Antibody-based methodology to assess the stability of whole cell pertussis vaccines (PSPT 2022)

Nicholas J. Mantis, Ph.D.
E-mail: nicholas.mantis@health.ny.gov
Introduction

Mantis Lab
Microbial Pathogenesis
Immunology and Mucosal Immunology
Vaccinology

Salmonella, cholera, borreliosis, toxins, SARS-CoV-2

Investigators
Dr. Jennifer Doering
Dr. Yetunde Adewunmi

Albany, New York, USA
Motivation

How do you assess the potency and stability of whole cell Pertussis (wP) within context of pentavalent and hexavalent vaccines?

In collaboration with Drs. David Volkin and Sangeeta Joshi (University of Kansas) with support from BMGF
The Kendrick Assay is designed to assess potency, but we have been unable to identify its applications to stability studies. The Kendrick Assay is also associated with other shortcomings.
Alternatives to Kendrick Test

Development of Pertussis Serological Potency Test
Serological assessment of antibody response induced by whole cell vaccine as an alternative to mouse protection in an intracerebral challenge model

Arno van der Ark, Ineke van Straaten-van de Kappelle, Arnoud Akkermans, Coenraad Hendriksen and Huib van de Donk
Laboratory for Control of Biological Products, National Institute of Public Health and Environmental Protection, P.O. Box 1, 3720 BA Bilthoven, The Netherlands

Whole-cell pertussis vaccine potency assays: the Kendrick test and alternative assays

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Dorothy Xing, Kevin Markey, Rose Gaines Das and Ian Feavers*
Division of Bacteriology, National Institute for Biological Standards and Control, Potters Bar, Hertfordshire, EN6 3QG, UK
*Author for correspondence. Tel.: +44 1707 641450 Fax: +44 1707 641540 ian.feavers@nibs.org
Adapting PSPT

Kendrick Test

PSPT
Multivalent Nature of DTwP
“Enhanced” PSPT at Wadsworth Center

PSPT

DTwP wP

DT TT FHA PRN AcT PTx

intranasal

CFU (lung)
We chose 1.2 OU for all vaccination studies going forward.
Antigen-specific Ab Titers (Day 30)
Intranasal challenge with *B. pertussis* (Day 30)

DTP vaccination results in ~4 log reduction in *B. pertussis* 18323 CFUs (day 4)
The “enhanced” PSPT (for research purposes only) provides serological dose response with whole cell ELISA, titers to different DTP antigens, and can be combined with intranasal *B. pertussis* (18323) challenge to assess relative degrees of clearance.
Further Simplifying wP Potency Assays

Kendrick Test

PSPT
Vaccine potency reflects the biochemical integrity of the antigen, adjuvant and its given formulation. With time, potency declines due to multiple factors, including loss of antigen integrity.
Decline in Vaccine Integrity Yields Low Quality Abs

Potency

High

Low

time, temperature, chemical, other

decline in antibody quality (and quantity)
Proof of Concept (Ricin toxin vaccine; RiVax™)

A. Thermal degradation
- Native (R)
- Partially degraded (R')
- Extensively degraded (R'')

B. Potency determination in animal model (survival)
- 12/12
- 6/12
- 0/12

C. RiCoE analysis

Monoclonal antibodies (MAbs) or a reference serum panel could be used to interrogate the conformational integrity of D, T and wP within DTP.

Ab-specific for intact antigen X, Y, Z
Probing RiVax Integrity by Competition ELISA (RICoE)

A. No competitor

B. Intact vaccine

C. Compromised vaccine

MAB

ricin  ricin  ricin

no inhibition

ricin  ricin  ricin

high inhibition

ricin  ricin  ricin

no or low inhibition
Probing RiVax Integrity by Competition ELISA with PB10

RiVax-Alhydrogel in liquid was incubated at 25°C for indicated time points then subjected to competition ELISA with PB10. Decline in “integrity” results in reduced potency, as reflected in lethal dose challenge.
Applications of Competitive ELISA to DTP

PetCoE

Enhanced PSPT

4°C 100°C

% Competition

Dilution (DTP)

Threshold

CFU (lung)

DT
TT
FHA
PRN
AcT
PTx
DTP at 4°C or 100°C was used as competitor with DTP antiserum for binding to ELISA plates coated with DTP. Boiled DTP was less effective competitor, suggesting a loss in integrity.
Thermal stress (accelerated decay) of DTP

4°C  100°C

Native DTP

DTP
Mice that were vaccinated with boiled DTP were less able to clear B. pertussis from lungs, as compared to DTP control mice.

The reduction in CFUs correlates with loss of vaccine integrity revealed by PetCo.
Serological analysis reveals different antibody profiles between DTP 4°C and 100°C. Sharp decline in TT and PRN titers, but little change in FHA, PT, ACT or LPS.
The differential stability of different DTP antigens raises questions about weak link in the chain regarding formulation optimization.
Interrogating DTP upstream may provide insight into vaccine potency and stability.
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Investigators
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Dr. Yetunde Adewunmi
Dr. David Volkin
Dr. Sangeeta Joshi

NIIMBL (USA)

Albany, New York, USA