Joint Committee on Vaccination and Immunisation
Statement on varicella and herpes zoster vaccines

Introduction

1. Following a request from the Secretary of State for Health for England* the committee considered vaccination strategies to protect groups of the population against the diseases caused by the varicella zoster virus – chickenpox (varicella) and shingles (herpes zoster). This statement summarises the evidence considered by the committee and the committee's conclusions and recommendations on a vaccination strategies against these diseases.

Background

Varicella

2. Varicella is a highly infectious disease caused by the varicella zoster virus. It is most common in younger children and is transmitted through direct contact between people or indirectly via airborne droplets. Chickenpox is usually a mild illness in children with most recovering quickly from the infection and suffering few symptoms and no complications. However, there is a greater risk of complications for infected neonates (infants less than four weeks old), adults, pregnant women or those who are immunocompromised – as detailed in the immunisation against infectious diseases (Green Book) varicella chapter.

3. Data from a sentinel group of GP practices in the UK suggest that most infections occur in children under 14 years of age. Within the last two decades an increasing proportion of infections have occurred in children under five years of age (Figure 1).[1] Seroprevalence data support age-related change in varicella infections toward younger age groups.[2]

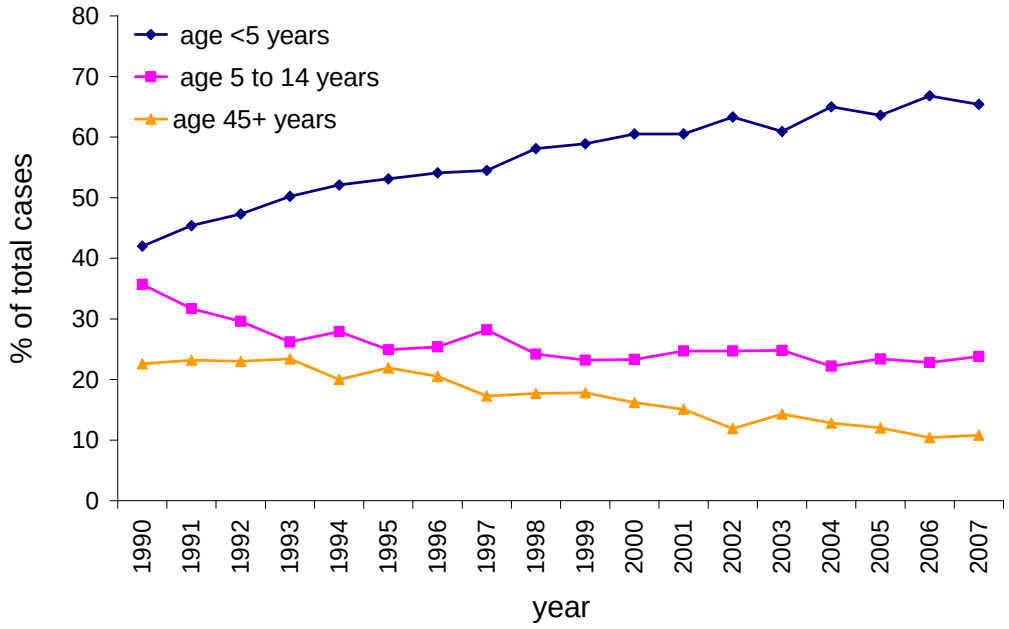

Figure 1: Change in distribution of varicella cases according to age – over time. Source: RCGP-BRU.

* Letter from Secretary of State for Health to JCVI (2009) http://www.dh.gov.uk/prod_consum_dh/groups/dh_digitalassets/@dh/@ab/documents/digitalasset/dh_104190.pdf

Herpes zoster

4. Whilst most teenagers and adults in the UK have immunity to re-infection from varicella zoster virus from having first contracted the infection as a child, some are susceptible to herpes zoster (shingles). This is caused by reactivation of varicella virus that has remained in the body in a dormant state within nerve cells. Reactivation is usually associated with immune system depression that can occur, for example, in older age, following therapy with immunosuppressant drugs or from HIV infection.

5. Herpes zoster tends to be more prevalent in adults, particularly with increasing age.[3] The first sign is usually pain in the affected area, followed by a rash of fluid-filled blisters that usually persist for about a week. However, pain may last longer should post herpetic neuraligia (PHN) develop, lasting for three to six months or years in some cases. Ophthalmic zoster develops when the viral infection is localised in or around the eyes and this condition is also often associated with long-term pain. Although herpes zoster is not caused by exposure to a person with varicella, varicella zoster virus can be transmitted from someone with herpes zoster.

