Serosurveillance of Varicella and Hepatitis B Infection after Reported Cases in Medical Students and the Relationship between Past Varicella Disease History and Immunity Status

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Objective: *To identify seroprevalence of varicella and the relationship with their histories of experiences of varicella diseases and to provide appropriate immunization against varicella, mumps, measles, rubella and hepatitis B to medical students.*
Material and Method: *All of the medical students were eligible for participation after informed consents. Immunization history against varicella, mumps, measles, rubella (MMR) and hepatitis B were obtained from a questionnaire. A blood sample was obtained from each student for IgG antibody against VZV by ELISA. Medical students with an uncertain history or no documentation of hepatitis B vaccination were tested for HBsAg and anti-HBcIgG by ELISA.*
Results: *There were 383 medical students enrolled. The mean age at enrollment was 21.6 years (median 21.4 years; range 18-25.8 years). Of 383 medical students, 372 (97.2%) had documents of receiving MMR immunizations. The blood samples were obtained from 374 of 383 (97.6%) medical students to identify the immunity against varicella zoster virus (VZV) and the seroprevalence rate was 92%. Using VZV IgG antibody detection as a standard test, history of experience of varicella disease provided positive predictive value of 99.3% (148/149). Of 383 medical students, 277 (72.3%) were tested for hepatitis B markers and 243 (87.7%) students showed negative results. The prevalence of HBsAg carriers was 0.01% (4/383).*
Conclusion: *Suboptimal immunities against vaccine preventable diseases could be demonstrated in the medical students including varicella and hepatitis B. New recommendations of immunizations against varicella, MMR and hepatitis B viruses for a particular group of the population were provided.*

Keywords: *Varicella, Hepatitis B, Measles, Mumps, Rubella, MMR, VZV, HBV, Immunity, Vaccine, Medical student, Seroprevalence, Carriers, Control*

J Med Assoc Thai 2012; 95 (Suppl. 5): S80-S85
Full text. e-Journal: *http://jmat.mat.or.th*

Varicella, mumps, measles, rubella and hepatitis B are contagious diseases which can occasionally occur in a hospital based setting[1]. At present, potentially high risk groups include health care workers (HCWs) and medical students who take care of the patients[2]. The Phramongkutklao Hospital's infection control policy recommended that all of HCWs must have immunity to varicella, mumps, measles, rubella and hepatitis B before working in the patient ward. Although, this policy is also applied to the medical students, there is no intensive monitoring. In the past year, a medical student who was working in the pediatric ward developed chickenpox. During the event, the authors provided post exposure prophylaxis to all of VZV susceptible patients who were admitted in that pediatric ward. As a result, it increased the risk for nosocomial VZV infection in patients and increased cost of hospitalization[3]. Another case was a fifth year medical student who had measles with pneumonia and needed hospitalization in the adult ward.

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To improve an effectiveness of hospital infection control, the knowledge of current medical students' immunity status against vaccine preventable diseases is needed. A cross sectional surveillance was conducted to assess their immunities against varicella and hepatitis B by history taking and serological testing. Since MMR was given to each student, the immunity of mumps, measles, rubella was assessed by only the history of past illness and document of previous vaccination. This knowledge also helps guiding improvement of infection control policy to identify susceptible medical students and define recommendations for appropriate immunization. The main objectives of the present study were 1) to identify seroprevalence of varicella and the relationship with their histories of experiences of varicella diseases 2) to provide appropriate immunization against varicella, mumps, measles, rubella and hepatitis B to medical students.

Material and Method

Study population

All of the medical students (second year-sixth year) who have studied in Phramongkutklao College of Medicine during May 2008-March 2009, were eligible for participation after informed consents. The following data were obtained from a questionnaire including age, gender, personal history and immunization history against varicella, mumps, measles, rubella and hepatitis B. Any written documentation of previous immunizations was requested and recorded.

Serological assays

A 5-ml of venous blood sample was obtained from each participant who gave informed consent for specific serum antibody analyses. IgG antibodies against VZV were determined by ELISA (enzyme-linked immunosorbent assay®, Wiesbaden, Germany) with declared sensitivity and specificity values of 92% and 100%, respectively.

In medical students with an uncertain history of immunization or no documentation of hepatitis B vaccination, the respective serum samples were tested for HBsAg and anti-HBcIgG by ELISA (Cobas®, Roche, USA) to distinguish between undocumented immunization and infection.

