Prevention of Community-acquired Pneumonia in the Adult Population: Better Immunization Strategies are Needed

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Conflict of interest disclosure statement

- Honoraria: Wyeth, Sanofi-Aventis, Abbott, Bayer and Pfizer
- Advisory boards: Oryx Pharmaceuticals, Bayer, Iroko, Abbott and Wyeth
- Sponsored trials: Genzyme, Wyeth, Merck, Optimer, BioCryst, Trius, Cempra and Arpida

Centre Hospitalier Universitaire de Sherbrooke

- 686-bed, academic, tertiary care center
- Two distinct sites
- 62 ICU beds
- One centralized microbiology lab.
- 32 000 admissions/year

- **Sherbrooke retrospective study on CAP**
  a) 1997-2008
  b) Adults (≥ 18 years) with a PAC primary Dx + compatible CXR (<48 hrs).
  c) N=3667

PNEUMONIA CASE STUDY

Pneumonia case study

- A 42 year old man presents to ER with a temperature of 39° C and a productive cough.
- Past Medical History:
  - Ruptured appendicitis 5 years ago.
- Lifestyle
  - Avg: one beer/day
  - Smoker: 1 pack/day for 20 years

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Pneumonia case study

- Lung examination reveals left lower lobe crackles, with decreased breath sounds.
- SaO_2=89%, pls=120/min, RR = 24/min, BP=N.
- GB= 18 000/mm^3
- RXP = LLL infiltrate.

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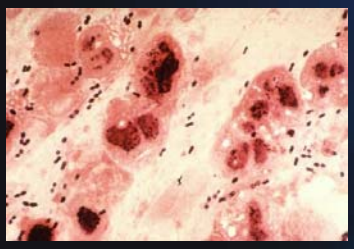
Pneumonia case study

- Sputum cultures are positive for an abundant growth of pneumococcus.
- A treatment of ceftriaxone + azithromycin is started. He improves rapidly, and is discharged on amoxicillin for 7 days. After one week of rest, he resumes his normal activities.



EPIDEMIOLOGY AND IMPACT OF COMMUNITY-ACQUIRED PNEUMONIA

Impact of CAP

- United States
  - 500 000 hospital admissions/year
- Canada
  - 1 million medical consultations/year
  - 60 000 hospital admissions/year

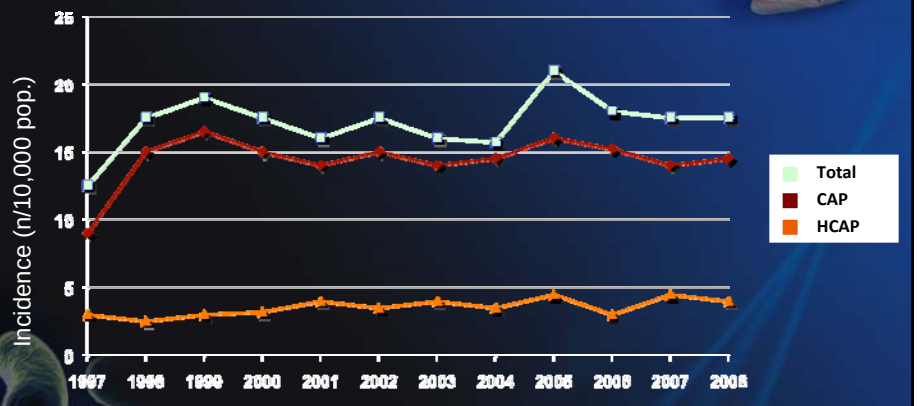
Fok et al. Can Respir J. 2002
Institut canadien d'information sur la santé
Association pulmonaire du Canada, 2001

Impact of CAP in Quebec 1990-2007

	20-39	40-59	60-79	≥80	Total
Cases (#)	17 380	33543	93878	66863	211664
Rate/100 000 pers.-year	44.0	90.4	493.0	1812.7	213.1
Length of hospital stay(days)	6.8	8.5	11.3	14.8	11.6
ICU (%)	6.3	9.9	9.7	6.7	8.5
Case-fatality rate (%)	1.6	3.6	8.9	18.3	10.4

De Wals et al. ICAAC 2010.

