

## NEW HUMAN PAPILLOMAVIRUS VACCINES

No. 42/43, 2006

The first vaccine against human papillomavirus (HPV) has now been approved for use in Denmark. The vaccine is targeted at HPV types 6, 11, 16 and 18. A bivalent HPV vaccine targeting types 16 and 18 is expected to reach the market shortly.

### HPV infection

HPV infection is a causative factor for development of cervical cancer. More than 99% of all cases of cervical cancer are caused by HPV. HPV infection is transmitted sexually and about 60-80% of all sexually active females and males have been infected at some point in their lives. The infection is frequently asymptomatic and disappears spontaneously, while it persists in some cases. Persisting HPV infection is the leading cause of cervical cancer and is also associated with other anogenital forms of cancer such as anal and penile cancer. Furthermore, HPV infection may cause severe cervical intra-epithelial neoplasia (CIN), which is a precursor of invasive cervical cancer, anal intraepithelial neoplasia, condylomas and larynx papilloma in children. HPV types 6 and 11 cause 90% of all condylomas.

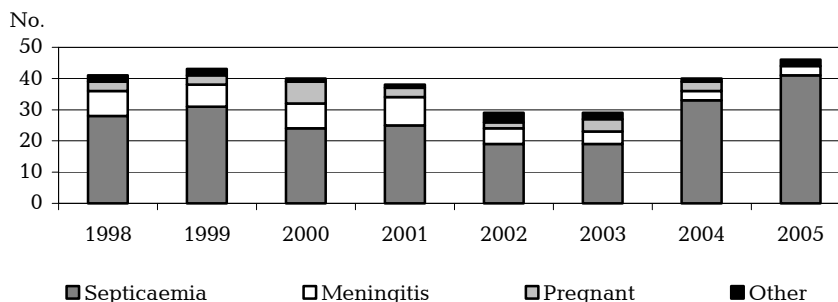
### The vaccines

Preliminary findings show that both vaccines yield 100% protection against the development of HPV 16/18 associated CIN grade II/III, i.e. the vaccines protect against persisting infections and associated cell changes caused by HPV types 16 and 18. These types cause 70% of all cases of cervical cancer. A protective effect has been observed for a period of 4.5 years after completion of the 3-dose series. Future studies will elucidate the long-term effects. The 4-valent vaccine has demonstrated 98% protection against condylomas caused by types 6 and 11 and has documented effect in children and adolescents aged 9 to 15 years and in females aged 16 to 26 years. The vaccination series consists of three separate doses, administered at 0, 2 and 6 months. All three doses must be administered within one year. The vaccine has been approved for both males and females.

### Who may be vaccinated?

As the vaccine is exclusively prophylactic, it should ideally be given prior to sexual debut. However, adults may potentially benefit from vaccination. Vaccination studies have not identified substantial adverse effects, neither in females who were not in-

Figure 1. Laboratory confirmed listeriosis cases, 1998-2005



fect, nor in females naturally infected with HPV prior to vaccination. It has also been demonstrated that females who have become infected with one or more of the HPV types included in the vaccine gain protection against the types they have not been naturally infected with. The exact effect of the vaccine in these cases is unknown at present. Even though vaccinations have yielded very promising results, a number of unanswered questions remain, for instance concerning long-term effect, consequences for screening programmes and economic issues. Consequently, the Danish National Board of Health has initiated the elaboration of a health technology assessment to gather knowledge facilitating the decision as to whether the vaccination should form part of a public prophylactic programme, and whether it should be included in the childhood vaccination programme. (K. Mølbak, Dept. of Epidemiology)

### LISTERIOSIS 1998-2005

Listeriosis is a food-borne infection caused by the bacterium *Listeria monocytogenes*. This bacterium is widespread in nature and present in a considerable number of unprocessed foods. Most people occasionally ingest foods containing listeria, mostly without falling ill. The disease presents as septicaemia, meningoencephalitis or as foetomaternal listeriosis with a risk of stillbirth or life-threatening infection of the neonate. The overall listeriosis mortality is about 25%. The disease is monitored via the laboratory notification system and was last covered in EPI-NEWS 34/98.

### Risk factors and sources of infection

Underlying disease or treatment entailing reduced cellular immune response predisposes listeriosis development. In addition to pregnancy, the classic risk factors are cancer, haematological diseases, diabetes, alcoholism, organ transplantation,

AIDS and age 60+ years. In contrast to the majority of other foodborne bacteria, *Listeria monocytogenes* can reproduce at refrigerator temperature. If sliced meat products or ready-to-eat products are contaminated with listeria, the bacteria may grow during storage. Patients typically become infected from ready-to-eat products, e.g. sliced meat cuts for sandwiches, soft cheese, fishery products and vegetables.

### Listeriosis development

In the period 1998-2005, the annual median was 40 cases (range 29-46), [Figure 1](#). In 2004 and 2005, 42 and 46 cases were notified, representing an increase compared with 2002-3. By 1 October 2006, 36 notifications had been received, which is a further increase. Identification by ribotyping and PFGE has shown that the increase is caused by various types. Consequently, it is unlikely that the increase is the result of a single outbreak. An epidemiological investigation in a county with a particularly high occurrence did not identify one single source of infection.

