The Immunological Response of Thai Infants to *Haemophilus influenzae* Type B Polysaccharide-Tetanus Conjugate Vaccine Co-administered in the Same Syringe with Locally Produced Diphtheria-Tetanus-Pertussis Vaccine

Angkool Kerdpanich MD*,
Yanee Hutagalung MD**, Veerachai Watanaveeradej MD*,
Hans L Bock MD**, Mark Steinhoff MD***

** Infectious Diseases Unit, Department of Pediatrics, Phramongkutklao Hospital, Bangkok, Thailand*
*** GlaxoSmithKline Biologicals, Rixensart, Belgium*
**** Johns Hopkins University, Baltimore, USA*

Objective: *Comparing the immunogenicity and reactogenicity of three vaccine combinations. These were GlaxoSmithKline Biologicals' (GSK)* Haemophilus influenzae *type b vaccine (Hib-TT;* Hiberix™*) administered with the local Government Pharmaceutical Organization's (GPO) diphtheria-tetanus-pertussis whole cell (DTPw) vaccine, Hib-TT mixed with GPO's DTPw vaccine, or Hib -TT mixed with GSKs' DTPw vaccine (*Tritanrix™*.*

Material and Method: *An open, randomized, controlled, single center study of three hundred and sixty infants. They were randomized into three groups to receive either Hib-TT;* Hiberix™ *mix with GPOs' DTPw vaccine (group 1), Hib-TT mixed with GPO's DTPw vaccine (group 2), or Hib -TT mixed with GSKs' DTPw vaccine (*Tritanrix™*; group 3) at two, four and six months of age.*

Result: *One month after the third dose, all subjects had antibodies level against Hib polyribosylribitol phosphate (PRP) ≥ 0.15* μg/ml. *All subjects except two (in group 2) had anti-PRP levels ≥ 1.0* μg/ml. *The geometric mean concentrations were similar in all three groups. Over 96% of the subjects in all three groups demonstrated an immunological response to diphtheria, tetanus, and pertussis antigens. There was no difference among the three groups in terms of severe local reaction and fever.*

Conclusion: *The present study showed that the combined vaccines produced an effective antibody response with no increase in reactogenicity compared to separately administrated vaccines.*

Keywords: *Combined vaccine, Haemophilus influenzae, Immunogenicity, DTPw*

J Med Assoc Thai 2007; 90 (7): 1330-6
Full text. e-Journal: *http://www.medassocthai.org/journal*

Combined vaccines are important tools in the control of preventable childhood infectious diseases. They offer the advantages of convenience, cost-effectiveness, and better compliance. The combined trivalent diphtheria, tetanus, whole-cell pertussis (DTPw) vaccine has been available since 1940s and has been part of the World Health Organization's (WHO) Expanded Program on Immunization (EPI) since the late 1970s. It is well established as part of the routine vaccine practice worldwide. The DTPw vaccine contains inactivated *Bordetella pertussis* bacteria, diphtheria and tetanus toxoids. Three doses of DTPw vaccine, given intramuscularly, are usually administered within the first six months of age.

Haemophilus influenzae type b (Hib) is the main pathogen causing meningitis in infants and young children and can cause other invasive infections such as pneumonia, empyema, suppurative arthritis, and cellulitis[1-4]. In the past, Hib infection caused considerable morbidity, long-term sequelae, mortality, and

Correspondence to : Kerdpanich A, Infectious Diseases Unit, Department of Pediatrics, Phramongkutklao Hospital, Bangkok 10400, Thailand. Phone: 0-2644-8971, Mobile: 084-703-8679, Fax: 0-2644-4135, E-mail: akpmk@yahoo.com

