

Longitudinal study of multi-site *Chlamydia trachomatis* infection in young, high-risk women



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Abstract

Chlamydia trachomatis (CT) is the most common bacterial sexually transmitted infection, and chronic or repeat infections can result in severe reproductive morbidities. CT is a significant public health problem because infection rates continue to rise and there is no vaccine. The endocervix is the primary site of infection in women, but recent reports suggest additional extra-genital reservoirs of infection, specifically the pharynx and rectum. In this study, I plan to evaluate (i) rates of single, dual, and triple infections in young, high risk women in New Orleans, (ii) if organisms are genetically similar at each site, and (iii) if oral and pharyngeal infections can spontaneously clear without antibiotic intervention, similar to that observed in genital infection. CT strains have been historically classified into serovars by differences in the major outer membrane protein (MOMP), which varies greatly between strains. Genetic similarities can be analyzed both within and between different serovars. High-risk women who have tested positive for CT infection at the LSU CrescentCare Sexual Health Clinic are tested for several STIs using nucleic acid amplification tests (NAATs). Endocervical, pharyngeal, and rectal swabs are collected, and genomic DNA is isolated and quantified. The *ompA* gene encoding the major outer membrane protein (MOMP) is amplified by polymerase chain reaction (PCR). Positive samples are then sequenced using forward and reverse primers, and full-length sequences are assembled from overlapping reads. The *ompA* genotype of the infecting strain is determined by aligning our sequences against those of defined clinical isolates in the NCBI BLASTn database. The *ompA* genotypes of many CT NAAT-positive patients in our cohort have been identified thus far. In addition, we have identified the genotypes of CT strains isolated from one woman who spontaneously cleared an infection without antibiotics, one woman who had a pharyngeal infection, and one woman with a rectal infection. The patient who was able to spontaneously clear genital infection and the patient with a pharyngeal infection were both found to have serovars that are fairly rare in our patient population, while the rectal infection was found to be a more common strain. We aim to learn more about the serovars infecting our patient population at these atypical sites to gain more insight about why CT successfully infects patients at these locations.