IgG antibody against VZV was performed at the Department of Medical Sciences, Ministry of Public Health, Thailand and positive result as interpreted according to cut-off point of OD-value which is the lot specific of each test kit. HBsAg and anti-HBcIgG were performed at Phramongkutklao Hospital and both Cut-off values $\geq$ 1.0 IU/ml were considered positive results.

To stop the continuation of epidemic after knowing a medical student diagnosed as measles, the authors provided one dose of MMR vaccine to all of the medical students before starting the present study. Therefore, antibodies for mumps, measles, rubella were not performed.

Statistical analysis

Statistical analysis was performed using STATA version 10. Categorical variables were analyzed. Use of the Pearson Chi-square test and p-value of less than 0.05 was considered to be statistically significant.

Results

Study population

There were 383 medical students enrolled. The mean age at enrollment was 21.6 years old (median 21.4 years; range 18-25.8 years) and 61.9% were males. All participants were tested for antibodies against VZV and HBV (Fig. 1).

Immunization status and seroprevalence

Mumps Measles Rubella (MMR)

Of 383 medical students, 372 (97.2%) had documents of receiving MMR immunizations, 78 (20.4%) students completed with at least 2 doses, 294 (76.8%) students received 1 dose and 11 (2.8%) students reported uncertain immunization history.

Varicella

The blood samples were obtained from 374 of 383 (97.6%) medical students to identify the immunity against varicella zoster virus (VZV) and the seroprevalence rate was 92%. Of students with a negative history of previous varicella disease, 87.2% had positive IgG antibodies against VZV (Table 1).

Using VZV IgG antibody detection as a standard test, history of experience of varicella disease provided sensitivity of 43% (148/344), specificity of 96.7% (29/30), positive predictive value of 99.3% (148/149) and negative predictive value of 12.9% (29/225).

Of 383 subjects, 13 (3.4%) had completed two doses of varicella vaccine and 2 of them became seronegative for varicella IgG antibodies. Of the 3 students who experienced of receiving varicella vaccine one dose, 1 student revealed seronegative for VZV. The seropositivities of varicella antibodies were 90% and 95.2% in male and female students respectively (p-value 0.07).

Table 1. Relationship between participant's experience of varicella disease and the serological immune status

Numbers of medical students with experience of varicella disease by history	VZV serological immune status Numbers of medical students		
	Yes	No	Total
Yes	148	1	149
No	196	29	225
Total	344	30	374

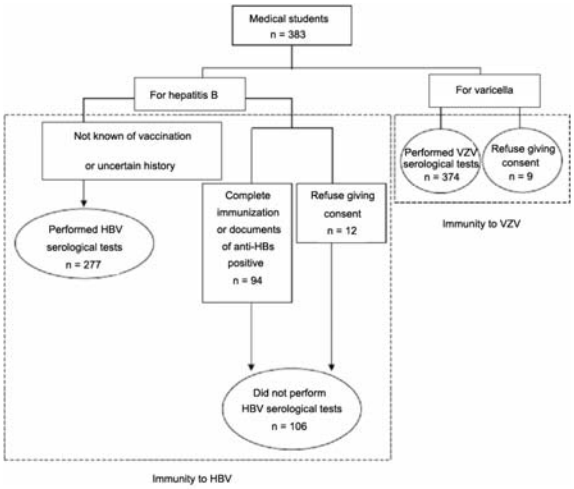

Fig. 1 Flowchart of the activities in studied population

Hepatitis B

Of 383 students, 94 had immunity for hepatitis B virus by documented immunization history of complete primary immunization series by at least three doses of hepatitis B vaccine (77 cases) or by documentation of anti-HBs positive (17 cases).

From 383 students, 277 who were not known of HBV vaccination or uncertain history gave consent and had their serum samples obtained for serological testing of hepatitis B. Two hundred and fourty-three (87.7%) students were negative for HBsAg and anti-HBcIgG. (Table 2) Four students had positive results of HBsAg and anti-HBcIgG. All of them were considered as chronic hepatitis B carriers and consultation were sent to the internist for further management. The seropositive rate of natural hepatitis B infection which was defined by the presence of anti-HBcIgG was 12.3%. Male gender gave a higher rate than female gender (16%, 6%; p-value 0.013).

Intervention for medical students' immunization

Recommendation for catch up immunization was provided to all of the medical students in the present study. For completing MMR vaccination, 294 (76.8%) students with documentation of getting one dose received an additional one dose and 11 (2.8%) students with uncertain history received two doses. For varicella immunization, all 30 of 383 (7.8%) students who were seronegative to VZV were recommended to immunize with two doses of varicella vaccine. Primary series of hepatitis B vaccine (3 doses) were recommended to 243 students who had negative results for both HBsAg and anti-HBcIgG..

