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LPSP News Letter

Lebanese Inter-hospital Pneumococcal Surveillence Program

Contacts

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Cooperation with MOH

This work is being done in collaboration with the Ministry of Health (MOH) with encouragement from the WHO-EMRO. The MOH sent letters to all hospitals in Lebanon requesting that they report any pneumococcal isolates from invasive pneumococcal disease cases to our program to arrange for shipment and serotyping of these organisms.

Funded by

A generous grant from PneumoADIP to Dr. Ghassan Dbaibo, American University of Beirut

Update on pneumococcal serotypes from Lebanon

After the late war on Lebanon, there were problems encountered with transportation. Many of the bridges connecting the various regions in Lebanon were destroyed. As a team, there were difficulties getting samples from distant hospitals. However, Lebanon revived again, bridges were rebuilt, and those samples were obtained in addition to new samples. We were able to have an additional 50 samples sent for serotyping, making a total number of samples of 97. Out of these 97 samples, 52 were serotyped, 15 were either S. viridans or failed to grow on subculture, and 30 are awaiting shipment for serotyping within the next month. The adjacent table shows the contributions from different hospitals.

Hospital Contribution List

30*	AUBMC	Dr George Araj
11	HAYKAL HOSPITAL	Dr. Ibrahim Nemer
9	MAKASSED GENERAL HOSPITAL	Dr. Tamima Jisr
6	RHUH	Dr. Rita Feghali
5	SAHEL GENERAL HOSPITAL	Dr. Wassim Serhal
5	ST. JOSEPH-DAWRA	Dr. Raymond Rohban
3	CENTRE HOSPITALIER DE NORD	Dr. Salam Samad
3	HAMMOUD HOSPITAL	Dr. Mohamad Zaatari
3	NINI HOSPITAL	Dr. Monzer Hamzeh
3	SACRE- COEUR	Dr. Antoine Haddad
3	ST.GEORGE	Dr. Ziad Daoud
2	RIZK HOSPITAL	Dr. Jacques Mokhbat
2	ISLAMIC HOSPITAL	Dr. Malak Naboulsi
2	YUSSEF	Dr. Mohamad Abdallah
2	RASSOUL Al-AZAM	Dr. Hosni Yazbeck
2	MONLA HOSPITAL	Dr. Ricardo Sarraf
1	BAHMAN	Dr. Mohamad Haidar
1	HAYAT HOSPITAL	Dr. Hadi Al-Amine
1	HOSPITAL NOTRE DAME DE SECOURS	Dr. George Abdel Nour
1	RIYAK HOSPITAL	Dr. Talal Araji
1	NOTRE DAME DE LA PAIX	Dr. Joseph Freifer
1	TAL-CHIHA HOSPITAL	Dr. Naziha Makhlouf

Table 1

* 8 out of these samples had been frozen during the period April 2003 to July 2005.

Following is a graphical depiction of the data we have so far.

Demographics

- Out of the 97 samples collected so far, 22 were under 2 years of age.
- There were 17 patients between the ages of 2 to 5 years.
- There were 9 patients between the ages of 6 to 20 years.
- There were 13 patients in the age group of 21 to 60 years.
- 36 patients were above 60 years of age.
- Almost 64% of the number of samples collected belonged to male patients.

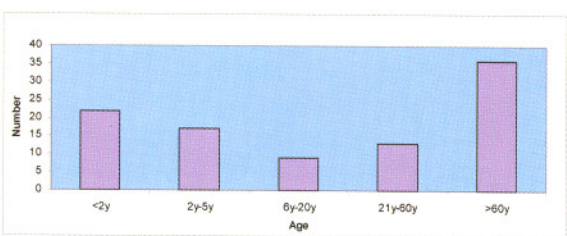

Figure 1. Distribution of invasive peumococcal disease (IPD) by age

Therefore, our data is similar to published data worldwide where the peak incidence of IPD is under the age of 2 years and above 60 years.

Demographics (Ctd)

- 72 out of the 97 samples were collected from blood, 12 from CSF, 7 from pleural fluid, 4 from abscess, 1 peritoneal fluid, and 1 from urine.
- This constitutes percentages of 74, 12, 7, 4 and 2 respectively.