Introduction

The pathogen and the problem

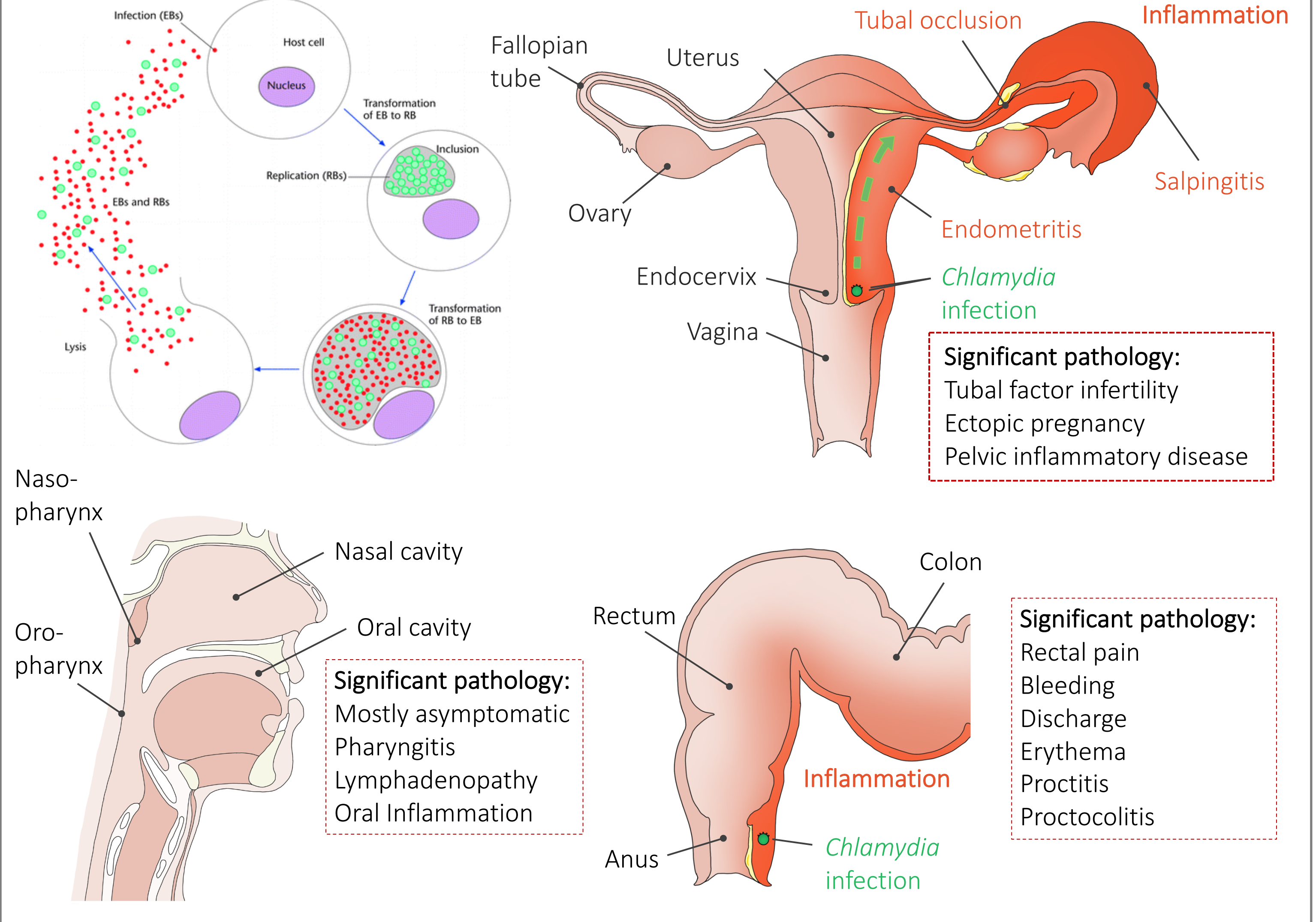
- Chlamydia trachomatis* (CT) is the most common bacterial STI. This past year, there were over 1.7 million new infections in the United States.
- In women, it primarily infects the endocervix, where infection can ascend into the uterus and fallopian tubes, causing significant pathology. It also increases the risk of transmission of HIV and other STIs.
- CT can also infect other mucosal sites outside of the endocervix, specifically, the rectum and pharynx.
- Over 90% of female genital infections are asymptomatic,³ which is problematic because these women don't know that they're infected and therefore don't seek medical care.
- The current strategy for detecting and treating asymptomatic endocervical infections is by frequent screening in clinics, but screening for extra-genital CT infections is not recommended as standard of care in the United States.

Immunity to *Chlamydia*

- Chlamydia*, as an obligate intracellular pathogen, possesses many strategies to evade immunity.⁶
- While the immune system is capable of naturally resolving infection in some cases, most of the pathology is caused by the sustained innate and cellular immune responses to chronic infection.⁵
- Some women have the ability to spontaneously clear infection in both genital and extra-genital sites without antibiotics,⁴ and we are currently investigating this mechanism.