CAP Incidence in adults, Sherbrooke



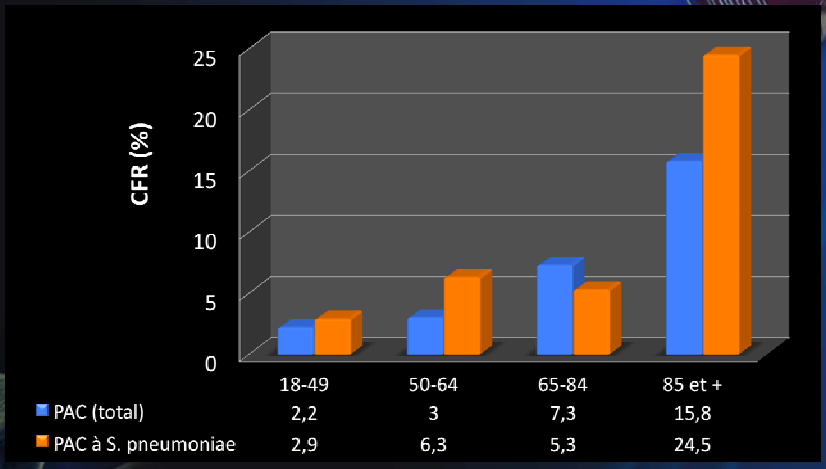
Grenier et al. ICAAC/IDSA Joint Meeting 2008

Economic impact

- Costs
  - U.S. : $9,7 billion/year (90% associated with hospital admissions)
- Median length of stay in Canada: 7 days (4-11)
- Average cost per hospital admission: US$25 218
- 10-20% of admitted patients will be admitted to an ICU

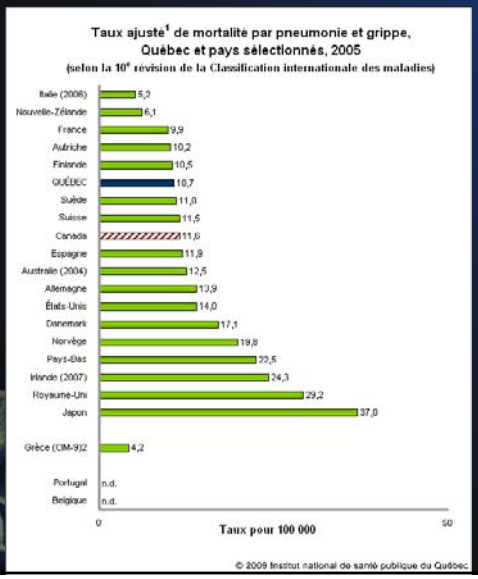
Feagan et al. CMAJ. 2000.
Kollef et al. Chest. 2005.
File et al. Postgrad Med. 2010
Marrie et al. Medicine. 2007