had a strong impact on healthcare costs in both developed and developing countries[5]. Hib vaccines, originally containing purified polyribosylribitol phosphate (PRP) capsular polysaccharide from Hib[6], were introduced in the mid 1980s. However, the vaccine was found to have variable efficacy in children younger than 18 months because of the nature of the immune response to the PRP polysaccharide. Subsequently, conjugated C vaccines were developed in which the pathogenic antigen is linked to a more immunogenic 'protein carrier', with the aim to improve efficacy. By the early 1990s, Hib conjugated vaccines were used to vaccinate infants. The introduction of effective vaccines, has resulted in the virtual disappearance of invasive Hib diseases and has markedly lowered the prevalence of upper respiratory carrier of Hib[7-10]. In 1997, WHO recommended the worldwide inclusion of Hib conjugated vaccines in infant immunization programs, as appropriate to national capacities and priorities[11]. This initiative requires the addition of another series of inoculations into the recommended schedule for infants and children. The complicated logistics of administering additional vaccines, each requiring several inoculations, may pose a significant barrier to the success of universal immunization. Compliance with vaccination schedules would be enhanced if Hib vaccines could be mixed with DTP vaccines for a single injection, without intensifying the reactogenicity and safety profile or causing interference with the immune response compared to the separate vaccines.

The present study was conducted to demonstrate the immunogenicity and reactogenicity of GlaxoSmithKline Biologicals 'Hib vaccine (Hib-TT; *Hiberix*™) administered separately or mixed with locally produced DTPw vaccine (GPO-DTPw), and to demonstrate the non-inferiority to GlaxoSmithKline Biologicals' extemporaneously mixed combination of DTPw (GSK-DTPw; *Tritanrix*™) and Hib-TT when given at 2, 4 and 6 months of age.

Material and Method

The present study was an open, randomized, phase II clinical trial, conducted at Phramongkutklao Hospital, Bangkok. The present study was approved by the National and Institutional Ethic Committees, and conducted according to the Declaration of Helsinki and Good Clinical Practice. Written informed consent was obtained from the parents or guardians prior to enrollment.

Healthy 6-12 week-old infants who had received two doses of hepatitis B vaccine at birth and 1 month of age were recruited. The subjects were excluded if they had a history of previous disease or vaccination against diphtheria, tetanus, pertussis, or *Haemophilus influenza* type B; if they had received a vaccine not foreseen in the present study protocol within 30 days prior to the present study start or after receiving a study vaccine. Additional exclusion criteria were history of allergic disease or reactions likely to be exacerbated by any component of the vaccine. The infants were also excluded if they had a history of chronic administration (more than 14 days) of immunosuppressants or other immune-modifying drugs prior to the first vaccine dose, continuing any chronic drug therapy during the present study period, confirmed or suspected immunosuppressive or immunodeficiency condition, including HIV infection, or administration of immunoglobulins or any blood products since birth or planned administration during the present study period. The infants were also excluded if they had any underlying condition such as major congenital defects or serious chronic illness, neurological disorders including seizure, or developed acute disease at the time of enrollment.

Study groups and Vaccines

The infants were randomized according to a 1:1:1 randomization scheme to receive either Government Pharmaceutical Organization's (GPO) local commercially available combined GPO-DTPw concomitantly with Hib-TT conjugated (*Hiberix*™) vaccine (group 1) or GPO-DTPw mixed with Hib-TT conjugated vaccine (group 2) or GSK-DTPw (*Tritanrix*™) mixed with Hib-TT conjugated vaccine (group 3).

Hib-TT conjugated (*Hiberix*™) and GSK-DTPw *vaccines (Tritanrix*™), were developed and manufactured by GlaxoSmithKline Biologicals, Rixensart, Belgium[12]. The GPO-DTPw vaccine was developed locally in Thailand. A single lot of each vaccine was used in the present study.

GSK-DTPw vaccine was supplied in 0.5 ml monodose vials, each containing a minimum of 30 IU, 60 IU, and 2 IU of diphtheria, tetanus, and inactivated *Bordetella pertussis* antigen, respectively. Hib-TT conjugated vaccine was supplied in 0.5 ml, and containing 10 µg *Haemophilus influenza* type b capsular polysaccharide conjugated to 20-40 µg Tetanus Toxoid. This vaccine was supplied as a freeze-dried pellet for reconstitution before use.