Multi-site infection

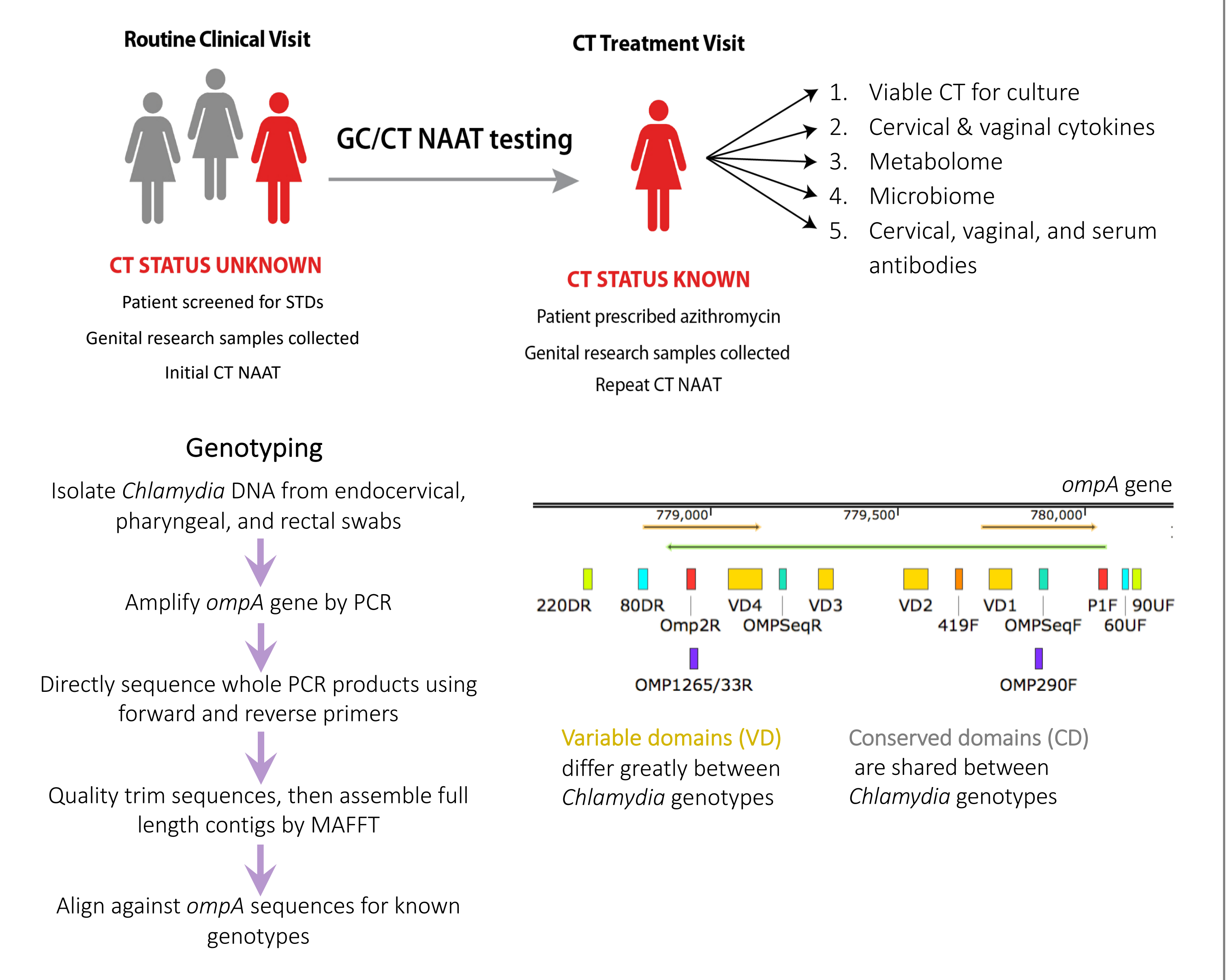
- C. trachomatis* is tropic for columnar epithelial cells, which are found in both the endocervix and the rectum.^{1,6} However, the specific cell type that CT infects in the oropharynx is unclear at this time.
- Extra-genital sites share many similarities with the endocervix but also differ in many ways, which presents the question of why *C. trachomatis* infects these sites and what pathology can be seen in these infections.
- Extra-genital infection can also lead to pathology. Rectal CT has been shown to cause rectal pain, bleeding, discharge/pruritis, erythema, and proctitis. Almost all pharyngeal CT infections are asymptomatic, but they have also been linked to pharyngitis, localized lymphadenopathy, and inflammation of the oral cavity.²
- Research has suggested that CT acts more as an opportunistic commensal in extra-genital sites than as a pathogen, as it does in the genital tract. CT avoids eliciting an inflammatory immune response and subsequent pathology in the GI tract because many of the usual effectors of the immune system are not present.²
- Untreated extra-genital infections may be transmitted to a sexual partner or to other sites in the same individual.³



