

# 2014 Research Annual Report

## Global Child Health



### Division Summary

#### RESEARCH AND TRAINING DETAILS

Number of Faculty	4
Number of Joint Appointment Faculty	4
Number of Support Personnel	11
Direct Annual Grant Support	\$3,067,875
Direct Annual Industry Support	\$325,297
Peer Reviewed Publications	11

#### CLINICAL ACTIVITIES AND TRAINING

### Division Photo



L to R: A Dawodu, E Schlaudecker, M Steinhoff

## Significant Accomplishments

### Environment and Diet Shown to Impact Breast Feeding

**Adekunle Dawodu, MB, BS**, and his group measured serum 25(OH)D levels in breast feeding mothers and infants from Cincinnati, Shanghai, China and Mexico City to compare these populations enrolled in the Global Exploration of Human Milk (GEHM) Study. The study was designed to explore effects of different environments and diets on human milk composition, infant nutrition, and health. Maternal vitamin D deficiencies were more common in Shanghai and Mexico than Cincinnati mothers. In contrast, infant vitamin D deficiencies were more common in Cincinnati and Mexico than in Shanghai. The study provided data that vitamin D deficiency is common in breastfeeding mothers and infants worldwide, though the prevalence in diverse populations depends upon sun exposure and Vitamin D supplementation behaviors. Abstracts from this work were presented in May at the Pediatric Academic Societies annual meeting and in April at Experimental Biology 2014.

### Study Examines Altered Immune Response to Influenza Immunization During Pregnancy

After discovering that pregnant women have lower antibody responses to influenza vaccine compared to non-pregnant women, **Elizabeth Schlaudecker, MD, MPH**, collaborated with **Fred Finkelman, MD**, in the Division of Immunobiology to further evaluate this immune response. They found that the antibody isotypes associated with antibody-dependent killing of virus were more likely to be decreased in pregnant women, possibly inhibiting their ability to mount a response against influenza. Many pregnant women had a combination of low IgG1 and high IgG4 that was not seen in non-pregnant women and is likely to provide poor protection against influenza infection. This suggests a need to reconsider approaches for immunizing pregnant women against influenza.

### Meningococcal Vaccine Appears Safe for Pregnant Women in Africa

Steve Black, MD, has collaborated with WHO and the INDEPTH research center in Navrongo, Ghana, to conduct the first evaluation of the MenAfriVac conjugate meningococcal A vaccine in pregnant women. Meningococcus type A causes large and devastating epidemics in an African “meningitis belt” that includes northern Ghana. The MenAfriVac vaccine was developed specifically to address this issue, however no information was available about the vaccine’s safety when given to pregnant women. Black compared the risk of adverse events in women who received the vaccine both to a historical control group and to pregnant women who elected not to receive this vaccine during the new program. Results presented to the WHO Global Advisory Committee on Vaccine Safety in June 2014 demonstrated that administering the vaccine was safe during pregnancy.

### **Neonatal Outcomes Study Earns Honor**

The Bruce P. Squires Award for 2014 was conferred for our publication entitled, “[Neonatal Outcomes after Influenza Immunization in Pregnancy](#),” which first appeared in February 2012 in the journal CMAJ. This was the first report of the effect of increased neonatal weight and reduced prematurity related to maternal immunization with influenza vaccine. This unique evidence from a randomized controlled trial showing that prevention of influenza in the mother results in substantial benefits for the fetus and newborn has now been replicated in numerous reports.

### **Nurturing Children’s Development Program Expands**

This partnership between Cincinnati Children’s and Procter & Gamble, which has supported research scholars and observers from China, Latin America, and Africa, was expanded this year to include one research scholar and four observers from India. So far, four observers have visited Cincinnati Children’s from India.

## **Research Highlights**

Steven Black, MD

The Risk of Narcolepsy following Adjuvanted Pandemic Influenza Vaccine

In this US CDC funded study, Dr. Steven Black and colleagues will evaluate the risk of narcolepsy following adjuvanted influenza vaccines. Three such vaccines were used during the 2009-2010 pandemic and one was associated with an increased risk of narcolepsy in children in several European studies. The goal of this project is to expand the scope of prior studies to include the other two adjuvanted vaccines by performing studies in Brazil, Taiwan, Canada, Israel, the Netherlands, Spain, and Argentina. The results of this study will inform the future use and selection of adjuvants for future pandemics. This study is a collaboration with the Brighton Collaboration in Switzerland and Erasmus University in the Netherlands.