### Commentary

If this year's trend continues, it will lead to an annual incidence of 8.5 cases per 1 million inhabitants; a high incidence compared with all other European countries. As the increase may be attributed to septicaemia cases and not meningitis cases, it is possible that blood culture practice may contribute to the described fluctuations. Unfortunately, the period from bacteria isolation to notification is often relatively long. Delayed dispatch of isolates to SSI causes unnecessary delay in typing analysis. To ensure rapid investigation of suspected outbreaks, it is essential that isolates be dispatched continuously.

(B. Smith, M. Kemp, DBMP,  
 K. Mølbak, Dept. of Epidemiology)

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## Individually notifiable diseases

Number of notifications received in the Department of Epidemiology, SSI (2006 figures are preliminary)

Table 1	Week 42 2006	Cum. 2006 <sup>1)</sup>	Cum. 2005 <sup>1)</sup>
AIDS	1	33	49
Anthrax	0	0	0
Botulism	0	0	0
Cholera	0	0	0
Creutzfeldt-Jakob	0	21	2
Diphtheria	0	0	0
Food-borne diseases	19	442	442
of these, infected abroad	0	105	107
Gonorrhoea	5	343	407
Haemorrhagic fever	5	343	407
Hepatitis A	1	29	52
of these, infected abroad	0	16	17
Hepatitis B (acute)	0	15	30
Hepatitis B (chronic)	2	257	112
Hepatitis C (acute)	1	7	1
Hepatitis C (chronic)	7	393	252
HIV	7	185	207
Legionella pneumonia	4	102	95
of these, infected abroad	0	29	40
Leprosy	0	0	0
Leptospirosis	0	8	10
Measles	0	28	2
Meningococcal disease	0	55	79
of these, group B	0	26	38
of these, group C	0	10	20
of these, unspec. + other	0	19	19
Mumps	0	16	7
Neuroborreliosis	5	62	67
Ornithosis	1	10	17
Pertussis (children < 2 years)	0	37	130
Plague	0	0	0
Polio	0	0	0
Purulent meningitis			
Haemophilus influenzae	0	1	1
Listeria monocytogenes	0	6	2
Streptococcus pneumoniae	0	66	95
Other aethiology	0	7	14
Unknown aethiology	0	17	15
Under registration	4	23	-
Rabies	0	0	0
Rubella (congenital)	0	0	0
Rubella (during pregnancy)	0	0	0
Shigellosis	2	49	87
of these, infected abroad	0	41	69
Syphilis	1	55	105
Tetanus	0	2	2
Tuberculosis	10	317	352
Typhoid/paratyphoid fever	0	24	30
of these, infected abroad	0	21	28
Typhus exanthematicus	0	0	0
VTEC/HUS	1	109	133
of these, infected abroad	0	36	46

<sup>1)</sup> Cumulative number 2006 and in corresponding period 2005

## Selected laboratory diagnosed infections

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

Table 2	Week 42 2006	Cum. 2006 <sup>2)</sup>	Cum. 2005 <sup>2)</sup>
Bordetella pertussis (all ages)	3	172	425
Gonococci	6	341	368
of these, females	1	61	39
of these, males	5	280	329
Listeria monocytogenes	3	42	31
Mycoplasma pneumoniae			
Resp. specimens <sup>3)</sup>	9	344	785
Serum specimens <sup>4)</sup>	12	301	630
Streptococci <sup>5)</sup>			
Group A streptococci	0	119	88
Group B streptococci	0	77	63
Group C streptococci	0	19	19
Group G streptococci	0	115	94
S. pneumoniae	10	771	893
Table 3	Week 40 2006	Cum. 2006 <sup>2)</sup>	Cum. 2005 <sup>2)</sup>
Pathogenic int. bacteria <sup>6)</sup>			
Campylobacter	52	2463	2948
S. Enteritidis	7	477	525
S. Typhimurium	10	315	431
Other zoon. salmonella	23	551	466
Yersinia enterocolitica	6	145	191
Verocytotoxin-producing E. coli	1	115	128
Enteropathogenic E. coli	16	237	218
Enterotoxigenic E. coli	4	197	300

<sup>2)</sup> Cumulative number 2006 and in corresponding period 2005

<sup>3)</sup> Resp. specimens with positive PCR

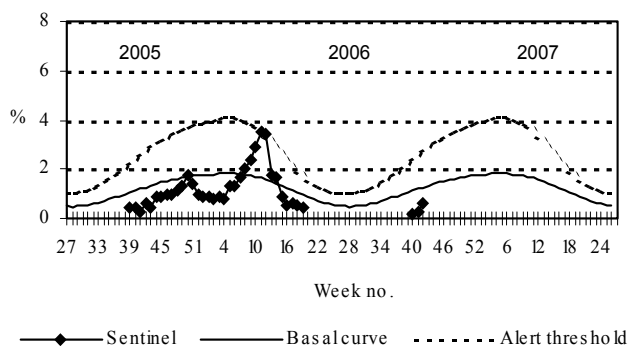
<sup>4)</sup> Serum specimens with pos. complement fixation test

<sup>5)</sup> Isolated in blood or spinal fluid

<sup>6)</sup> See also [www.germ.dk](http://www.germ.dk)

## Sentinel surveillance of the influenza activity

Weekly percentage of consultations, 2005/2006/2007



Sentinel: Influenza consultations (as percentage of total consultations)

Basal curve: Expected frequency of consultations under non-epidemic conditions

Alert threshold: Possible incipient epidemic