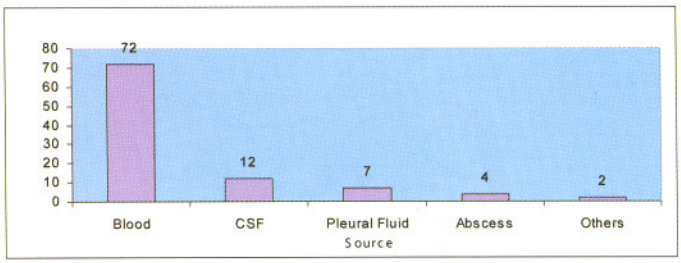

Figure 2. Sources of Isolates of IPD
* Others: Urine, peritoneal fluid

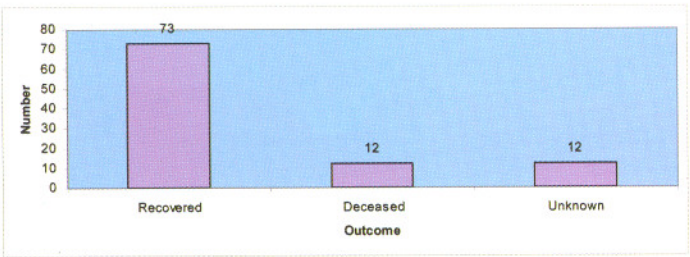

Figure 3. Outcomes of IPD

- Out of the 97 samples, 75% of the subject's conditions resolved after treatment. However, 12 % died.
- It is worth to note that the deceased ranged from neonates to older subjects. The rest of the patient's outcomes are unknown.

- The majority of patients had pneumonia making up a percentage of 51% out of the collected samples.
- Meningitis accounted for 14%.
- Sepsis accounted for 22% out of the samples collected.

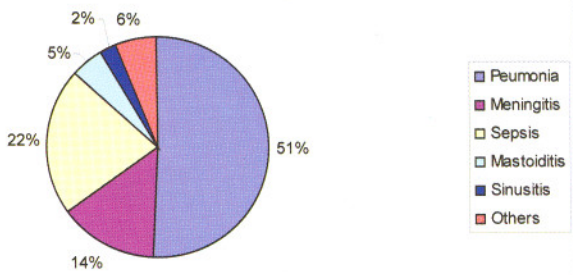

Figure 4. Clinical Syndromes Associated with *S.pneumoniae*

Serotypes

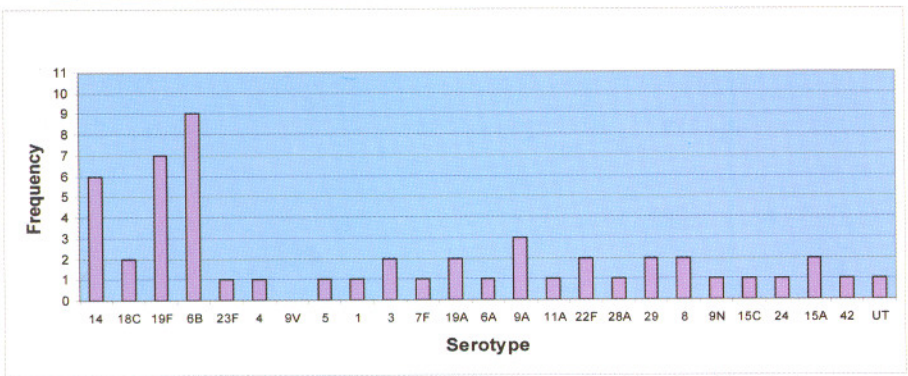

Figure 5. Serotype Distribution (serotypes covered by 7-valent vaccine, 11-valent, 13-valent in sequence)

- The most prevalent serotype was 6B which accounted for 9 out of the 52 serotyped samples.
- The second and third most common serotypes were19F and 14, being found in 7 and 6 samples respectively.

- It is worthwhile to note that serotypes that caused other diseases (corneal abscess, peritonitis), one was caused by serotype 8, and one by serotype 19F respectively.
- Pneumonia and meningitis cases were caused by many serotypes. Therefore, the commercial vaccine would have prevented infection with the three most common serotypes but a substantial number of cases caused by other serotypes would have still occurred.