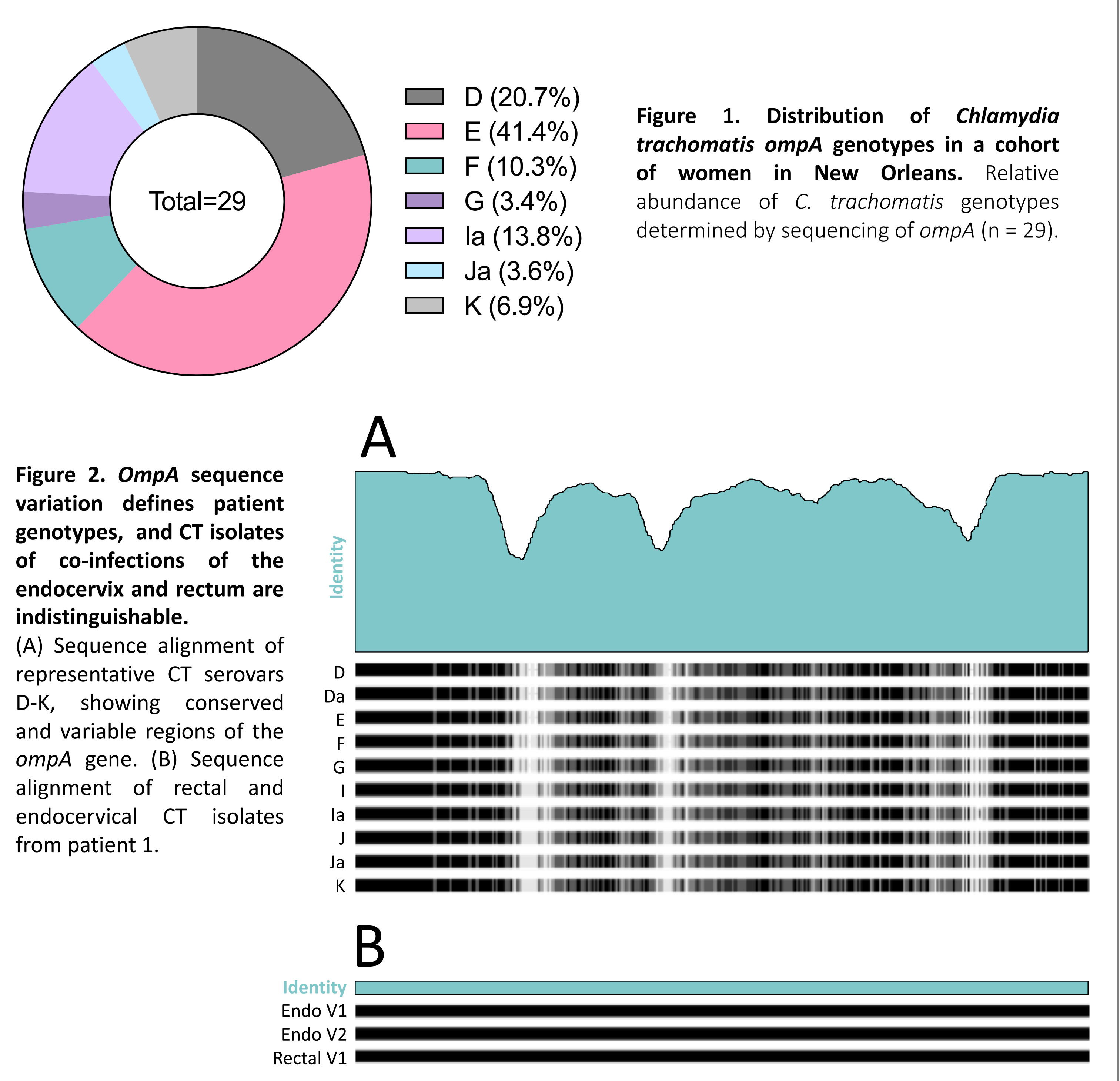
Hypothesis

We hypothesize that multi-site CT infections are genetically similar at each location and that infections in these locations be spontaneously cleared without antibiotic intervention, as is observed in genital infections.

Methods



Results



Results

Table 1. Persistence and clearance of multi-site *Chlamydia* infections. Persistence of *C. trachomatis* infections at the endocervix and the rectum (bold). Clearance associated with *C. trachomatis* infection in the pharynx as compared to the endocervix (dotted).

	Patient 1		Patient 2		Patient 3		Patient 4		Patient 5	
	V1	V2	V1	V2	V1	V2	V1	V2	V1	V2
Pharyngeal	-	nd	-	-	+	+	+	-	+	-
Endocervical	+	+	+	+	+	-	+	+	+	-
Rectal	+	+	+	+	+	-	nd	nd	nd	nd