Table 2. Serological tests for hepatitis B virus in 277 medical students

Serology for hepatitis B virus	Numbers of medical students n = 277
Anti-HBcIgG positive/HBsAg positive	4 (1.4%)
Anti HBcIgG positive/HBsAg negative	30 (10.9%)
Anti HBcIgG negative /HBsAg negative	243 (87.7%)

Discussion

Vaccines against hepatitis B (HBV), mumps-measles-rubella (MMR) were included in national EPI of Thailand in the year 1992 and 1997 respectively. In fact, one dose of isolated measles vaccine at 9 months of age was included in EPI in 1984. Two doses of MMR were recommended in 1997 and most of the people in the same generation as these medical students' age did not receive the second dose. The efficacy of single dose measles vaccination at 9 months of age could be as low as 66%[4]. The cost for MMR vaccine was 5 US dollars per dose and the cost for antibody detection for all these 3 diseases were 3 times more expensive. Therefore, all of the medical students were offered 1 dose of MMR vaccine without evaluating their pre-existing antibodies, to prevent the measles epidemic

from the index case. The efficacy of single dose measles vaccination at 12 months of age or older could be as high as 95%[5] and last 10-15 years[6,7]. However, one study showed only 81.9% of seropositive rate among a Thai population aged 15-19 years old[8]. The prevalence of chronic HBsAg carriers in general population declined from 6-10%[9,10] to 1.4% in the year before and 10 years after respectively integration of hepatitis B vaccine to EPI in Thailand[11]. All of the studied population were born prior to the integration and most of them were not hepatitis B immunized. The prevalence of HBsAg carrier in the present study was 0.01% (4 of 383 students). The low prevalence might indicate the good adherence to standard precautions for sharp equipment related procedures according to the Hospital's infection control policy.

VZV infection is an occupational hazard for susceptible HCWs and can be easily transmitted to the patients[12-16]. Varicella vaccine has not been included in the Thai EPI and < 5% of these medical students had received vaccine against VZV. However, most of them (92%) were seropositive to VZV. This finding was similar to those from the previous studies which showed the seroprevalence rates of 78-84%[17-19]. Giving history of experience varicella disease provided a high rate of seropositivity (PPV 99.3%) and should need no further immunization[12,20-24].

One of the important factors of vaccine-preventable infectious disease outbreak in hospitals is inadequate immunization in medical students[11-14]. From this present study, the new recommendations for our medical students include.

1) Two-dose of MMR vaccines, at least 1 month apart are recommended. Persons who previously received a single dose or had uncertain immunization history must receive at least 1 dose of MMR vaccine, one month prior to working in the ward.

2) Three-doses of hepatitis B vaccines are recommended. Persons who had uncertain immunization history should be tested for HBsAg and anti- HBc. This person should receive the full course of hepatitis B vaccine unless either of his/her HBsAg or anti-HBcIgG becomes positive.

3) Two-dose of varicella vaccines, at least 3 months apart are recommended unless there has been a history of experiencing varicella disease. Persons who had uncertain immunization history or uncertain history of experiencing varicella disease should be tested for antibody against VZV before determination of vaccine requirement.

In conclusion, suboptimal immunities against vaccine preventable diseases were demonstrated in the medical students including varicella and hepatitis B. Post exposure prophylaxis with a single dose of measles/ MMR vaccine should be considered in order to control measles after a reported case, where a particular group of population had incomplete immunization.

Acknowledgement

This work was financially supported by Student affairs, Phramongkutklao College of Medicine, Bangkok, Thailand. The authors wish to thank all the volunteers for their generous participation. Thanks to the Department of Medical Sciences, Ministry of Public Health, Thailand for their excellent laboratory supports.

Potential conflicts of interest

Phramongkutklao Hospital's Foundation under Her Royal Highness Princess Maha Chakri Sirindhorn's Patronage.

