LIPSP News Letter
Lebanese Inter-hospital Pneumococcal Surveillance Program

Funded by

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Contents

Hard Times

The recent Israeli war on Lebanon was brutal. Many people died, many lost their loved ones, their homes, business, and other property. Many hospitals and medical centers suffered shortage of proper medication, fuel, and human resources. The dreams of many were shattered.

We offer our condolences to those of you who suffered losses during the war.

As many have noticed, we did not have contact with the different hospitals and medical centers over Lebanon during the war because we felt that the program would not be a priority during these hard times. However, with the cessation of war, we hope to resume our function normally and to make up for lost time.

Our First Baby Streps!

In December 2004, the World Health Organization-Eastern Mediterranean Regional Office (WHO-EMRO) held a meeting in Cairo where the status of pneumococcal disease and prevention in countries of the Middle East and North Africa (MENA) region was discussed. It was obvious at the meeting that there was a severe lack of data from our region. As a recommendation of that meeting, MENA countries were asked to set up surveillance systems for invasive pneumococcal disease in order to determine the burden of disease caused by *Streptococcus pneumoniae* and the prevalent serotypes responsible for the majority of the cases. This information would be of great help for the WHO and for individual countries to make recommendations about current and future pneumococcal vaccines.

In Lebanon, no published data could be found about serotypes of *Streptococcus pneumoniae* causing invasive or even non-invasive disease. The currently available conjugated vaccine was introduced to the Lebanese market without any information about the usefulness of this vaccine in Lebanon and the coverage it provides. In February 2005, a proposal was submitted to pneumoADIP, a non-governmental organization that is part of the Global Alliance for Vaccines and Immunizations (GAVI), to set up a pilot surveillance program for *Streptococcus pneumoniae* in Lebanon with a principal aim to determine the prevalent serotypes causing invasive disease. This proposal was funded in June 2005 and the pilot network of seven hospitals was initiated in October 2005.

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Table 1: Serotypes and antibiotic sensitivity of the initial batch of isolates of S. pneumoniae collected by our program (New) or stored at the AUBMC medical microbiology laboratory by Dr. George Araj (Frozen).

	Date	Age	Source	SEROTYPE	C	TE	SXT	VA	E	PG	PG MIC	TX	TX MIC
Frozen	6-Apr-03	2	Blood	14	S	S	R	S	S	R	3	I	1.5
	16-Apr-04	70	Blood	19A	R	I	R	S	S	S	0.064	S	0.064
	14-Dec-04	10m	Blood	24	S	S	S	S	S	S	0.047	S	0.047
	29-Mar-05	2	Blood	15C	S	I	I	S	S	I	0.5	S	0.38
	7-Apr-05	68	Blood	1	S	S	R	S	S	S	0.032	S	0.032
	21-Apr-05	84	Blood	9A	R	S	R	S	S	R	4	I	2
	3-Jul-05	69	Blood	6B	S	R	I	S	R	I	0.125	S	0.125
	15-Jul-05	2	Blood	14	S	R	R	S	R	R	6	R	3
New	10-Oct-05	73	Blood	11A	S	S	R	S	S	R	6	I	1.5
	18-Oct-05	83	Blood	3	S	S	S	S	S	S	0.047	S	0.032
	21-Nov-05	8	Blood	22F	R	S	S	S	S	S	0.047	S	0.064
	6-Dec-05	2	CSF	18C	S	S	R	S	S	S	0.047	S	0.047
	10-Dec-05	74	Blood	3	S	I	S	S	S	S	0.023	S	0.012
	10-Dec-05	66	Blood	Viridans Streptococcus									
	14-Dec-05	3	Blood	14	S	R	R	S	R	R	6	I	2
	21-Dec-05	2	Blood	14	S	S	R	S	S	I	1.5	S	1
	15-Feb-06	86	Blood	Viridans Streptococcus									

C:Chloramphenicol TE:Tetracycline SXT:TMP/SMZ VA:Vancomycin E:Erythromycin PG:Penicillin TX:Ceftriaxone

Table 2: The following table shows the samples collected between January 1st and June 30th, 2006.