Adekunle Dawodu, MBBS, FRCPCH

In a study funded by Qatar National Research Fund, Adekunle Dawodu, MB, BS, in collaboration with researchers in Qatar is evaluating the effect of maternal vitamin D (vD) supplementation alone to prevent vitamin D deficiency in Qatari breastfeeding infants and mothers. 160 healthy Qatari breastfeeding mother-infant pairs will be randomized at one month postpartum to either receive 6000 IU/day vD3 plus infant receives placebo or mother to receive 600 IU/day vD3 and infant receives 400 IU/day vD3 drops for six months. Vitamin D and Calcium levels will be monitored in the mother and infant, and milk vitamin D content will be measured. The study will provide the first data in a high-risk population on whether supplementing mothers alone with high dose vD can safely achieve normal vD status in both the mother and nursing infant, which would be generalizable to other populations.

Elizabeth Schlaudecker, MD, MPH

Dr. Schlaudecker's research continues to focus on the immunologic responses to maternal immunization. After completing a comprehensive epidemiologic study of the etiology and seasonality of viral respiratory infections in rural Honduras, she has shifted focus to prevention of these infections with maternal immunization. Her recent work has demonstrated antibody persistence in mothers one year after pneumococcal immunization in pregnancy, as well as a significantly decreased antibody response to influenza immunization in pregnant women. In collaboration with Dr. Mark Steinhoff and Monica McNeal, she evaluated influenza-specific IgA levels in breast milk and demonstrated that they were significantly higher in influenza vaccinees compared to pneumococcal controls for at least six months postpartum. She also demonstrated that greater exclusivity of breastfeeding in the first six months of life significantly decreased the expected number of respiratory illness with fever episodes in infants of influenza-vaccinated mothers, but not in infants of pneumococcal-vaccinated mothers.

Dr. Schlaudecker continues to study the immunologic response to influenza immunization in pregnant women with the support of a K12 Child Health Research Career Development Award from the NIH. She investigated the IgG isotype responses to influenza immunization in Dr. Sing Sing Way's laboratory with the mentorship of Dr. Fred Finkelman in the Division of Cellular and Molecular Immunology and demonstrated an altered isotype profile in pregnant women compared to non-pregnant women consistent with a decreased response to the vaccine. She is also investigating immunologic responses to immunization in breast milk with Cincinnati Children's Vaccine and Treatment Evaluation Unit (VTEU).

Mark Steinhoff, MD

Working with colleagues at icddr in Dhaka, Bangladesh and the University of Washington, Dr. Steinhoff analyzed serum specimens from mothers and infants in Bangladesh to evaluate the transfer of natural antibodies to RSV and their concentrations in the infant. These data showed that higher levels of antibody transferred to the infant were associated with reduced risk of infant infection due to RSV. These data regarding the stability of RSV antibody in pregnancy and the efficient transfer to the infants suggest that maternal RSV immunization in the third trimester has the potential to provide protective levels of antibodies to prevent RSV infection in young infants.

A retrospective analysis of surveillance data from the state of Georgia covered 8,393 live births from January 2005 through December 2008. The analysis showed that maternal influenza vaccine was associated with reduced odds of preterm birth and with protection against SGA births, ranging from odds ratios of 0.22 to 0.15. Maternal vaccination was associated with reduced odds of preterm birth ranging from 0.34 -0.30. The vaccine effects varied by socio demographic characteristics.

## Significant Publications

Geng Q, Zhang T, Ding Y, Ta Y, Lin Y, Wang Y, **Black S**, Zhao G. **Molecular characterization and antimicrobial susceptibility of *Streptococcus pneumoniae* isolated from children hospitalized with respiratory infections in Suzhou, China.** *PloS One*. 2014 9:e93752.

China does not currently utilize any pneumococcal vaccine routinely in children but does utilize antibiotics profusely in this age group. This study was conducted to evaluate the potential impact of a vaccination program and to evaluate the impact of antibiotic use on pneumococcal epidemiology in China.

Monangi N, Slaughter JL, **Dawodu A**, Smith C, Akinbi HT. **Vitamin D status of early preterm infants and the effects of vitamin D intake during hospital stay.** *Arch Dis Child Fetal Neonatal Ed*. 2014 99(2):F166-8.

Vitamin D intake of 400 IU/day is recommended for infants to achieve serum 25(OH)D concentrations of 50 nmol/L. In this study, serum 25(OH)D was 50 nmol/L in 64% of preterm infants at birth and 35% at the time of

discharge. Low serum 25(OH)D concentration is common in preterm infants at discharge from neonatal intensive care unit. The publication highlights that the current neonatal nutritional strategies for early preterm infants may be insufficient to achieve the recommended vitamin D intake and the target serum 25(OH)D concentration.