The GPO-DTPw vaccine was supplied as a multidose per vial each 0.5 ml containing 30 Lf, 6 Lf, and 20,000 million cells of diphtheria toxoid, tetanus

toxoid, and *Bordetella pertussis*, respectively.

Vaccines were administered by deep intramuscular injection in the left deltoid region at 2, 4, and 6 months of age in groups 2 and 3, and in bilateral deltoid region in the concomitant vaccination group 1. The duration of each subject's participation in the present study was seven months.

Assessment of immunogenicity

Blood samples were taken prior to the first dose of vaccination and 1 month after completing the full vaccination course for antibody measurement against diphtheria, tetanus toxoid, Bordetella pertussis, and Hib antigens. All antibody levels were measured by enzyme-linked immunosorbent assay (ELISA) at GSK Biologicals' central laboratory (Rixensart, Belgium). The protective level at 0.1 IU/ml was used as assay cut-off for diphtheria and tetanus antibodies. For *Bordetella pertussis* toxoid (BPT) antibodies, seropositivity was used at 15 EL.U/ml. The Hib PRP cut-off was set at 0.15 μg/ml.

Assessment of reactogenicity

All subjects were observed closely for at least 30 minutes after each vaccination. Solicited local symptoms (pain, redness, and swelling) at the injection site and solicited general symptoms (fever, drowsiness, loss of appetite, and restlessness/fussiness) were recorded on diary cards for 4 days following vaccination. Serious adverse events were recorded up to one month following vaccination. A 3-point scale was used for grading the intensity of symptoms; grade 1: an adverse event that is easily tolerated causing minimum discomfort or not interfering with everyday activities, grade 2: an adverse event that is sufficiently discomforting to interfere with normal everyday activities, grade 3: an adverse event that prevents normal, everyday activities

Statistical analysis

Immunogenicity: Analysis was performed on two cohorts: total and according to protocol (ATP) cohorts with analysis on ATP cohort considered as the primary analysis. Seroprotection/ seropositivity rates and Geometric mean concentrations/titers (GMC/GMT) for antibodies against all vaccine antigens were calculated with 95% confidence intervals (CI), at each blood sampling time point.

Inferential analysis: Equivalence between the treatment groups and the control group was demonstrated by calculating the standardized asymptotic 95% CI for the between-group treatment differences in seroprotection rates/vaccine response rates for each antigen and verifying that the confidence limits were within pre-defined clinical limits [-10%, 10%]. Similarly, 95% CI for the ratio of GMTs between groups (treatment group/control) was computed and compared with pre-defined clinical limits (1.5 fold difference) to verify equivalence of groups.

Reactogenicity: Analysis was performed only on the ATP reactogenicity cohort. The overall incidence of solicited symptoms during the 4-day follow-up period vaccination was tabulated with exact 95% CI. The incidence, relationship to vaccination and intensity of unsolicited symptoms was also tabulated.

Exploratory analysis: Fisher's exact test was performed to compare the incidence of any solicited local symptom, any severe solicited local symptom, incidence of fever and incidence of each of the solicited local symptom in the three groups.

Results

Three hundred and sixty infants were enrolled in the present study and were randomized to one of the three study groups (120 subjects/group). The demographic characteristics for all three-vaccination groups were similar. Twenty-four infants (6.6%; 8 in group 1, GPO-DTPw + HibTT; 6 in group 2, GPO-DTPw/Hib-TT; 10 in group 3, GSK-DTPw/Hib-TT) were not included in the immunogenicity analysis, due to protocol violation or non-compliance with either the vaccination or blood-sampling schedule.

Immunogenicity results

One month after completing the full vaccination course, all subjects (ATP-cohort) in all three groups had anti-PRP antibody concentrations ≥ 0.15 μg/ml. Moreover, all except two subjects (in group 2) had anti-PRP antibody concentrations ≥ 1 □g/ml. The measured GMCs were high (above 15 mg/ml) and similar in all three groups (Table 1).