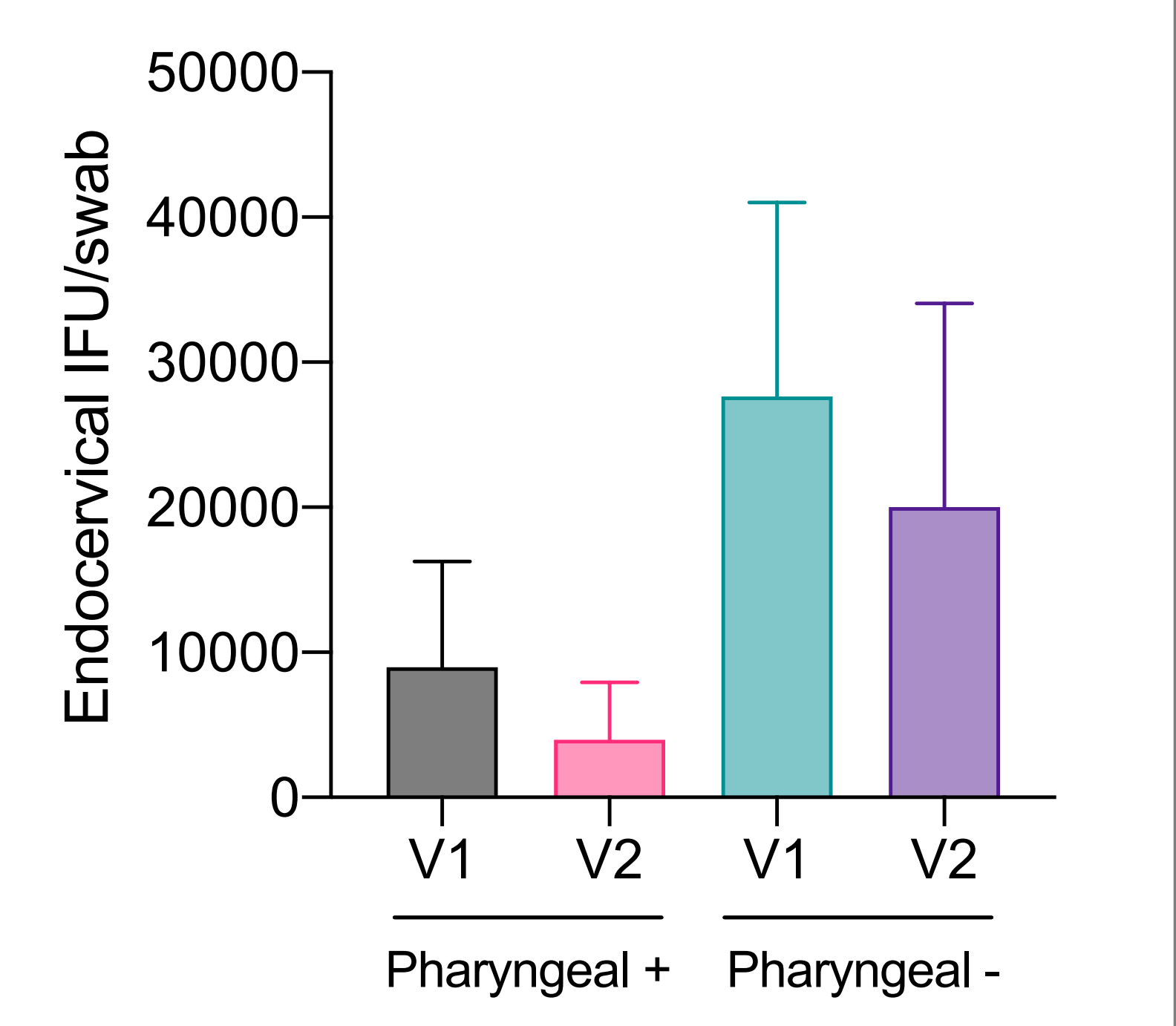
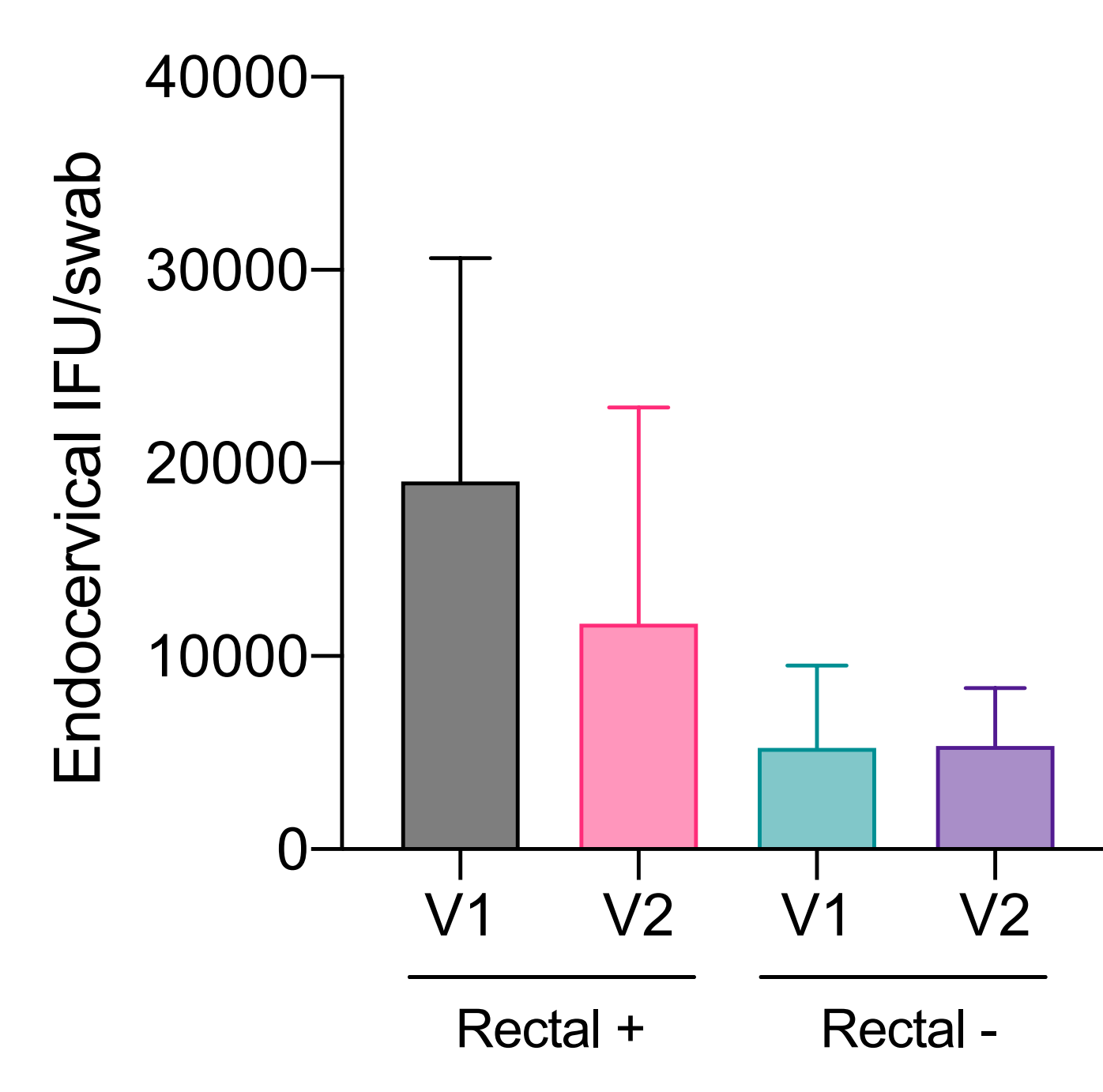


