

Using a combination of physico-chemical methods we extracted, purified and characterized cell-surface polysaccharides of *C. difficile* and *C. jejuni* and used them in conjugate vaccine preparations.

We discovered that *C. difficile* and *C. jejuni* produce distinctive cell-wall polysaccharides that when integrated into vaccine formulations were capable of eliciting antibodies that prevented the corresponding disease in animal models.¹⁻² *C. difficile* ribotypes were found to expose a common polysaccharide (named PS-II) composed of hexasaccharide phosphate repeating blocks. After its discovery, PS-II quickly attracted the attention of many researchers as a *C. difficile* vaccine target. In our hands, a PS-II conjugate vaccine protected about 90% of mice challenged with *C. difficile* spores.³ In the case of *C. jejuni*, a multivalent approach was needed, as each serotype complex expressed a specific polysaccharide. The prototype *C. jejuni* polysaccharide-based vaccine was shown to fully protect against *C. jejuni* diarrhea in a monkey model⁴ and preliminary data from a phase 1 clinical trial has demonstrated its safety in humans. Recently, we have discovered that certain regions of *C. jejuni* polysaccharides containing methyl phosphoramidate (MeOPN) linkages are highly immunogenic.⁵ A MeOPN galactose synthetic construct (left) reacted with antisera from *C. jejuni* serotypes containing MeOPN at primary positions, and was found to have more bactericidal activity than the native polysaccharide vaccine.

The gastric pathogens *C. difficile* and *C. jejuni* expose specific cell-wall polysaccharides that when converted into glycoconjugate vaccines are capable of fighting the corresponding bacterial infection in animal models. Such polysaccharide based vaccines have the potential to control disease and colonization.

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4. Guerry P, Poly F, Riddle M, et al. Campylobacter polysaccharide capsules: virulence and vaccines. Front Cell Infect Microbiol. 2012 Feb 15;2:7.
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Clinical Trials of Vaccines Administered During Pregnancy

Flor Munoz-Rivas, MD
Baylor College of Medicine
Houston, TX

Objectives: Explain the concept of maternal immunization as a strategy to prevent infectious diseases in mothers and infants. Discuss the rationale and methodology associated with studying vaccines for administration during pregnancy.

Abstract: Immunization of women during pregnancy is an accepted strategy to protect mothers and infants against infectious diseases during a period of high vulnerability. As a public health intervention, maternal immunization has the potential to reduce the morbidity and mortality associated with pathogens that affect the mother, the newborn, or both. Maternal immunization with tetanus, pertussis and influenza vaccines results in direct protection of the mother and the newborn infant. Group B streptococcus and Respiratory Syncytial Virus (RSV) are infections that could be prevented through immunization of pregnant women with safe and effective vaccines that are currently under clinical investigation. The rationale, safety, effectiveness, acceptability, and potential impact of vaccination of women during pregnancy will be reviewed in this presentation. Challenges associated with the development and implementation of clinical trials of vaccines administered during pregnancy will be discussed.

References:

1. Munoz, FM, Sheffield JS, Beigi RH, et al. Research on vaccines during pregnancy: protocol design and assessment of safety. *Vaccine*. 2013 Sep 13;31(40):4274-9.
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3. Munoz, FM. The challenges of pregnancy in clinical trials for vaccines. Editorial. *Clin. Invest.* (2014) 4(2), 103–105.
4. Beigi RH, Fortner KB, Munoz FM, et al. Maternal immunization: opportunities for scientific advancement. *Clin Infect Dis*. 2014 Dec 15;59 Suppl 7:S408-14.
5. Munoz FM, Weisman LE, Read JS, et al. Assessment of safety in newborns of mothers participating in clinical trials of vaccines administered during pregnancy. *Clin Infect Dis*. 2014 Dec 15;59 Suppl 7:S415-27.

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Safety Monitoring in Immunization in Pregnancy Efforts at NIH

Richard L. Gorman, MD
National Institute of Allergy and Infectious Diseases
National Institutes of Health
Bethesda, MD

Objective: Review safety monitoring in maternal immunization studies sponsored by DMID/NIH, and how these efforts may align with the tools developed by the GAIA consortium.

Abstract: Key knowledge gaps identified during DMID sponsored studies were addressed by subject matter experts during consensus-building conferences. The output from these discussions were toxicity grading tables for laboratory tests, and adverse events grading tables of pregnancy and neonatal outcomes.

Although overlapping in the topics of interest, DMID and GAIA efforts differ in the scope. DMID Tables do not provide ontology of terms and definitions, or the assessment of diagnostic certainty, that is especially relevant for studies in MLICs. Standardized definitions and tools to evaluate and report 21 most critical adverse events in pregnancy and neonatal period are provided by the GAIA consortium. Thus, GAIA and NIH efforts are complementary and if combined could improve quality of data generated in clinical trials, harmonize reporting and facilitate meta-analyses across multiple studies.

Reference:

1. Keller-Stanislawski B, Englund JA, Kang G, et al. Safety of immunization during pregnancy: a review of the evidence of selected inactivated and live attenuated vaccines. *Vaccine*. 2014 Dec 12;32(52):7057-64.

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NVAC Initiatives

Saad B. Omer, MBBS, MPH, PhD
Emory University
Atlanta, GA

Objective: Discuss updates on recent National Vaccine Advisory Committee (NVAC) initiatives regarding maternal immunization

Abstract: NVAC is working to identify barriers to and opportunities for developing vaccines for pregnant women and make recommendations to overcome these barriers. There are several current scientific and structural barriers for developing vaccines and countermeasures for pregnant women.¹

One barrier is a lack of a broadly accepted ethical framework for guiding clinical research in pregnancy. Therefore, IRBs often resort to categorizing most intervention research in pregnancy as high risk, often without a balanced consideration of the risks of not performing the research. Hence, there is a need for development and articulation of a pregnancy specific ethical framework that can offer guidance to investigators and IRBs.