**Schlaudecker EP**, Steinhoff MC, Omer SB, McNeal MM, Roy E, Arifeen SE, Dodd CN, Raqib R, Breiman RF, Zaman K. **IgA and neutralizing antibodies to influenza A virus in human milk: A randomized trial of antenatal influenza immunization.** *PLOS One*. 2013 8(8):e70867.

This publication is the first demonstration that breastfeeding in the first six months of life significantly decreased the expected number of respiratory illness with fever episodes in infants of influenza-vaccinated mothers.

**Steinhoff MC**, MacDonald N, Pfeifer D, Muglia LJ. **Influenza vaccine in pregnancy: policy and research strategies.** *Lancet*. 2014 383(9929):1611-3.

This commentary invited by the editor of Lancet summarizes the effects of influenza vaccine in pregnancy and outlines new research strategies.

Richards JL, Hansen C, Bredfeldt C, Bednarczyk RA, **Steinhoff MC**, Adjaye-Gbewonyo D, Ault K, Gallagher M, Orenstein W, Davis RI, Omer SB. **Neonatal outcomes after antenatal influenza immunization during the 2009 H1N1 influenza pandemic: Impact on preterm birth, birth weight, and small for gestational age birth.** *Clin Infect Dis* 2013 56(9):1216-22.

Working with several colleagues, this was an analysis of Kaiser Permanente data during the 2009 influenza A H1N1 virus epidemic. The analysis of 3,327 births, of which 1,125 received flu vaccine showed that there were 37% lower odds of being born preterm, and the mean birthweight of infants of influenza-vaccinated mothers was 45g greater than that of the unvaccinated mothers. These findings support US and WHO vaccine policy to prioritize pregnant women during the 2009 influenza pandemic.

## Division Publications

1. Adedinsewo DA, Noory L, Bednarczyk RA, Steinhoff MC, Davis R, Ogbuanu C, Omer SB. **Impact of maternal characteristics on the effect of maternal influenza vaccination on fetal outcomes.** *Vaccine*. 2013; 31:5827-33.
2. Black S. **The role of health economic analyses in vaccine decision making.** *Vaccine*. 2013; 31:6046-9.
3. Black S. **Immunisation against meningococcus B.** *Lancet*. 2013; 382:858.
4. Black S, Margarit I, Rappuoli R. **Preventing newborn infection with maternal immunization.** *Sci Transl Med*. 2013; 5:195ps11.
5. Chavez MA, Shams N, Ellington LE, Naithani N, Gilman RH, Steinhoff MC, Santosham M, Black RE, Price C, Gross M, Checkley W. **Lung ultrasound for the diagnosis of pneumonia in adults: a systematic review and meta-analysis.** *Respir Res*. 2014; 15:50.
6. Dodd CN, Romio SA, Black S, Vellozzi C, Andrews N, Sturkenboom M, Zuber P, Hua W, Bonhoeffer J, Buttery J, Crawford N, Deceuninck G, de Vries C, De Wals P, Gutierrez-Gimeno MV, Heijbel H, Hughes H, Hur K, Hviid A, Kelman J, Kilpi T, Chuang SK, Macartney K, Rett M, Lopez-Callada VR, Salmon D, Gimenez-Sanchez F, Sanz N, Silverman B, Storsaeter J, Thirugnanam U, van der Maas N, Yih K, Zhang T, Izurieta H, Global HNGBSC. **International collaboration to assess the risk of Guillain Barre Syndrome following Influenza A (H1N1) 2009 monovalent vaccines.** *Vaccine*. 2013; 31:4448-58.
7. Gupta A, Mathad JS, Yang WT, Singh HK, Gupte N, Mave V, Bharadwaj R, Zaman K, Roy E, Bollinger RC, Bhosale R, Steinhoff MC. **Maternal pneumococcal capsular IgG antibodies and transplacental transfer are low in South Asian HIV-infected mother-infant pairs.** *Vaccine*. 2014; 32:1466-72.

8. Monangi N, Slaughter JL, Dawodu A, Smith C, Akinbi HT. **Vitamin D status of early preterm infants and the effects of vitamin D intake during hospital stay**. *Arch Dis Child Fetal Neonatal Ed*. 2014; 99:F166-8.
9. Schlaudecker EP, Steinhoff MC, Omer SB, McNeal MM, Roy E, Arifeen SE, Dodd CN, Raqib R, Breiman RF, Zaman K. **IgA and neutralizing antibodies to influenza a virus in human milk: a randomized trial of antenatal influenza immunization**. *PLoS One*. 2013; 8:e70867.
10. Steinhoff MC. **Assessments of vaccines for prenatal immunization**. *Vaccine*. 2013; 31 Suppl 4:D27-30.
11. Steinhoff MC, MacDonald N, Pfeifer D, Muglia LJ. **Influenza vaccine in pregnancy: policy and research strategies**. *Lancet*. 2014; 383:1611-3.