References

1. Chazan B, Colodner R, Teitler N, Chen Y, Raz R. Varicella zoster virus in health care workers in northern Israel: seroprevalence and predictive value of history of varicella infection. Am J Infect Control 2008; 36: 436-8.
2. Baer G, Bonhoeffer J, Schaad UB, Heininger U. Seroprevalence and immunization history of selected vaccine preventable diseases in medical students. Vaccine 2005; 23: 2016-20.
3. Carapetis JR, Russell DM, Curtis N. The burden and cost of hospitalised varicella and zoster in Australian children. Vaccine 2004; 23: 755-61.
4. John S, Sanghi S, Prasad S, Bose A, George K. Two doses of measles vaccine: are some states in India ready for it? J Trop Pediatr 2009; 55: 253-6.
5. Markowitz LE, Orenstein WA. Measles vaccines. Pediatr Clin North Am 1990; 37: 603-25.
6. Krugman S. Present status of measles and rubella immunization in the United States: a medical progress report. J Pediatr 1977; 90: 1-12.
7. Markowitz LE, Preblud SR, Fine PE, Orenstein WA. Duration of live measles vaccine-induced immunity. Pediatr Infect Dis J 1990; 9: 101-10.
8. Tharmaphornpilas P, Yoocharean P, Rasdjarmrearn-sook AO, Theamboonlers A, Poovorawan Y. Seroprevalence of antibodies to measles, mumps, and rubella among Thai population: evaluation of measles/MMR immunization programme. J Health Popul Nutr 2009; 27: 80-6.
9. Punyagupta S, Olson LC, Harinasuta U, Akarawong

K, Varawidhya W. The epidemiology of hepatitis B antigen in a high prevalence area. Am J Epidemiol 1973; 97: 349-54.
10. Thongcharoen P, Panpatana P, Wasi C, Jatikavanich V, Chandanayingyong D, Yongchaiyud U, et al. The incidence of hepatitis B surface antigen in tropical infections and liver diseases in Thailand. J Med Assoc Thai 1976; 59: 546-9.
11. Chongsrisawat V, Yoocharoen P, Theamboonlers A, Tharmaphornpilas P, Warinsathien P, Sinlaparatsamee S, et al. Hepatitis B seroprevalence in Thailand: 12 years after hepatitis B vaccine integration into the national expanded programme on immunization. Trop Med Int Health 2006; 11: 1496-502.
12. Holmes CN. Predictive value of a history of varicella infection. Can Fam Physician 2005; 51: 60-5.
13. Pavlopoulou ID, Daikos GL, Tzivaras A, Bozas E, Kosmidis C, Tsoumakas C, et al. Medical and nursing students with suboptimal protective immunity against vaccine-preventable diseases. Infect Control Hosp Epidemiol 2009; 30: 1006-11.
14. Germann D, Matter L. Increasing the immunization rate against measles, mumps, and rubella in medical students at the University of Berne. Schweiz Med Wochenschr 1999; 129: 499-507.
15. Loutan L, Maitre B, Zuber P. Are medical students sufficiently vaccinated? Results of a serological survey and of vaccine coverage. Soz Praventivmed 1994; 39: 86-92.
16. Rowan MS, Carter AO, Walker VJ. Immunization policies in Canadian medical schools. CMAJ 1994; 151: 957-61.
17. Poland GA, Nichol KL. Medical students as sources of rubella and measles outbreaks. Arch Intern Med 1990; 150: 44-6.
18. Kowitdamrong E, Pancharoen C, Thammaborvorn R, Bhattarakosol P. The prevalence of varicella-zoster virus infection in normal healthy individuals aged above 6 months. J Med Assoc Thai 2005; 88 (Suppl 4): S7-11.
19. Migasena S, Simasathien S, Desakorn V, Phomrat B, Suntharasamai P, Pitisuttitham P. Seroprevalence of varicella-zoster virus antibody in Thailand. Int J Infect Dis 1997; 2: 26-30.
20. Bhattarakosol P, Chantarabul S, Pittayathikhun K, Mung-mee V, Punnarugsa V. Prevalence of anti-varicella zoster IgG antibody in undergraduate students. Asian Pac J Allergy Immunol 1996; 14: 129-31.
21. Holmes CN, Iglar KT, McDowell BJ, Glazier RH. Predictive value of a self-reported history of varicella infection in determining immunity in adults. CMAJ 2004; 171: 1195-6.
22. Lieu TA, Black SB, Takahashi H, Ray P, Capra AM, Shinefield HR, et al. Varicella serology among school age children with a negative or uncertain history of chickenpox. Pediatr Infect Dis J 1998; 17: 120-5.
23. Boulianne N, Duval B, De Serres G, Deceuninck G, Masse R, Couillard M. Most ten-year-old children with negative or unknown histories of chickenpox are immune. Pediatr Infect Dis J 2001; 20: 1087-8.
24. Harel Z, Ipp L, Riggs S, Vaz R, Flanagan P. Serotesting versus presumptive varicella vaccination of adolescents with a negative or uncertain history of chickenpox. J Adolesc Health 2001; 28: 26-9.