CAP Case-fatality rate (CFR)-Sherbrooke



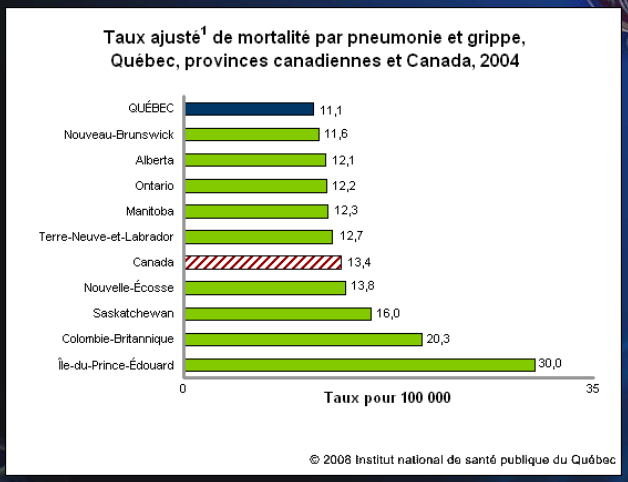
Valiquette et al. Unpublished data

CFR – CAP and Flu



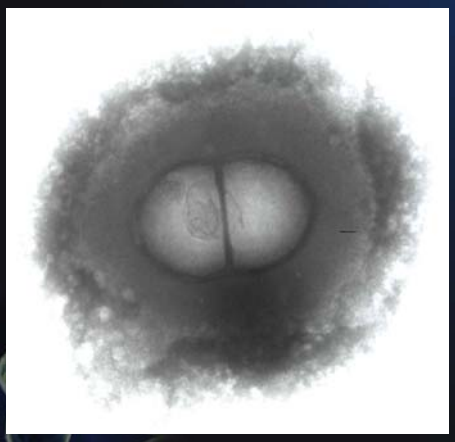
#6 cause of mortality in Canada

CFR – CAP and Flu



CAP – MICROBIOLOGY

Streptococcus pneumoniae



Bar = 100 nm

- Diplococcus
- Capsule
  - Protection
  - 90 serotypes
  - Target for vaccines

CAP microbiology

Bacteria most frequently associated with CAP are:

1) *Streptococcus pneumoniae* (15-80%);
2) *Haemophilus influenzae* (1-40%)
3) *Staphylococcus aureus* (3-14%)

Bacteria associated with CAP, Sherbrooke	CAP (n=1217)
H. influenzae	298 (25)
H. parainfluenzae	167 (14)
M. catarrhalis	45 (4)
Enterobacteriaceae	50 (4)
P. aeruginosa	41 (3)

Torres et al. In: Respiratory Infections, 2007.
Valiquette et al. Unpublished data.

Treatment

- Initial antibiotic therapy is always empirical: no rapid test to identify pathogens.
- Modified according to several factors:
  - Exposure
  - Resistance
  - Underlying diseases, risk factors
- Patient must improve within 72 hours.

Mandell et al. Clin Infec Dis, 2007.

Treatment recommendations

- Inpatients, non-ICU
  - Respiratory fluoroquinolones (Strong recommendation, Level 1)

  OR
  - β-lactam + macrolide (Strong recommendation, Level 1)

Mandell et al. Clin Infec Dis, 2007.

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CAP prevention in adults

- 23-valent polysaccharide pneumococcal vaccine (PPV-23) is recommended in adults $\geq$ 65.
- Useful to prevent bacteremic CAP, not CAP at large.

Canadian Immunization Guide, 7th Edition, 2006

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INTRODUCTION TO VACCINOLOGY

Definitions

- Immunity: the ability of an organism to resist disease
- Antigen (Ag) : a substance that when introduced into the body stimulates the production of antibodies (Ab).
- Immunological memory: the repeated encounter with an antigen leads to a stronger immune response.
- Vaccine : a substance given to stimulate the body's production of antibodies and provide immunity vs. a disease, prepared from the agent that causes the diseases, or a synthetic substitute.

Canadian Immunization Guide, 7th Edition, 2006

Different types of vaccines

- Live attenuated vaccine : MMR
- Whole inactivated vaccine : Hepatitis A
- Protein purified inactivated vaccine : Influenza
- Conjugated inactivated vaccine : Pneumococcus (13-valent, 10-valent+Hflu, and 7-valent)
- Polysaccharide inactivated vaccine : PPV-23

Canadian Immunization Guide, 7th Edition, 2006

Polysaccharide vaccines

- Production and purification of polysaccharide antigens from pathogens' capsule.
- Direct stimulation of B lymphocytes leading to AB production **without immunological memory.**
- Since no T cells are activated, poorly immunogenic in children < 2 y.o.

Canadian Immunization Guide, 7th Edition, 2006

Conjugated vaccines

- Polysaccharides are fixed to a protein.
- Induces a T-cell dependent immune response.
- Antibodies have more affinity and are more active.

Canadian Immunization Guide, 7th Edition, 2006

Immunization schedule

Table 4: Routine Immunization Schedule for Adults (≥ 18 Years of Age) Not Immunized in Childhood

Timing	Tdap	Td	MMR	Var	Men-C	Pneu-C-23	HPV	Inf
First visit	▲		■	●	(◉)	(◘)	✲	(✲)
2 months later		◧	(■)	●			✲ (Females, 14-26 years)	
6-12 months later		◧					✲	
10 years later		◧						

Canadian Immunization Guide, 7th Edition, 2006

IMPACT OF IMMUNIZATION PROGRAMS

Impact in Canada

Table 2. Incidence of Select Vaccine-Preventable Diseases in Canada – Pre-vaccine Era Compared with Five Most Recent Years