Over 96% of the subjects in all three groups achieved anti-diphtheria sero-protection rates. Anti-diphtheria GMCs were 1.123 IU/ml, 0.833 IU/ml and 0.932 IU/ml in groups 1, 2 and 3 respectively. All subjects in all three groups developed sero-protection against tetanus with high GMCs in all three groups (Fig. 1).

One month after the full vaccination course, 97-99% of subjects in all three groups developed seropositivity for anti-BPT antibodies. GMCs were 75.5 EL.U/ml, 66.1 EL.U/ml, and 72.7 EL.U/ml in groups 1, 2, and 3, respectively (Fig. 1).

Table 1. Percentage of subjects with anti-PRP antibody concentrations ≥ 0.15 μg/ml and ≥ 1.0 μg/ml and GMCs

Group	Timing	N	≥ 0.15 μg/ml		≥ 1.0 μg/ml		GMC (95% CI)		
			n	%	n	%	μg/ml	LL	UL
1	Pre	111	101	91.0	16	14.4	0.356	0.296	0.428
	Post	112	112	100.0	112	100.0	17.655	14.495	21.504
2	Pre	110	97	88.2	18	16.4	0.352	0.290	0.426
	Post	111	111	100.0	109	98.2	15.285	12.253	19.068
3	Pre	110	100	90.9	21	19.1	0.408	0.338	0.492
	Post	110	110	100.0	110	100.0	15.447	13.298	17.943

Group 1 received GPO DTPw + GSK Hib at 2, 4 and 6 months of age
Group 2 received GPO DTPw/GSK Hib at 2, 4 and 6 months of age
Group 3 received GSK DTPw/GSK Hib at 2, 4 and 6 months of age
N: number of subjects with available results
n (%): Number (percentage) of subjects with antibody concentrations above the cut-off
95%CI, LL, UL: 95% confidence interval; Lower Limit; Upper Limit
Pre: Day 0; Post: One month after the third dose
GMC: geometric mean concentration

