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NATIONAL SURVEILLANCE OF COMMUNICABLE DISEASES

Editor: Peter Henrik Andersen
Dept. of Epidemiology
Statens Serum Institut • 5 Artillerivej • DK 2300 Copenhagen S

Tel.: +45 3268 3268 • Fax: +45 3268 3874
www.ssi.dk • epinews@ssi.dk • ISSN: 1396-4798

DANISH STUDIES ON THE EFFICIENCY AND SAFETY OF CHILDHOOD VACCINES

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Before a vaccine is introduced, its efficiency and safety are tested in a number of clinical trials, known as phase 1 to phase 3 studies.
After its introduction, the efficiency and safety of the vaccine are tested in a real-world context, the so-called phase 4 trials.
Statens Serum Institut has developed a research database comprising vaccination information on all Danish children born since 1990. In combination with information from national health registers, e.g. on hospital admissions, this database is an essential research resource. These tools have made it possible to perform a series of register-based cohort studies to explore the efficiency and safety of the vaccines comprised by the Danish Childhood Vaccination Programme.
The below sections outline some of the main study results.

Efficiency of the Haemophilus influenzae type b (Hib) vaccination
The Hib vaccine was introduced into the Danish Childhood Vaccination Programme in 1993. Prior to its introduction, the Hib bacterium constituted one of the main factors causing childhood meningitis.
A cohort study including more than ½ million Danish children demonstrated that the vaccine provided excellent protection against Hib meningitis. The overall effect of the introduction to the programme was at least a 98% improvement compared with the pre-vaccination situation. This improvement was achieved owing to the direct effect of the vaccine, and the indirect effect of the so-called flock immunity. The concept of flock immunity denotes the situation in which unvaccinated persons are protected, because the bacterium cannot circulate in a predominantly vaccinated population.
The study showed a measurable flock immunity effect already 6 months after the introduction of the Hib vaccine, and after 3½ years, flock immunity had yielded a 94% protection rate for unvaccinated children compared with the period prior to the introduction of the vaccine.

Whooping cough vaccination efficiency
In 1997 the previously used whole-cell whooping cough vaccine was replaced by an acellular whooping cough vaccine with an improved adverse event profile.
In a cohort study comprising more than ½ million Danish children it was determined that the protection rate for admissions caused by whooping cough after 1, 2 and 3 doses of whooping cough vaccine was 37%, 72% and 93%, respectively. The protection rate for whooping cough that did not require hospitalisation, i.e. milder cases, was marginally lower: 78% after 3 doses, EPI-NEWS 34/04.
The efficiency of the acellular mono-component vaccine used in Denmark is at par with other types of whooping cough vaccine used abroad.

Measles, mumps and rubella vaccine and autism
Since the late 1990s the measles, mumps and rubella (MMR) vaccine has been linked to autism. Particularly in Great Britain this caused concern among parents which led to insufficient vaccination coverage. In Denmark, a decrease in the MMR vaccination coverage was also observed in this context, EPI-NEWS 49/97.
A cohort study including more than ½ million Danish children found no association between MMR and autism EPI-NEWS 14/04.

Mercury in vaccines and autism
Ethyl mercury is a thiomersal component used in very small amounts as a preservative in some vaccines. In the US, attention has been drawn to the levels of ethyl mercury given in connection with the US childhood vaccination programme, as these exceed the threshold values for other types of organic mercury. As high doses of mercury damage nerve tissue, speculations arose concerning a possible association between ethyl mercury in vaccines and the occurrence of autism.
In the Danish Childhood Vaccination Programme, only the formerly used whole-cell whooping cough vaccine contained ethyl mercury, and only in a specified period of time. It was therefore possible to perform a comparative study of this vaccine with and without ethyl mercury.
A cohort study including nearly ½ million Danish children detected no association between ethyl mercury and the occurrence of autism.

Childhood vaccines and type 1 diabetes
Childhood vaccines have been suspected of causing type 1 diabetes (T1D). This hypothesis was based primarily on the correlation in time between an increase in T1D in children over recent decades and the simultaneous expansion of some vaccination programmes.
In a cohort study including more than 700,000 children born in Denmark in the period 1990-2000, no evidence was found to support an association between the vaccines of the Danish Childhood Vaccination Programme and development of T1D.

Childhood vaccines and non-specific infectious diseases
It has been suggested that vaccine exposure may overload the immune system and therefore render the child susceptible to infectious diseases.
In a cohort study comprising approx. 800,000 children born in Denmark 1990-2001, the possible association between Danish childhood vaccines and admission with infectious diseases was explored. Vaccinated children did not have an increased risk of infectious diseases such as upper respiratory infections, pneumonia, CNS infections, diarrhoea, etc.

