Maternal death from influenza in tropical Thailand

Pipat Thongnoi, Prabda Praphasiri, Fatimah S Dawood, Kim A Lindblade

At 0033 h on Sept 9, 2015, a 17-year-old Thai woman, 33 weeks and 4 days into her first pregnancy and no medical history of note, presented to the emergency room of Phon Thong district hospital with a 1 day history of fever, cough, and sore throat. On presentation she was febrile (temperature 39·2°C) and tachycardic (pulse 129 beats per min) with a respiratory rate of 22 breaths per min and blood pressure 130/81 mm Hg. She was diagnosed with bronchitis, prescribed amoxicillin, paracetamol, and bromhexine, and discharged home.

She attended a scheduled antenatal care clinic appointment the next morning at 0800 h and was afebrile (temperature 37·1°C). Ultrasonography showed twin infants with estimated bodyweights of 1900 g and 2000 g and on stress test fetal heart beats were normal. She returned to hospital for a third time at 2030 h after experiencing contractions. On examination, her cervix was found to be dilated to 3 cm. She was febrile (39·0°C) and tachycardic (pulse 136 beats per min), with a respiratory rate of 20 breaths per min and blood pressure 144/81 mm Hg. At 2045 h, her blood pressure rose to 150/100 mm Hg and she reported mild dyspnoea. Fetal heart monitoring showed fetal tachycardia. At 2100 h, her respiratory rate increased to 28 breaths per min with oxygen saturation (SpO_2) 86% on room air and 96% on 10 L oxygen. Fine crepitations were noted on lung examination, and she was started on ceftriaxone. At 2130 h, before being transferred to the provincial hospital, she developed tachycardia (pulse 140 beats per min), tachypnoea (respiratory rate 30 breaths was found to have three dead infants in utero. Real-time PCR of her lung and heart tissue were positive for influenza A (H3N2) virus and negative for influenza B virus and 16 other common respiratory viruses. Haemoculture did not grow any pathogens. The family confirmed that she had not been vaccinated against influenza during her pregnancy.

Pregnant women are at increased risk for severe complications from influenza, including maternal death and adverse fetal outcomes.[1,2] Presence of multiple fetuses might increase the potential for complications because they further reduce maternal tidal volume and lung function, particularly in the third trimester. In Thailand, 26 deaths of pregnant women associated with influenza have been reported since 2009 (Bureau of Epidemiology, Ministry of Public Health, personal communication), but as influenza testing is not routine, the real number of influenza deaths in pregnancy is likely to be much higher. Only five (19%) of these cases had underlying chronic disease. Thailand's clinical practice guidelines recommend early initiation of antivirals before laboratory confirmation for influenza-like illness in high-risk groups, including pregnant women, to prevent severe complications.[3] Our patient became ill in September, at the typical peak of influenza transmission in Thailand, and presented within 48 h of illness onset, when antivirals are most effective at preventing severe disease. Both hospitals that treated this patient had oseltamivir in stock. However, as influenza was not suspected by her treating physicians, she was not given antiviral treatment. Influenza has not

Lancet 2017; 389: 571–72

Phon Thong hospital, Roi Et province, Thailand (P Thongnoi MD); Influenza Program, Thailand Ministry of Public Health – US Centers for Disease Control and Prevention Collaboration, Nonthaburi, Thailand (P Praphasiri PhD, K A Lindblade PhD); and Influenza Division, Centers for Disease Control and Prevention, Atlanta, Georgia, USA (K A Lindblade, F S Dawood MD)

Correspondence to: Dr Prabda Praphasiri, Thailand MOPH-US CDC Collaboration, Ministry of Public Health, Nonthaburi 11000, Thailand hpu3@cdc.gov

Slide courtesy of Assoc.Prof.Surasith Chaithongwongwatthana

Recommendation of influenza vaccines for pregnant women

	USA	Thailand
tivated influenza	Any trimester	2nd or 3rd trimester

If pregnant women has influenza

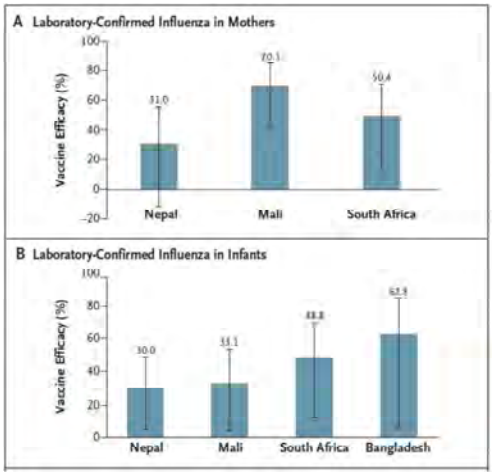
Increase risk of fetal death HR 1.9 (95% CI 1.1 to 3.4)

N Engl J Med 2013;368

Increase risk of hospitalization OR 2.4 (95% CI 1.2 to

Vaccine 2017;35:

fficacy of influenza vaccine during pregnancy



Omer SB. *N Engl J Med* 2017;376:1256-67.