Date	Age	Hospital	Source	Diagnosis
8-Mar-06	86	St. Joseph	Blood	Acute Bronchitis
30-Mar-06	4	AUBMC	Pleural Fluid	Pneumonia, Pleural Effusion
5-May-06	2	Centre Hosp. Du Nord	Blood	Pneumonia
9-May-06	9d	RHUH	CSF	Meningitis
18-May-06	94	Centre Hosp. Du Nord	Blood	Pneumonia
24-May-06	4	Haykal Hospital	Blood	Sinusitis
27-May-06	3	Haykal Hospital	Urine	UTI
30-May-06	4	Makassed Hospital	Blood	Pneumonia
2-Jun-06	1'6"	Notre Dame de la Paix	Pleural Fluid	Pneumonia, Empyema
3-Jun-06	1' 6"	Haykal Hospital	Blood	Pneumonia
7-Jun-06	5	Haykal Hospital	Blood	Pneumonia
13-Jun-06	63	AlRassoul AlAzam	Blood	Cervical adenitis
17-Jun-06	37	Rizk Hospital	Pleural Fluid	Pneumonia, Pleural Effusion
18-Jun-06	1	El-Yussef	CSF	Meningitis
23-Jun-06	23	Haykal Hospital	CSF	Meningitis
28-Jun-06	2m	Sahel Hospital	CSF	Meningitis

*The shaded cells were not stored because of failure to grow on subculture or wrong identification at home center

First LIPSP Meeting at Movenpick Hotel

We took the opportunity of the annual meeting of the National Collaborative Perinatal Neonatal Network (NCPNN) organized by Dr. Khalid Yunis, who is the program manager of LIPSP, to organize the first national meeting of the Lebanese Pneumococcal Surveillance Program on May 12th 2006 at the Movenpick Hotel, Beirut. *(continue on page 2)*

Our First Baby Streps!

Early Results from LIPSP

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Isolates of Streptococcus pneumoniae from invasive sites (pleural fluid, blood, CSF, etc…) were collected from different hospitals and medical centers in different geographic regions of Lebanon. The number of samples was disappointingly small. These samples were cultured, isolated, studied in terms of antibiotic sensitivity and their serotypes were identified in collaboration with Dr. Guillermo Pimentel at Naval Medical Research Unit No. 3 (NAMRU3) in Cairo.

An additional group of isolates from invasive disease were kindly provided by Dr. George Araj at AUBMC who had stored them over the past three years. Table 1 shows the results of serotyping and antibiotic sensitivity for these isolates. Of course, the small sample number does not allow us to draw any conclusions at this point and a much larger sample will be needed. Table 2 summarizes the data of new samples collected by our program between January and June of this year showing an accelerated contribution by new member hospitals that have joined the program. These samples will be serotyped in the coming months once we have a sufficient number to justify the shipping costs.

An early reading of our results shows that there is a propensity of invasive streptococcus disease in children (<4 years) and elderly (> 60 years) as in other countries (Figure 1). When the serotypes are examined we find that, similar to other developing countries as well as developed countries, serotype 14 appears to be very common. However, no other serotype appears to be dominant (Figure 2). But caution should stop us from further conclusions until we collect more samples.

The graphs below represent the distribution of *S. Pneumoniae* collected by Age and Serotype:

Fig: 1

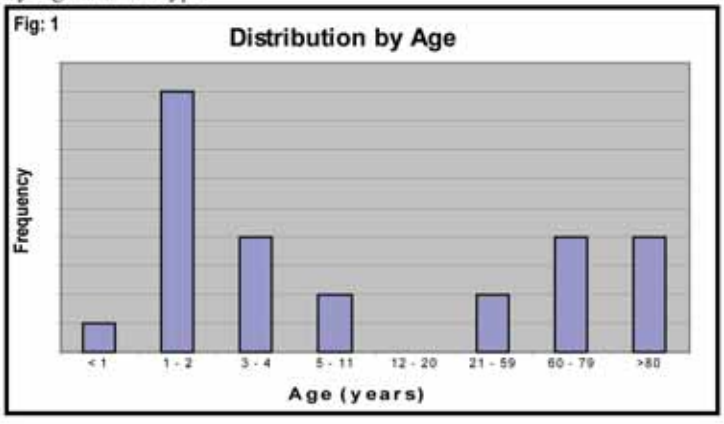
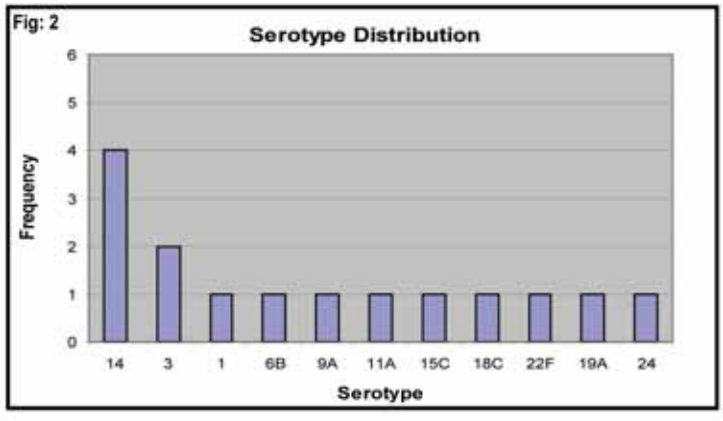


Fig: 2



First LIPSP Meeting in Movenpick Hotel

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We invited Pediatricians, Microbiologists, and Infectious Disease Specialists from various districts of Lebanon to attend the meeting. More than 40 participants were able to attend and a significant number of those who could not attend expressed interest in joining the network. During the meeting, Dr. Ghassan Dbaibo gave a presentation explaining the aims of the Lebanese Pneumococcal Surveillance Program, the rationale behind it, and the strategy for data collection as well as an update about the program's accomplishments. He invited those in attendance and their hospitals to be active collaborators in this project. Following the presentation, a discussion ensued and several ideas were shared and comments and suggestions were made to enhance the program. The name of the program was changed to the Lebanese Inter-hospital Pneumococcal Surveillance Program (LIPSP) based on a suggestion and approval of the participants. At the end of the meeting, a package was distributed to the audience and subsequently mailed to those unable to attend. This package included a summary of the project's protocol, a sample of the case report form, and a contact list of the program personnel. At the same time, contact information was gathered from the audience to enhance feedback and ensure weekly contact with them.

Special Thank You

We would like to thank all of you who have contributed to our study and those who kept us in the back of their minds during their daily patient care. A special Thanks for submitting samples to: Dr. Ibrahim Nemer, Dr. Raymond Rohban, Dr. Joseph Freifer, Dr. Ricardo Sarraf, Dr. Mohammad Zaatari, Dr. Jaques Mokhbat, Dr. Hassan Mallat, Dr. Ghaith Makhoul, Dr. Tamima El-Jisr, Dr. Mariam Rajab, Dr. Wissam Serhal, Dr. Salam Samad, Dr. Housni Yazbek, and Dr. Mohammad Abdallah.

A big THANK YOU to Dr. Georges Araj and Mr. Hasan Beyh for technical help, and to Dr. Dolla Sarkis and Dr. Raymond Mikhael for organizational help and support.

Rapid Review

Pneumococcal infections, including meningitis, pneumonia, and otitis media are major causes of childhood morbidity and mortality worldwide. In the United States alone, it is estimated that pneumococci account for 3000 cases of meningitis, 50,000 cases of bacteremia, 500,000 cases of pneumonia, and 7 million cases of otitis media. Globally, approximately 1.2 million deaths due to pneumococcal pneumonia and meningitis are believed to occur among young children every year; mostly in developing countries.

There is lack of epidemiological data documenting the pneumococcal disease burden in all populations. However, the available data shows that underprivileged children, especially those in developing countries, bear the highest morbidity and mortality from pneumococcal disease.