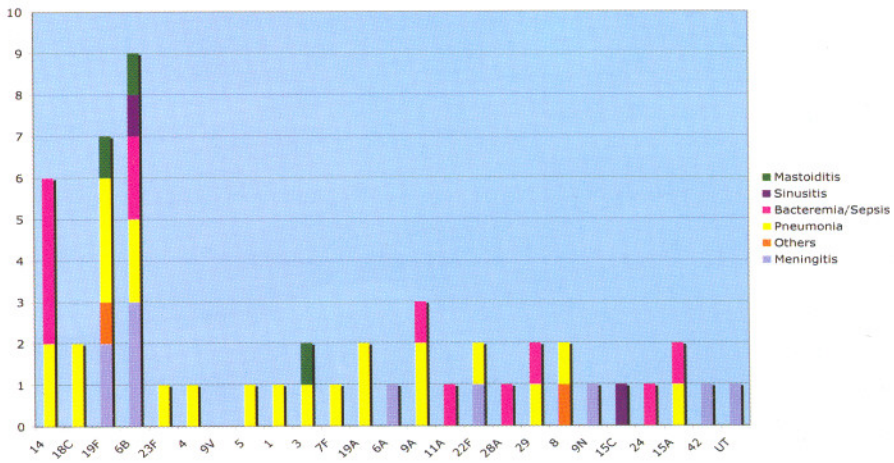

Figure 6. Serotype distributions by disease

Sensitivity and Resistance

- There was a 15% resistance to penicillin. Serotype 14 accounted for the majority of those. 35% were sensitive, and the other 50% showed intermediate sensitivity.
- 80% were sensitive to ceftriaxone.
- All strains were sensitive to vancomycin.
- 70% were sensitive to erythromycin.
- 55% were resistant to TMP/SMZ, 35% were sensitive, and other 10% showed intermediate sensitivity.
- As for tetracycline, 65% were sensitive, 27% were resistant, 7% were of intermediate sensitivity, and 1% were unknown.
- 90% of our samples were sensitive to chloramphenicol.

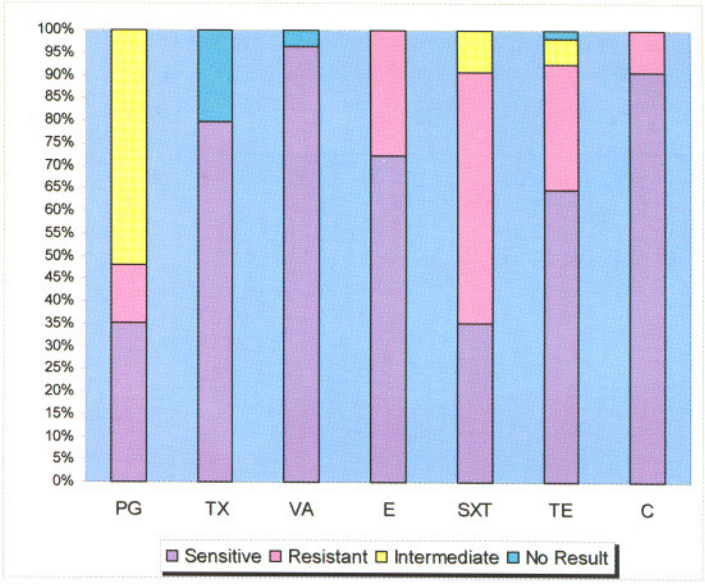

Figure 7. Sensitivity and Resistance

Vaccine coverage

- Commercially available heptavalent vaccine covers for the following serotypes: 4, 9V, 14, 19F, 23F, 18C, and 6B.
- 26 out of the 52 serotyped cases were caused by the serotypes found in the heptavalent vaccine. Therefore, the commercially available vaccine would have potentially prevented 50% of the infections in all age groups, and 57% in patients less than or equal to 2 years of age.
- The 11-valent vaccine under development covers an additional four serotypes: 1, 5, 3, 7F. This would have prevented 60% of infections in all age groups.
- A 13-valent vaccine is now in clinical trials and has been demonstrated to be highly immunogenic. It covers an additional 2 strains: 6A, 19A. In our data, that would have prevented 65% of infections in all age groups.

Conclusion

This pilot data underscores the importance of collecting national data and determining the predominance of specific serotypes and, by extension, the suitability of marketed vaccines. We seem to be positioned in the middle of two extremes when it comes to vaccine coverage. In some Asian countries the heptavalent vaccine coverage was reported to be around 40% whereas in the USA, it was reported to be 85-88%. Our numbers remain small for making firm conclusions but we hope to keep this program ongoing so that a sufficient sample size will be obtained. Importantly, the expanding use of the vaccine in Lebanon is expected to alter the serotype predominance with time. This will be something to watch for in the future.

Changing Epidemiology of Invasive Pneumococcal Disease Among Older Adults in the Era of Pediatric Pneumococcal Conjugate Vaccine

In 2000, a conjugate vaccine targeting 7 pneumococcal serotypes was licensed for young children. The purpose of the study is to determine the incidence of invasive pneumococcal disease, disease characteristics and the spectrum of patients acquiring these illnesses in adults aged 50 years or older. Results showed that in this category of subjects, incidence of disease caused by the 7 conjugate vaccine serotypes declined 55%, did not change for the serotypes present only in the polysaccharide vaccine, whereas for the serotypes not present in either vaccines, it increased somewhat. The use of the 7 valent vaccine in children has substantially benefited older adults. (Catherine A. Lexau, Ruth Lynfield et al. JAMA 2005;294:2043-2051)

Save Lives with Pneumococcal Vaccine !!!