		Pre-vaccine era*		2000-2004**	
Disease	Details	5-year average annual incidence per 100,000	Peak annual number of cases	5-year average annual incidence per 100,000	Peak annual number of cases
Diphtheria	Diphtheria toxoid introduced in 1926, routine infant immunization since 1930, national notifiable diseases reporting began in 1924	1925-29 84.2	1925-29 9,010	0.0	1
Invasive *Haemophilus influenzae* type b (Hib) in children < 5 years of age	PRP vaccine introduced in 1986, currently approved Hib PRP-T and PRP-OMP conjugate vaccines introduced in 1991/92, national notifiable diseases reporting of invasive Hib disease began in 1986	1986-90 22.7	1986-90 526	0.9	17
Measles	Live vaccine approved in 1963, MMR universal infant program implemented in 1983, 2 dose MMR introduced 1996/97, no notifiable diseases reporting from 1959-68	1950-54 369.1	1950-54 61,370	0.2	199
Mumps	Vaccine approved in 1969, MMR universal infant program implemented in 1983, 2 dose MMR introduced 1996/97, no notifiable diseases reporting from 1960-85	1950-54 248.9	1950-54 43,671	0.3	202
Pertussis	Whole cell pertussis vaccine approved in 1943, acellular pertussis vaccine replaced whole cell in 1997-98, adolescent/adult acellular formulation approved in 1999	1938-42 156.0	1938-42 19,878	10.4	4,751
Paralytic poliomyelitis	IPV approved in 1955, OPV approved in 1962 and in use in Canada until 1997, IPV used exclusively from 1998-present	1950-54 17.3	1950-54 1,584	0	0

Canadian Immunization Guide, 7th Edition, 2006

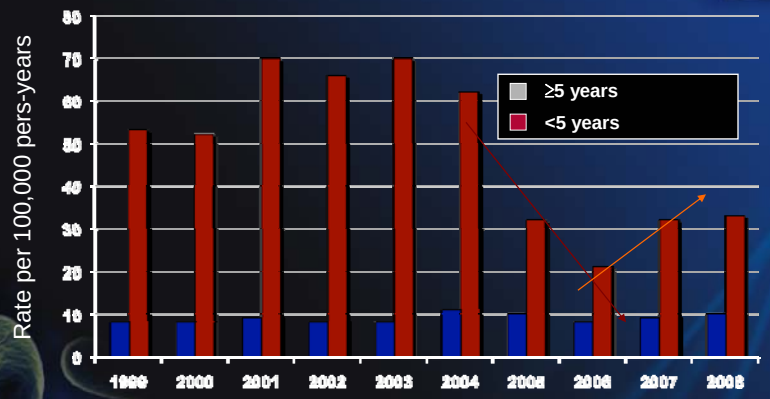
ANTI-PNEUMOCOCCAL IMMUNIZATION

Anti-pneumococcal vaccines licensed in Canada

Vaccines	Included serotypes	Protein	Year
PCV-7 (Prevnar®)	4, 6B, 9V, 14, 18C, 19F, 23F	CRM 197	2001
PHiD-CV (Synflorix®)	1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F, 23F	Protein D	2009
PCV-13 (Prevnar13®)	1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, 23F	CRM 197	2010
PPV-23 (Pneumovax® Pneumo 23®)	1, 2, 3, 4, 5, 6B, 7F, 8, 9N, 9V, 10A, 11A, 12F, 14, 15B, 17F, 18C, 19A, 19F, 20, 22F, 23F, 33F	N/A	1998