Influenza vaccine for Thai pregnant women

All year round supply
Start 2019

What is the estimated influenza vaccine coverage in Thai pregnant women?

<10%	20%
40%	60%

61% รู้จักวัคซีนไข้หวัดใหญ่
42% ยินดีฉีดวัคซีนไข้หวัดใหญ่
4% ได้รับวัคซีนในการตั้งครรภ์ครั้งนี้

Ditsungnoen D, et al. *Vaccine* 2016;34:

27-day-old infant with cough and cyanosis

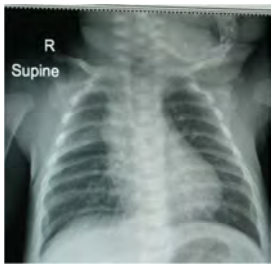
PTA frequent, severe, spasmodic cough, occasional cyanosis

His father had a prolonged cough.

Febrile, intermittent severe cough with central cyanosis

ung: clear

CBC: Hct 44.5%,
WBC: 35,640/mm3 (N 32%, L 60%, M 6%, Eo 2%),
platelet 180,000/mm3
ESR: 2 mm/hr

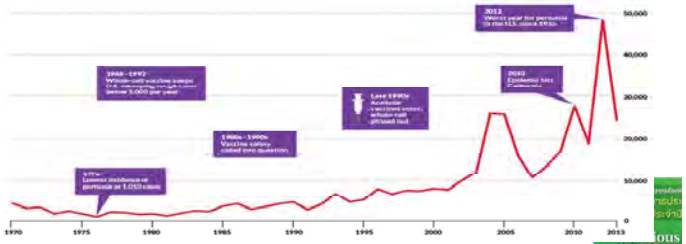


PCR for *B. pertussis*: positive

Recommendation of pertussis vaccines for pregnant women

	USA	Thailand
or Td	**1 dose Tdap each pregnancy** @ GA 27-36 week	**1 dose Tdap each pregnancy** during 3rd trimester

ooping cough
ouncing back
e 2010



Efficacy of Tdap vaccine during pregnancy

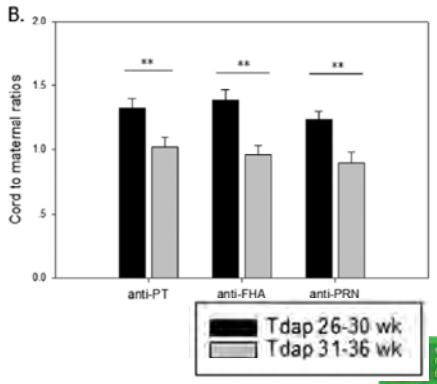
California Immunization Registry, 2013-2014

Efficacy to prevent pertussis in the first 2 months

Timing of Prenatal Tdap	Adjusted VE (95% CI), %
27-36 wk gestation	85.4 (33.0–96.7)
Any time during pregnancy	63.8 (10.6–85.4)

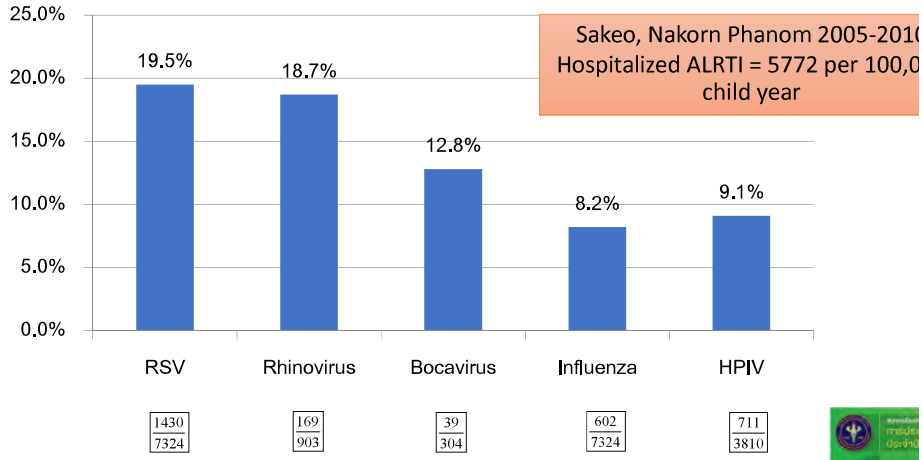
Winter K, et al. *Clin Infect Dis* 2017;64:3-8.