การสำรวจความชุกของภูมิคุ้มกันต่อโรคอีสุกอีใสและไวรัสตับอักเสบบีหลังพบรายงานโรคอีสุกอีใสในนักเรียนแพทย์และความสัมพันธ์ของการมีภูมิคุ้มกันต่อโรคอีสุกอีใสกับการให้ประวัติการเป็นอีสุกอีใสมาก่อน

เดชวิจิตร์ สุวรรณภักดี, ชลิดา เลาหพันธ์, วิศัลย์ มูลศาสตร์, ประสงค์ ล้อมทอง, ณัฐ ไกรโรจนานนท์, พฤษพงศ์ ศรีสวัสดิ์, วีระชัย วัฒนวีรเดช

วัตถุประสงค์: *ศึกษาความชุกของระดับภูมิคุ้มกันต่อไวรัสอีสุกอีใสและความสัมพันธ์กับประวัติการเป็นอีสุกอีใสในอดีตและให้วัคซีนตามความเหมาะสมในการป้องกันโรคอีสุกอีใส หัด หัดเยอรมัน คางทูม และไวรัสตับอักเสบีในนักเรียนแพทย์*

วัสดุและวิธีการ: *เป็นการศึกษาเชิงพรรณนาโดยประวัติการรับวัคซีนอีสุกอีใส หัด หัดเยอรมัน คางทูม และไวรัสตับอักเสบีของนักเรียนแพทย์ทุกราย จะถูกบันทึกในแบบสอบถาม นักเรียนแพทย์ทุกรายจะได้รับการตรวจภูมิคุ้มกันต่อไวรัสอีสุกอีใสโดยวิธี ELISA สำหรับโรคตับอักเสบีในรายที่จำประวัติวัคซีนไม่ได้หรือไม่มีการบันทึกการได้รับวัคซีนไวรัสตับอักเสบีในอดีตจะได้รับการตรวจ HBsAg และ anti-HBc โดยวิธี ELISA ก่อนพิจารณาให้คำแนะนำด้านวัคซีน*

ผลการศึกษา: *มีนักเรียนแพทย์เข้าร่วมการศึกษาทั้งสิ้น 383 ราย อายุเฉลี่ย 21.6 ปี (พิสัย 18-25.8 ปี) ร้อยละ 97.2 (372 คน) มีประวัติเคยได้รับวัคซีนหัด หัดเยอรมัน คางทูมมาก่อน กรณีของอีสุกอีใส นักเรียนแพทย์ 374 คนจาก 383 คน คิดเป็นร้อยละ 97.6 ได้รับการเจาะเลือดตรวจภูมิคุ้มกันชนิด IgG ต่อไวรัสอีสุกอีใสและพบว่าร้อยละ 92 มีภูมิคุ้มกันแล้ว เมื่อประเมินความสัมพันธ์ของการให้ประวัติการเป็นอีสุกอีใสในอดีต โดยใช้การมีภูมิคุ้มกันต่อไวรัสอีสุกอีใสเป็นมาตรฐานเปรียบเทียบพบว่ามีค่าพยากรณ์ผลบวก (PPV) ร้อยละ 99.3 กรณีของไวรัสตับอักเสบีนักเรียนแพทย์ 277 คน ได้รับการตรวจเลือด HBsAg และ anti-HBc พบว่า 243 คน คิดเป็นร้อยละ 87.7 ไม่มีภูมิคุ้มกันต่อไวรัสตับอักเสบีและพบความชุกของการเป็นพาหะต่อไวรัสตับอักเสบีเรื้อรังร้อยละ 0.01*

สรุป: *ระดับภูมิคุ้มกันที่ไม่เพียงพอในการป้องกันโรคที่ป้องกันได้ด้วยวัคซีนเกิดได้ในนักเรียนแพทย์ทั้งที่เกิดจากไวรัสอีสุกอีใสและไวรัสตับอักเสบี การศึกษานี้ทำให้เกิดคำแนะนำใหม่ในการเสริมสร้างภูมิคุ้มกันต่อไวรัสอีสุกอีใส หัด หัดเยอรมัน คางทูมและไวรัสตับอักเสบีสำหรับนักเรียนแพทย์ก่อนขึ้นปฏิบัติงานบนหอผู้ป่วย*