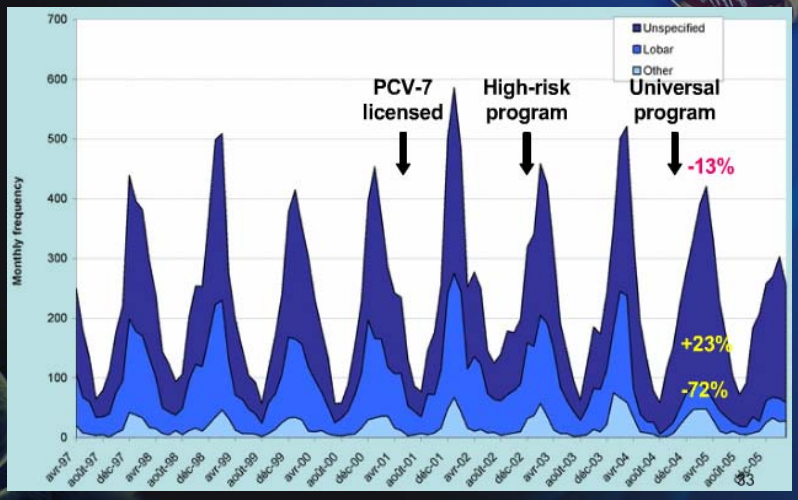
* Indicated in children, only.

Impact of PCV7 immunization program– IPD



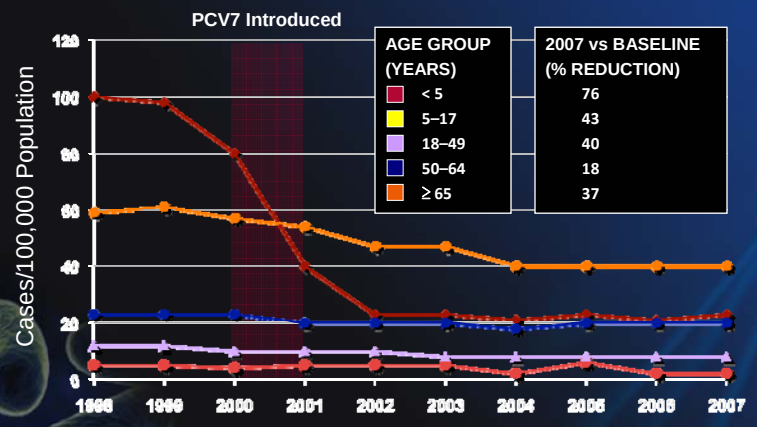
Quebec Ministry of Health, Registry of Notifiable Diseases

Impact of PCV7 immunization program – CAP



DeWals et al. *Pediatr Infect Dis J. 2008*

Indirect effect of PCV7 programs in adults on IPD



Pilishvili T, et al. *J Infect Dis*. 2010

Anti-pneumococcal immunization in adults

- Coverage rates are sub-optimal in adults, Quebec data

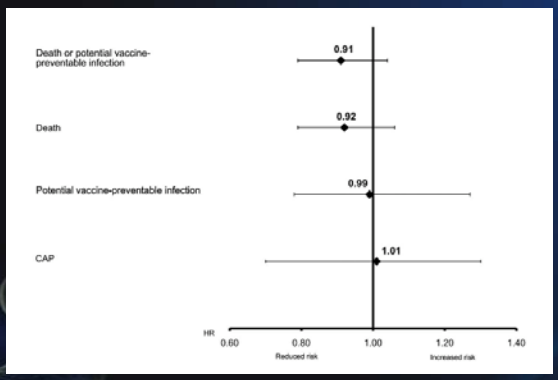
Vaccination vs. influenza and pneumococcus 2007-2008, Québec	
Vaccines and special groups	***Coverage rate***
Influenza (≥ 60 years)	60%
Influenza (50-59 years + chronic disease)	44%
Pneumococcus (≥ 65 years)	

- No significant decrease in IPD and CAP rates (direct or indirect effect).

Institut National de Santé du Québec, 2010

PPV23 impact is very limited on CAP

- Recent study in Alberta.
- 2950 patients hospitalized for a CAP between 2000-2002.
- Follow-up for 5 years : CAP and CFR.



Johnstone J, et al. *Clin Infec Dis*. 2010

Conclusion

- Pneumonia is the most frequent infection in Canada and is associated with a significant CFR.
- Pneumococcus is the most frequent bacteria associated with CAP in all age groups.

Conclusion

- Prevention is an essential strategy in infectious disease management.
- Immunization is one of the most efficient components of prevention programs.
  - Against CAP and IPD in children
  - Limited efficacy of PPV23
- Better vaccines to prevent pneumococcal infections in adults are urgently needed .