Figure 3. Patients with rectal co-infections have higher endocervical CT burdens. Comparison of endocervical *Chlamydia* load from the screening and treatment visits of patients that tested positive or negative for rectal infection by NAAT.

Figure 4. Patients with a pharyngeal co-infections have lower endocervical CT burdens. Comparison of endocervical *Chlamydia* load from the screening and treatment visits of patients that tested positive or negative for pharyngeal infection by NAAT.

Conclusions

- Like endocervical infections, extragenital *C. trachomatis* infections can spontaneously clear without antibiotic intervention.
- Pharyngeal infection appears to be associated with spontaneous clearance both in the pharynx and at other sites, which may be due to oral *Chlamydia* infections eliciting a stronger immune response.²
- Rectal and endocervical infection appear to have similar trends in persistence. This makes sense because many rectal-endocervical co-infections come from auto-inoculation.
- Further investigation will be necessary to determine the role that *ompA* genotypes play in multi-site *C. trachomatis* infections.

Future directions

- Future studies will determine the effect of the state of the vaginal microbiome, as well as the amount of *C. trachomatis* infection present, in the spontaneous clearance of infection.
- As more histological information and patient samples arise, more can be learned about the mechanisms that underlie rectal and pharyngeal infection.
- Future studies might look at the relationships between infections at multiple sites and how they might influence each other.
- Finally, it will be important to study the long-term pathology of persistent extra-genital CT infections.

References

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