Commentary
In addition to statutory surveillance, research is important for the assessment of the efficiency and safety of any vaccination programme.
The cohort studies have contributed to build prevention evidence by testing e.g. hypotheses concerning the safety of various vaccines. The studies on autism and T1D are good examples of such evidence.
Research-based quality assurance of vaccines and vaccination programmes presupposes that the data are available at the individual level. It would therefore be expedient to record all Danish vaccinations in a database corresponding to those used for the recording of other prescription drugs. Such initiative would also facilitate surveillance of the efficiency and safety of the numerous influenza vaccines which are administered ahead of the annual influenza season.
Physicians are required to report adverse events to the Danish Medicines Agency in accordance with current provisions, www.lmst.dk. Furthermore, all EU notifications are collected at the European Medicines Agency, www.emea.europe.eu, which continuously monitors pharmaceutical safety.
(A. Hviid, Department of Epidemiological Research)

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Individually notifiable diseases

Number of notifications received in the Department of Epidemiology, SSI (2008 figures are preliminary)

Table 1	Week 13 2008	Cum. 2008 [1]	Cum. 2007 [1]
AIDS	1	10	10
Anthrax	0	0	0
Botulism	0	0	0
Cholera	0	0	0
Creutzfeldt-Jakob	0	4	2
Diphtheria	0	0	0
Food-borne diseases	2	71	135
of these, infected abroad	1	18	23
Gonorrhoea	5	81	98
Haemorrhagic fever	0	0	0
Hepatitis A	0	14	10
of these, infected abroad	0	5	4
Hepatitis B (acute)	0	3	7
Hepatitis B (chronic)	0	43	68
Hepatitis C (acute)	0	3	2
Hepatitis C (chronic)	3	101	82
HIV	5	53	76
Legionella pneumonia	4	25	27
of these, infected abroad	0	10	4
Leprosy	0	0	0
Leptospirosis	0	1	4
Measles	1	5	1
Meningococcal disease	0	17	17
of these, group B	0	6	8
of these, group C	0	4	5
of these, unspec. + other	0	7	4
Mumps	0	12	3
Neuroborreliosis	0	18	25
Ornithosis	0	1	1
Pertussis (children < 2 years)	1	25	25
Plague	0	0	0
Polio	0	0	0
Purulent meningitis			
Haemophilus influenzae	0	0	1
Listeria monocytogenes	0	1	5
Streptococcus pneumoniae	0	26	34
Other aethiology	0	10	5
Unknown aethiology	0	7	5
Under registration	5	8	-
Rabies	0	0	0
Rubella (congenital)	0	0	0
Rubella (during pregnancy)	0	0	0
Shigellosis	0	16	13
of these, infected abroad	0	14	6
Syphilis	3	31	26
Tetanus	0	0	0
Tuberculosis	7	98	86
Typhoid/paratyphoid fever	0	9	3
of these, infected abroad	0	7	3
Typhus exanthematicus	0	0	1
VTEC/HUS	3	28	46
of these, infected abroad	1	8	14

[1] *Cumulative number 2008 and in corresponding period 2007*

Selected laboratory diagnosed infections

Number of specimens, isolates, and/or notifications received in SSI laboratories

Table 2	Week 13 2008	Cum. 2008 [2]	Cum. 2007 [2]
Bordetella pertussis			
(all ages)	1	35	41
Gonococci	3	94	86
of these, females	0	19	13
of these, males	3	75	73
Listeria monocytogenes	1	6	15
Mycoplasma pneumoniae			
Resp. specimens [3]	1	35	211
Serum specimens [4]	3	44	219
Streptococci [5]			
Group A streptococci	8	43	39
Group B streptococci	0	23	24
Group C streptococci	0	3	4
Group G streptococci	8	32	32
S. pneumoniae	48	343	369
Table 3	**Week 11 2008**	**Cum. 2008 [2]**	**Cum. 2007 [2]**
MRSA	30	127	-
Pathogenic int. bacteria [6]			
Campylobacter	31	365	492
S. Enteritidis	1	60	60
S. Typhimurium	9	75	59
Other zoon. salmonella	8	150	113
Yersinia enterocolitica	1	44	64
Verocytotoxin-producing E. coli	2	30	49
Enteropathogenic E. coli	4	21	34
Enterotoxigenic E. coli	4	62	31

[2] *Cumulative number 2008 and in corresponding period 2007*

[3] *Resp. specimens with positive PCR*

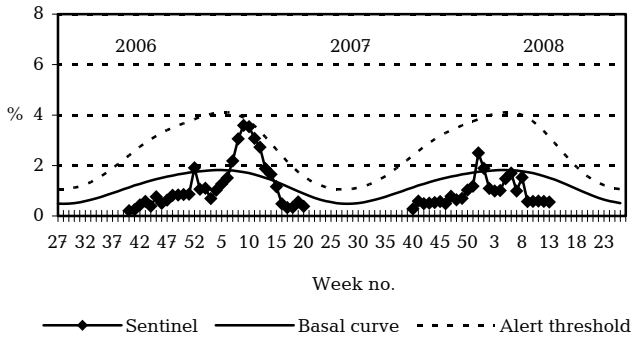
[4] *Serum specimens with pos. complement fixation test*

[5] *Isolated in blood or spinal fluid*

[6] *See also www.germ.dk*

Sentinel surveillance of the influenza activity

Weekly percentage of consultations, 2006/2007/2008



Sentinel:	Influenza consultations (as percentage of total consultations)
Basal curve:	Expected frequency of consultations under non-epidemic conditions
Alert threshold:	Possible incipient epidemic

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