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
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 immunosorbert 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-HBeIgG 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-HBeIgG were performed at Phramongkutklao Hospital and both Cut-off values ≥ 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

<table>
<thead>
<tr>
<th>Experience of varicella disease by history</th>
<th>VZV serological immune status</th>
<th>Numbers of medical students</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>Yes</td>
<td>148</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>196</td>
</tr>
<tr>
<td></td>
<td>Total</td>
<td>344</td>
</tr>
<tr>
<td>No</td>
<td>Yes</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>29</td>
</tr>
<tr>
<td></td>
<td>Total</td>
<td>30</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>374</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Serology for hepatitis B virus</th>
<th>Numbers of medical students</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anti-HBcIgG positive/HBsAg positive</td>
<td>4 (1.4%)</td>
</tr>
<tr>
<td>Anti HBcIgG positive/HBsAg negative</td>
<td>30 (10.9%)</td>
</tr>
<tr>
<td>Anti HBcIgG negative /HBsAg negative</td>
<td>243 (87.7%)</td>
</tr>
</tbody>
</table>

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 forty-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.

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%\(^{49}\). 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- HBe. This person should receive the full course of hepatitis B vaccine unless either of his/her HBsAg or anti-HBeIgG 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.

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Potential conflicts of interest

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การสำรวจความชุกของภูมิคุ้มกันต่อโรคอีสุกอีใสและไวรัสตับอักเสบบีหลังพบรายงานโรคอีสุกอีใสในนักเรียนแพทย์และความสัมพันธ์ของการมีภูมิคุ้มกันต่อโรคอีสุกอีใสกับการให้ประวัติการเป็นอีสุกอีใสมาก่อน

เคธีรัตน์ ศรัทธาภิญโญศิริ, ชมิตา เล่าพันธ์, วิสิทธิ์ ยุทธศาสตร์, ประสิทธิ์ ติมพอง, ณัฐ ไกรโรจนานนท์, พฤทธิ์ศรี วัชรินทร์, วัฒนา วัฒนาภิริยกิจ

วัตถุประสงค์: ศึกษาความชุกของระดับภูมิคุ้มกันต่อไวรัสอีสุกอีใสและความสัมพันธ์กับประวัติการเป็นอีสุกอีใสในอดีต และให้วัคซีนตามความเหมาะสมในการป้องกันโรคอีสุกอีใส หวัง หัดเยอรมัน คางทูม และไวรัสตับอักเสบบีในนักเรียนแพทย์

วัสดุและวิธีการ: เป็นการศึกษาเชิงพรรณนาโดยประวัติการรับวัคซีนอีสุกอีใส หวัง หัดเยอรมัน คางทูม และไวรัสตับอักเสบบีของนักเรียนแพทย์ทุกราย จะถูกบันทึกในแบบสอบถาม นักเรียนแพทย์ทุกรายจะได้รับการตรวจภูมิคุ้มกันต่อไวรัสอีสุกอีใสโดยวิธี ELISA สำหรับโรคตับอักเสบบีรายที่จำประวัติวัคซีนไม่ได้หรือไม่มีการบันทึกการให้วัคซีนที่ไวรัสตับอักเสบบีในอดีตจะได้รับการตรวจ HBsAg และ anti-HBc โดยวิธี ELISA กรมพิจารณาให้คำแนะนำด้านวัคซีน

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

สรุป: ระดับภูมิคุ้มกันที่ไม่เพียงพอในการป้องกันไวรัสที่ป้องกันโดยวัคซีนที่เกิดในนักเรียนแพทย์ที่เกิดจากไวรัสอีสุกอีใสและไวรัสตับอักเสบบี การศึกษานี้ทำให้เกิดคำแนะนำใหม่ในการเสริมสร้างภูมิคุ้มกันต่อไวรัสอีสุกอีใสหวัง หัด เล่าพันธ์ คางทูมและไวรัสตับอักเสบบีสำหรับนักเรียนแพทย์ก่อนขึ้นปฏิบัติงานบนหอผู้ป่วย