## Faculty, Staff, and Trainees

### Faculty Members

**Mark Steinhoff, MD**, Professor

**Leadership** Division Director, Global Child Health

**Research Interests** Maternal Immunization, Infant Infections

**Steven Black, MD**, Professor

**Research Interests** Vaccine Safety

**Adekunle Dawodu, MD**, Professor

**Leadership** Director, International Patient Coordination

**Research Interests** Vitamin D Supplementation

**Elizabeth Schlaudecker, MD, MPH**, Assistant Professor

**Research Interests** Maternal Immunization

## Division Collaboration

Vitamin D nutritional status of breastfeeding mothers and infants (Adekunle Dawodu, MD)

**Section of Neonatology, Perinatal and Pulmonary Biology** » Ardythe Morrow, PhD

Research involving: a) vitamin D nutritional status of preterm infants, and b) vitamin D supplementation of breastfeeding infants (Adekunle Dawodu, MD)

**Section of Neonatology, Perinatal and Pulmonary Biology** » Henry Akinbi, MD

Research involving the effect of vitamin D nutrition during pregnancy on fetal growth (Adekunle Dawodu, MD)

**Section of Neonatology, Perinatal and Pulmonary Biology** » Vivek Narendran, MD, MRCP, MBA and Teresa Seto, MD

**Biostatistics and Epidemiology** » Colleen Mangeot, MS

IgG isotype and cytokine analysis after influenza immunization in pregnant women (Elizabeth Schlaudecker, MD, MPH)

**Allergy and Immunology** » Fred Finkelman, MD

Planning and evaluation of influenza infection in pregnant animal models (Mark Steinhoff, MD)

**Section of Neonatology, Perinatal and Pulmonary Biology** » Suhas Kallapur, MD



Evaluation of body fluid metabolic patterns for the detection of infections (Mark Steinhoff, MD)

**Pathology and Laboratory Medicine** » Lindsey Romick-Rosendale, PhD

Assessing the etiology of respiratory infections in Malawi [Fogarty Project] (Mark Steinhoff, MD)

**Emergency Medicine** » Michelle Eckerle, MD, Richard Ruddy, MD, and Charles Schubert, MD

Training to maintain neonatal resuscitation skill in Kenya (Mark Steinhoff, MD)

**Hospital Medicine** » Amy Rule, MD, Brian Volck, MD, and Charles Schubert, MD

Hepatitis B in HIV-positive subjects in Botswana (Mark Steinhoff, MD)

**Infectious Diseases** » Kathleen Ryan, MD and Elizabeth Schlaudecker, MD, MPH

Neonatal resuscitation training in Ghana (Mark Steinhoff, MD)

**Section of Neonatology, Perinatal and Pulmonary Biology** » Kimberly Carpenter, MD and Laurel Moyer, MD

Effect of infant Streptococcus pneumoniae vaccine on growth of infants in Dhaka (Mark Steinhoff, MD)

**Biostatistics and Epidemiology** » Bin Zhang, MD

Effect of maternal influenza vaccine on birth weights in Dhaka (Mark Steinhoff)

**Biostatistics and Epidemiology** » Mekibib Altaye, MD

## Grants, Contracts, and Industry Agreements

### Grant and Contract Awards

Annual Direct

#### BLACK, S

##### Clinical Immunization Safety Assessment

Centers for Disease Control and Prevention

200-2012-53661

09/29/13-09/28/17

\$39,256

##### Enhanced Evaluation of Risk of Narcolepsy Associated with Pandemrix and Arepanrix

Centers for Disease Control and Prevention(Brighton Collaboration Foundation)

200-2012-53425

09/29/12-09/28/14

\$117,176

#### DAWODU, A

##### Maternal Vitamin D Supplementation to Prevent Vitamin D Deficiency in Mothers and Their Infants

Hamad Medical Corporation (Qatar National Research Fund)

11/20/13-11/19/16

\$78,630

#### STEINHOFF, M

##### Mother's Gift Field Trial

Bill & Melinda Gates Foundation

50274

12/11/08-11/30/15

\$2,832,813

Current Year Direct

**\$3,067,875**

Industry Contracts	
DAWODU, A	
Procter and Gamble	\$280,346
STEINHOFF, M	
Pfizer, Inc.	\$44,951
Current Year Direct Receipts	
\$325,297	
Total	
\$3,393,172	