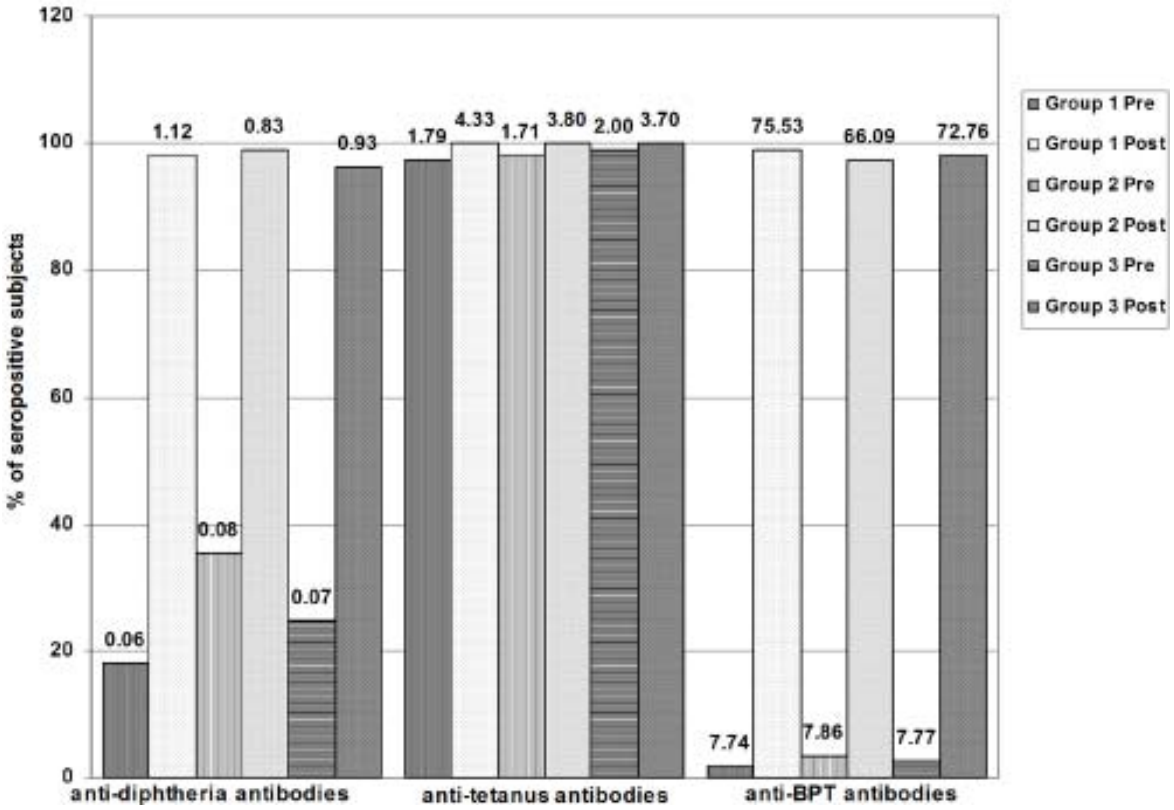

Fig. 1 Percentage seropositivity and GMC levels pre-dose 1 and one month post-dose 3
Label values are the GMCs
GMC unit of anti-diphtheria and anti-tetanus antibody = IU/ml
GMC unit of anti-BPT antibody = EL.U/ml

Reactogenicity results

The safety evaluation included data from 357 subjects. Eight subjects (2 in group 1, 5 in group 2, and 1 in group 3) reported serious adverse events during the present study. None was considered by the investgator to be causally related to vaccination. The number of subjects reporting any solicited/unsolicited local and generalized symptoms was similar in all groups. Pain at the injection site was the most frequent solicited local symptom both in terms of any or grade 3 intensity (grade 3 intensity was defined as spontaneously painful or crying when the limb was moved) during the 4-day follow-up period in all three groups. There were no significant differences among the three groups in terms of incidence of grade 3 pain. Grade 3 fever (> 39.5ºC) occurred in 1.7%, 3.3%, and 1.7% of subjects in Groups 1, 2, and 3, respectively. The differences were not statistically significant.

Discussion

In the present study, all subjects in the three vaccination groups recorded concentrations of anti-PRP $\geq$ 0.15 μg/ml, which is widely accepted as being the conservative threshold level of protection[13,14]. Whereas a serum concentration $\geq$ 1.0 μg/ml is believed to correlate with long term protection[13]. Using this cut-off level, the Thai subjects included in the present study demonstrated a high overall immunogenicity against anti-PRP antibodies irrespective of whether the study vaccines were administered combined or separately. The present results confirmed the previous studies showing a high immunogenicity to PRP antigen when Hib and DTPw vaccines were given in combination[15-17]. Anti-PRP antibody GMCs in the subjects, who received combination vaccines, were somewhat lower than those in the group who received vaccines in a separate arm (17.0 μg/ml in group 1 vs. 15.2 μg/ml and 15.4 μg/ml in groups 2 and 3, respectively). This finding has been observed previously when the subjects given the vaccines in the same syringe had statistically significantly lower Hib GMCs[16-18]. Nevertheless, these observations are not clinically relevant since the GMC level is high above the protective level.

The GMCs of antibodies against the DTP components were slightly, but consistently lower for all three components in the mixed vaccination groups. However, the differences were neither statistically nor clinically significant and are similar to those observed in another study[15].

Generally, the presented data of local DTPw mixed with GSK Biologicals' Hib vaccine are consistent with the results of combining GSK Biologicals' Hib with a commercially available DTPw vaccine in the UK[18].