Streptococcus pneumoniae has 90 capsular polysaccharide serotypes. Their distribution varies with age, disease manifestation, and geography.

Data from different studies have suggested that different serotypes of *Streptococcus pneumoniae* favor particular clinical syndromes, age-groups, or geographic regions. For example:

- Serotypes 7V, 9V and 11V cause relatively more pneumonia than meningitis.
- Vaccine serotypes account for a higher proportion of invasive disease isolates from young children than of isolates from older children and adults.

Vaccines

The pneumococcal polysaccharide vaccine (PS) was the first vaccine to be introduced. It is safe but poorly immunogenic especially in children under 2 years of age.

Infants' poor immunological response to the pneumococcal PS vaccine led to the development of pneumococcal conjugate vaccines (PCVs). These conjugate vaccines are made from the coupling of purified capsular PS with a protein carrier, thus increasing the immunogenicity of the polysaccharide vaccine, and creating a T-cell-dependent immune response.

There are now two vaccines on the market, the previously mentioned 23-valent polysaccharide vaccine (Pneumovax) and the 7-valent vaccine (Prevenar).

The 7-valent and the 9-valent PCVs employ the diphtheria CRM197 protein carrier, while the 11-valent PCV employs the diphtheria and tetanus PncD/T11 carrier protein. The 7-valent PCV (Prevenar) contains serotypes: 4, 6B, 9V, 14, 18C, 19F, and 23F. In addition to the serotypes included in the 7-valent vaccine, the 9-valent PCV includes serotypes 1 and 5, and the 11-valent PCV adds serotypes 3 and 7F. The 9-valent and the 11-valent PCVs - currently in development - are likely to be more appropriate for developing countries because of their wider serotype coverage.

Impact

The Active Bacterial Core surveillance (ABCs) data in the United States indicate that the rate of invasive pneumococcal disease in the non-vaccinated decreased considerably in the 5 years after the introduction of 7-valent PCV in the year 2000. This indicated a considerable herd-immunity effect for this vaccine.

Data from the Center of Disease Control (CDC) concluded that over the first 5 years of use, the vaccine has cost $7500 per life-year saved which was shown to be relatively cost-effective in terms of cost per quality-adjusted life-year saved.

Preliminary evidence indicates that pneumococcal conjugate vaccine formulation will need to be customized for use in developing countries because 40-60% of serotypes that cause invasive disease are not covered by the currently available vaccine.

Surprise…

Streptococcus pneumoniae is showing early signs of escape from the current vaccine. By way of natural selection, there is evidence now of an increase in pneumococcal disease caused by non-vaccine serotypes through "serotype replacement" although the frequency of these "replacement serotypes" remains very low. If serotype replacement increases over time, it is possible that the efficacy of the vaccine could decline in the future.

Reference Articles

1. Which Pneumococcal Serogroups Cause the Most Invasive Disease: Implications for Conjugate Vaccine Formulation and Use, Part I, William P. Hausdorff, John Bryant, Peter R. Paradiso, and George R. Siber, *Clinical Infectious Diseases* 2000;30:100-121

2. The Contribution of Specific Pneumococcal Serogroups to Different Disease Manifestations: Implications for Conjugate Vaccine Formulation and Use, Part II, William P. Hausdorff, John Bryant, Carolyn Kloek, Peter R. Paradiso, and George R. Siber, *Clinical Infectious Diseases* 2000;30:122-140.

3. Recent Advances In Pneumococcal Vaccination of children, Fiona M. Russel & E. K. Mulholland, *Annals of Tropical Paediatrics* (2004) 24,283-294.

LIPSP Members

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Dedication

We dedicate this first issue to Dr. Charbel Salem and Dr. Mohamad Sayyad who were instrumental in setting up the surveillance program.

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How Can You Contribute?

- Recruit hospitals or colleagues to join the program, especially from less represented areas.

- Share with members of LIPSP any ideas, relevant new data, or publications to include in this newsletter.

- Contact us as soon as you have an isolate from an otherwise sterile site (Blood, CSF, Pleural Fluid, Middle Ear Fluid by Tympanostomy, etc…)