GAVI (Global Alliance for Vaccines and Immunization) is a public-private partnership focused on increasing children's access to vaccines in poor countries. Partners include the GAVI Fund, national governments, UNICEF, WHO, The World Bank, the Bill & Melinda Gates Foundation, the vaccine industry, public health institutions and nongovernmental organizations (NGOs).

In late March, GAVI sent letters to all 72 GAVI eligible countries (the 72 poorest countries in the world) asking if they would be interested in introducing pneumococcal conjugate vaccine, beginning with the 7-valent vaccine, between 2008 and 2010. The vaccine will be provided at a very low cost, around 30-50 cents per dose.

By the end of May, 30 of the 72 GAVI eligible countries expressed interest, a non-binding commitment in introducing the vaccines by 2010. Responses came mainly from countries where >33% of all the childhood pneumococcal deaths occurs worldwide.

Millions of lives could be saved through earlier and faster access to pneumococcal vaccines.
WHO, UNICEF and others will play critical roles in supporting countries to make the vaccine available. (June 18th, 2007 Pneumo Alert)

Q&A1

Do children who are diagnosed with invasive pneumococcal disease still need to receive pneumococcal conjugate vaccine?

Yes. There are several different serotypes of *Streptococcus pneumoniae* that cause disease in children. A child who has had pneumococcal disease has only developed antibody against one serotype.

New Advances in Pneumococcal Vaccination

A retrospective study published in October 2006 showed that people over 60 years of age vaccinated by the Pneumococcal vaccine (Pneumovax PV) have reduced risk of both pneumonia and influenza-related diseases. Moreover, Pneumococcal vaccine reduced the morbidity of influenza-related diseases more than the influenza vaccine itself. This could have a major impact by reducing the economic burden on medical care providers. (A. Blay, H. Bessler, A.Lahad, et al. *Vaccine*, 25(2007) 1071-1075).

Two types of vaccines are currently available in the market: Pneumovax, the 23 valent polysaccharide vaccine, and Prevenar, the 7-valent conjugate vaccine. Both of these vaccines have their limitations; they cover only a certain number of strains. To overcome this problem, new ideas for vaccination are currently under investigation:

Q&A2

A 2-month-old was mistakenly given PPV instead of PCV. What should be done?

PPV is not effective in children less than 24 months of age. PPV given at this age should not be considered to be part of the pneumococcal vaccination series. PCV should be administered as soon as the error is discovered

Q&A3

When should a child undergoing splenectomy receive pneumococcal vaccine(s)?

It is preferable that the child have antibody to pneumococcus at the time of the procedure, so administer the appropriate vaccine prior to splenectomy if possible:

- Children 2-59 months of age should receive one or more doses of PCV if not up to date already for this vaccination.
- Children >2 years of age should receive PPV regardless of whether they also received PCV.
- Children >5 years will generally receive only PPV.

Doses of PCV and PPV given at age 2-5 years should be separated by an interval of at least 8 weeks

- In May 2007, a study was published emphasizing the efficacy of a single intranasal dose of a live-attenuated *S. pneumoniae* vaccine in generating both mucosal and systemic protection in mice. (Aoife M. Roche, Samantha J. King, and Jeffrey N. Weiser. *Infection and Immunity*, May 2007, p.2469-2475)

- The discovery of immunogenic surface antigens, common to all strains represents the basis of a pan-genomic vaccine which will confer protection against pneumococcus independently of the serotype. (Michele Anne Barocchi, Stefano Censini, Rino Rappuoli. *Vaccine*,25 (2007) 2963-2973)

- Studies were made on mice by administering heat inactivated *S. pneumoniae* type 4 with or without cholera toxin at various mucosal sites. It was found that intranasal immunization was superior to either oral, gastric or colonic antigen delivery with regard to induction of serum Ig G, Ig A as well as saliva Ig A antibodies specific for *S. pneumoniae*. This suggests a cellular link between nasal induction site and distal mucosal effective sites. Thus, an efficient intranasal vaccine can protect us against both systemic infections and death. (Benedicte K. R. Hvalbye, Ingeborg S. Aaberge, et al. *Infection and Immunity*, Sept. 1999, 4320-4325)

WHO

We were approached by the WHO during the month of June 2007 to provide them with our data. They were precisely interested in data from children younger han 5 years of age. We have provided this data and also submitted an application for funding for the next two years.It is currently being reviewed.

Acknowledgment:

Last but not least, we would to like to extend our gratitude to all those who contributed samples and helped in making this work possible.