Interestingly, the present study recorded a high percentage of anti-PRP and anti-tetanus antibodies pre-vaccination, due to the transplacental transfer of high maternal antibody levels. This is also seen in a lesser extent for anti-diphtheria. Although Hib vaccine is not recommended in pregnant women in Thailand, two doses of tetanus vaccine are routinely administered during pregnancy. Thus, the evidence of anti-PRP antibody levels in their mothers is naturally acquired, showing a sign of the prevalence of Hib infection. Inhibitory effects have been reported following immunization with tetanus and diphtheria toxoids[19,20], pertussis[21], conjugated Hib[22] and hepatitis A vaccines[23]; with every vaccine administered in the presence of significant titers of maternal antibodies. Significant inhibitory effects on infant antibody responses reflected by lower sero-conversion rates and/or GMT in infants immunized in the presence of high levels of maternal antibodies were found. However, this inhibition of B-cell mediated immune response is determinant-specific, and leaves infant T-cell responses largely unaffected by these transferred antibodies[24,25]. That leads to efficient immunological priming. This induces infant antibody response as soon as maternal antibody titers decline below the infant response threshold and can serve as an excellent basis for future response[24,25]. Thus, neonatal priming and early boosting with vaccine formulation optimized for sufficient early life immunogenicity and maximal safety profiles, could allow better control of the huge infectious disease burden in early life[24,25].

Despite the presence of high maternal anti-PRP and anti-tetanus antibodies, Hib conjugated and tetanus vaccines can overcome the theoretical inhibitory effect, as demonstrated by all subjects developing antibodies against tetanus and PRP antigen after completing their primary schedule. These findings are consistent with those of Englund et al (2003) where Hib conjugated vaccine was administered to pregnant women and high anti-PRP levels were demonstrated in their infants[26]. The present study demonstrated that the impact of increased levels of Hib antibodies in infants at the time of primary Hib immunization did not appear to interfere with vaccine efficacy. However, higher antibody levels in infants at the time of immunization may transiently decrease the infant's antibody response to active immunization after the first or second immunization, although overall, the antibody response

to PRP conjugated vaccines after the series of vaccines was similar to controls[26].

In contrast to anti-PRP and anti-tetanus antibodies, insignificant pre-vaccination anti-diphtheria and anti-BPT antibody titers were found. This confirms the waning immunity after routine immunization of DTP vaccine in childhood and supports the recommendation for pertussis booster vaccination in adults.

There were no significant differences among the three study groups with respect to the incidence of severe local symptoms, fever, or other systemic reactions. This confirms that the local GPO-DTPw vaccines can be mixed with GSK Biologicals' Hib-TT vaccine without increasing the frequency and severity of reactions usually seen following DTPw vaccination.

The present study confirmed that GSK Biologicals' Hib-TT conjugated vaccine combined with local commercially available GPO-DTPw vaccine, given as a single injection, is safe and immunogenic. Following regulatory approval, this new combined vaccine could facilitate the introduction of Hib vaccine into the National EPI by reducing the number of required injections and subject visits, lowering costs, and ultimately increasing subject compliance and vaccine coverage.

