas are necessary to justify why she will be looking at HPV susceptibility. Naturally, it is expected that immune compromise will lead to susceptibility to pathogens, such as viruses, in general. But we realize why Isabella is focusing on HPV in particular when she states: “In developing countries, there is often a high prevalence of HPV and cervical cancer, as well as a high rate of pre-labor, elective CSs.” Going back to the fact that Caesarean sections are performed in excess in particular developing countries, which she introduced in the first paragraph, she provides a compelling reason for exploring the link between Caesarean section immune consequences and HPV in particular, since we see high rates of unnecessary Caesarean section use and high prevalence of HPV and cervical cancer *in the same areas*.

Overall, Isabella effectively integrates her scholarly motive, as a biology student, with the popular motives of understanding disease patterns. This is particularly relevant in scientific writing, for it allows the author to communicate seemingly inaccessible ideas with both general and expert audiences. In general, motive serves not only to inspire the writer to undertake a project but to allow that writer to communicate her inspiration to the reader, which we see in Isabella’s introduction.