- Cord blood to maternal ratio



Wanlapakorn N, et al. *Vaccine* 2018;36:1453-9

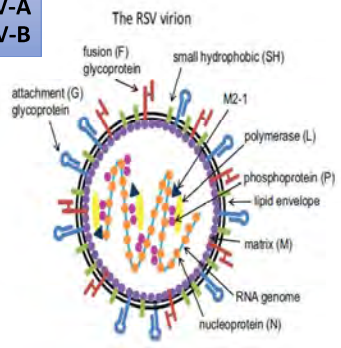
RSV is the most common cause of hospitalized ALRI in children <5 year



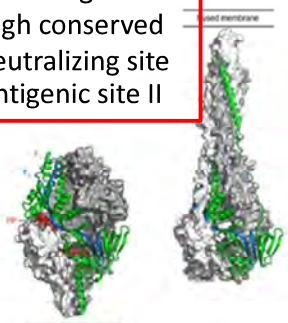
Hasan R. Pediatr Infect Dis J. 2014 33:e45-52.

RSV vaccine development

RSV-A
RSV-B



F protein
- Immunogenic
- High conserved neutralizing site
- Antigenic site II



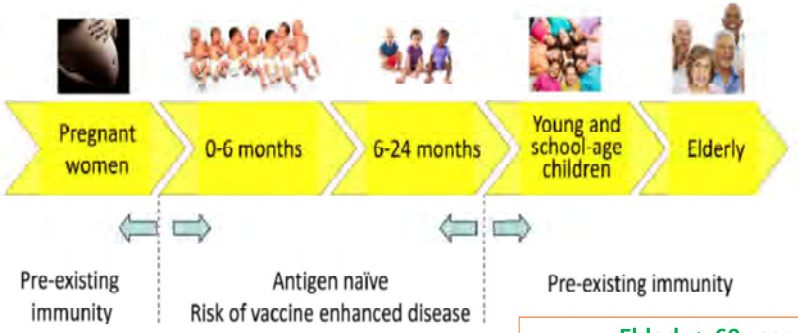
Family Paramyxoviridae
Single strand RNA envelope virus

Pre-fusion Post-fusion

DeVincenzo JP. N Engl J Med. 2015;373(21):2048-58.

RSV vaccine development

To prevent severe lower respiratory tract infection in infants



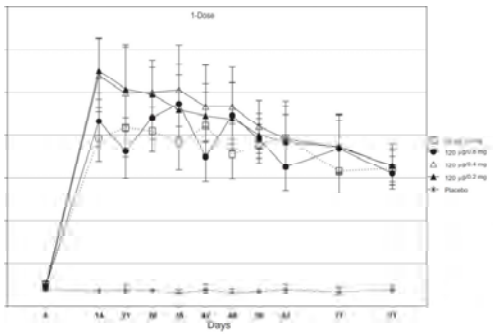
ax: RSV post-nanoparticle
SV pre-F (60ug)

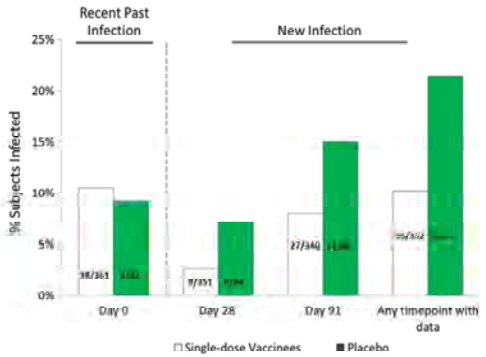
GSK: ChAd155-RSV F,M,M2

Elderly > 60 year
Novavax: RSV Post-F nanoparticle
Medimmune: RSV post F Phas

Graham BS. Vaccine 2016; 3353-3541. Jorge C. Human vaccine Immun 2018;7:

RSV vaccine development in pregnant women





e 3: RSV vaccine in pregnant women during 3rd trimester 120 ug
ein with 0.4 mg of aluminum is ongoing

August A. Vaccine 2017;3749.

Take home message

accines are for every stage of life.

accine for both infectious diseases and cancer prevention.

accine must be integrated in antenatal care services to reduce infant ortality rate esp during the first few months of live.

hai EPI: HPV for adolescent girl and influenza vaccine for pregnant wor

Vaccine is just a tool.
Immunization is the path for real impact!