References

1. Moxon ER, Rappuoli R. Haemophilus influenzae infections and whooping cough. Lancet 1990; 335: 1324-9.
2. World Health Organization. Bacterial meningitis - United Kingdom. Wkly Epidemiol Rec 1985; 60: 146-7.
3. Dajani AS, Asmar BI, Thirumoorthi MC. Systemic Haemophilus influenzae disease: an overview. J Pediatr 1979; 94: 355-64.
4. Todd JK, Bruhn FW. Severe Haemophilus influenzae infections. Am J Dis Child 1975; 129: 607-11.
5. Asensi F, Otero MC, Perez-Tamarit D, Miranda J, Pico L, Nieto A. Economic aspects of a general vaccination against invasive disease caused by Haemophilus influenzae type b (Hib) via the experience of the Children's Hospital La Fe, Valencia, Spain. Vaccine 1995; 13: 1563-6.
6. Anderson P, Peter G, Johnston RB Jr, Wetterlow LH, Smith DH. Immunization of humans with polyribophosphate, the capsular antigen of Hemophilus influenzae, type b. J Clin Invest 1972; 51: 39-44.
7. Peltola H, Kilpi T, Anttila M. Rapid disappearance of Haemophilus influenzae type b meningitis after routine childhood immunisation with conjugate vaccines. Lancet 1992; 340: 592-4.
8. Jonsdottir KE, Steingrimsson O, Olafsson O. Immunisation of infants in Iceland against Haemophilus influenzae type b. Lancet 1992; 340: 252-3.
9. Booy R, Hodgson S, Carpenter L, Mayon-White RT, Slack MP, Macfarlane JA, et al. Efficacy of Haemophilus influenzae type b conjugate vaccine PRP-T. Lancet 1994; 344: 362-6.
10. Adams WG, Deaver KA, Cochi SL, Plikaytis BD, Zell ER, Broome CV, et al. Decline of childhood Haemophilus influenzae type b (Hib) disease in the Hib vaccine era. JAMA 1993; 269: 221-6.
11. The Children's Vaccine Initiative and the global programme for vaccines and immunization: introduction of new vaccine. Wkly Epidemiol Rec 1997: 72: 240-2.
12. Clemens SC, Azevedo T, Homma A. Feasibility study of the immunogenicity and safety of a novel DTPw/Hib (PRP-T) Brazilian combination compared to a licensed vaccine in healthy children at 2, 4, and 6 months of age. Rev Soc Bras Med Trop 2003; 36: 321-30.
13. Kayhty H, Peltola H, Karanko V, Makela PH. The protective level of serum antibodies to the capsular polysaccharide of Haemophilus influenzae type b. J Infect Dis 1983; 147: 1100.
14. Claesson BA, Schneerson R, Robbins JB, Johansson J, Lagergard T, Taranger J, et al. Protective levels of serum antibodies stimulated in infants by two injections of Haemophilus influenzae type b capsular polysaccharide-tetanus toxoid conjugate. J Pediatr 1989; 114: 97-100.
15. Watemberg N, Dagan R, Arbelli Y, Belmaker I, Morag A, Hessel L, et al. Safety and immunogenicity of Haemophilus type b-tetanus protein conjugate vaccine, mixed in the same syringe with diphtheria-tetanus-pertussis vaccine in young infants. Pediatr Infect Dis J 1991; 10: 758-63.
16. Ferreccio C, Clemens J, Avendano A, Horwitz I, Flores C, Avila L, et al. The clinical and immunologic response of Chilean infants to Haemophilus influenzae type b polysaccharide-tetanus protein conjugate vaccine coadministered in the same syringe with diphtheria-tetanus toxoids-pertussis vaccine at two, four and six months of age. Pediatr Infect Dis J 1991; 10: 764-71.
17. Avendano A, Ferreccio C, Lagos R, Horwitz I, Cayazzo M, Fritzell B, et al. Haemophilus influenzae type b polysaccharide-tetanus protein conjugate vaccine does not depress serologic responses to

diphtheria, tetanus or pertussis antigens when co-administered in the same syringe with diphtheria-tetanus-pertussis vaccine at two, four and six months of age. Pediatr Infect Dis J 1993; 12: 638-43.
18. Jones IG, Tyrrell H, Hill A, Horobin JM, Taylor B. Randomised controlled trial of combined diphtheria, tetanus, whole-cell pertussis vaccine administered in the same syringe and separately with Haemophilus influenzae type b vaccine at two, three and four months of age. Vaccine 1998; 16: 109-13.
19. Sarvas H, Kurikka S, Seppala IJ, Makela PH, Makela O. Maternal antibodies partly inhibit an active anti-body response to routine tetanus toxoid immunization in infants. J Infect Dis 1992; 165: 977-9.
20. Bjorkholm B, Granstrom M, Taranger J, Wahl M, Hagberg L. Influence of high titers of maternal antibody on the serologic response of infants to diphtheria vaccination at three, five and twelve months of age. Pediatr Infect Dis J 1995; 14: 846-50.
21. Englund JA, Anderson EL, Reed GF, Decker MD, Edwards KM, Pichichero ME, et al. The effect of maternal antibody on the serologic response and the incidence of adverse reactions after primary immunization with acellular and whole-cell pertussis vaccines combined with diphtheria and tetanus toxoids. Pediatrics 1995; 96: 580-4.
22. Daum RS, Siber GR, Ballanco GA, Sood SK. Serum anticapsular antibody response in the first week after immunization of adults and infants with the Haemophilus influenzae type b-Neisseria meningitidis outer membrane protein complex conjugate vaccine. J Infect Dis 1991; 164: 1154-9.
23. Dagan R, Amir J, Mijalovsky A, Kalmanovitch I, Bar-Yochai A, Thoelen S, et al. Immunization against hepatitis A in the first year of life: priming despite the presence of maternal antibody. Pediatr Infect Dis J 2000; 19: 1045-52.
24. Siegrist CA. Mechanisms by which maternal antibodies influence infant vaccine responses: review of hypotheses and definition of main determinants. Vaccine 2003; 21: 3406-12.
25. Siegrist CA. Neonatal and early life vaccinology. Vaccine 2001; 19: 3331-46.
26. Englund JA, Glezen WP. Maternal immunization with Haemophilus influenzae type b vaccines in different populations. Vaccine 2003; 21: 3455-9.

การตอบสนองของระบบภูมิคุ้มกันของเด็กไทย ต่อการให้วัคซีนป้องกันโรคฮิปผสมกับวัคซีนป้องกันโรคคอตีบ ไอกรน และบาดทะยัก ขององค์การเภสัชกรรม

อังกูร เกิดพาณิช, ญาณี ฮูทะกาลุง, วีรชัย วัฒนะวีรเดช, ฮานส์ บอกค์, มาร์ค สไตน์ฮอฟ

การศึกษาแบบเปิด ในอาสาสมัครเด็กไทยจำนวน 360 ราย เพื่อประเมินระดับภูมิคุ้มกัน และ ผลข้างเคียงต่อวัคซีนที่มีการสุ่มให้ ในสามกลุ่ม กลุ่มที่1: ได้รับวัคซีนฮิปของบริษัทแกล็กโซสมิทไคล์น (Hiberix™) ร่วมกับวัคซีน DTPw ขององค์การเภสัชกรรม(ฉีดแยกคนละข้าง) กลุ่มที่ 2: ได้รับวัคซีนฮิปของบริษัทแกล็กโซสมิทไคล์นร่วมกับวัคซีน DTPw ขององค์การเภสัชกรรม(ฉีดรวมในเข็มเดียวกัน) และกลุ่มที่ 3:ได้รับวัคซีนฮิปร่วมกับวัคซีน DTPw ของบริษัทแกล็กโซสมิทไคล์น (ฉีดรวมในเข็มเดียวกัน) โดยให้ในอาสาสมัครเมื่ออายุ 2, 4 และ 6 เดือน ตามลำดับ

จากการศึกษาพบว่าเด็กทุกรายในทุกกลุ่มการศึกษามีการตอบสนองต่อ anti PRP $\geq$ 0.15 μg/ml และเด็กเกือบ ทุกรายที่มี anti PRP $\geq$ 1.0 μg/ml โดยมีระดับ GMT ใกล้เคียงกันในทั้ง 3 กลุ่ม นอกจากนี้ยังพบว่ามากกว่าร้อยละ 96 ของกลุ่มศึกษา มีการตอบสนองของระบบภูมิคุ้มกันต่อโรคคอตีบ ไอกรน และบาดทะยัก ทั้งนี้ไม่พบความแตกต่างกันในผลข้างเคียง เฉพาะที่ที่รุนแรง หรือ ไข้

การศึกษานี้สรุปได้ว่าการให้วัคซีนฮิปของบริษัทแกล็กโซสมิทไคล์น ร่วมกับวัคซีน DTPw ขององค์การเภสัชกรรม (ฉีดรวมในเข็มเดียวกัน)สามารถกระตุ้นระบบภูมิคุ้มกันได้ดีและไม่ก่อให้เกิดผลข้างเคียงเพิ่มขึ้น