6. Age-specific incidence rates of shingles have been estimated using a number of different GP-based sources[4] including: the Royal College of General Practitioners (RCGP) Weekly Returns Service;[5] the fourth Morbidity Survey in General Practice (MSGP-4),[6] and the General Practice Research Database.[3] Data from these GP-based studies suggest that over 50,000 cases of shingles occur in people aged 70 years and above (Table 1). The severity of shingles generally increases with age and can lead to PHN (Table 2) and hospitalisation. Studies have estimated ophthalmic zoster to occur in 10-20 per cent of shingles cases[7] with around four per cent of the cases resulting in long-term sequelae.[8] Around one in 1000 shingles cases is estimated to result in death in people aged 70 years and above.

Tables 1 and 2 below provide data on the estimated incidence according to age and the burden of disease in England and Wales.

Age Group	Herpes zoster cases	Post herpetic neuralgia cases	Herpes zoster deaths	Cases hospitalised
60-64	18,765	1,696	1	149
65-69	16,189	1,858	1	161
70-74	15,720	2,355	1	242
75-79	14,376	2,874	3	321
80-84	11,614	3,157	7	352
85+	11,987	6,270	43	522
Total	88,652	18,210	55	1746

Table 1. Burden of disease in the immunocompetent population England and Wales (population 2007).[4]

Age Group	Incidence per 100,000 per year (general)	Percentage developing post herpetic neuralgia after 90 days	Proportion hospitalised first diagnosis (first three diagnosis)	Mean number of days in hospital (median)
60-64	706	9%	0.8% (1.3%)	9 (4)
65-69	791	11%	1.0% (1.7%)	8 (5)
70-74	876	15%	1.5% (2.4%)	11 (5)
75-79	961	20%	2.2% (3.8%)	14 (7)
80-84	1046	27%	3.0% (5.2%)	17 (9)
85+	1216	52%	4.4% (8.1%)	22 (13)

Table 2. Estimated annual age-specific incidence, hospitalisation rate, length of inpatient stay, Burden of disease in the immunocompetent population England and Wales (population 2007). Data taken from from van Hoek AJ, Gay N, Melegaro A *et al.* (2009) Estimating the cost-effectiveness of vaccination against herpes zoster in England and Wales.[4]

Vaccines

7. The following vaccines are available and licensed in the UK for the prevention of varicella:
    - Varilrix® - manufactured by GlaxoSmithKline, and
    - Varivax® - manufactured by Sanofi Pasteur MSD;

    and for herpes zoster:
    - Zostavax® - manufactured by Sanofi Pasteur MSD.

    In order for the vaccines to be licensed for use in Europe by regulators their safety and efficacy are extensively evaluated and demonstrated in large clinical trials involving many thousands of subjects. [9-12] The efficacy and safety data are summarised in the Summary of Product Characteristics. [13-15]

JCVI consideration

8. A JCVI varicella and herpes zoster subgroup met in December 2007, April 2008 and March 2009 to consider the potential use of these vaccines in vaccination programmes in the UK. The JCVI considered the minutes of the subgroup meetings in February 2008, June 2008 and October 2009[†]. The evidence considered by the Subgroup and the JCVI is listed at Appendix A.

9. Two vaccination strategies were examined: a combined varicella and herpes zoster programme and a herpes zoster only programme.

10. Epidemiological modelling predicts that a national childhood immunisation programme against varicella using either a one or two dose schedule combined with a single dose herpes zoster vaccination programme for older people would result in a large reduction of varicella should vaccination coverage be relatively high for all vaccinations (> 70-80%). However, a significant number of break through infections are predicted with a one dose childhood schedule, it is predicted that both strategies could lead to an increase in herpes zoster incidence for the first 40 to 60 years following the introduction of a vaccination programme. This is because epidemiological evidence suggests that immunity in adulthood is boosted by the exposure to children infected by varicella zoster virus.[16,17] Without this natural boosting, current levels of immunity in adulthood may no longer be maintained.[18 19] Vaccinations against herpes zoster would only be expected to partly offset this increase, as the expected increase in herpes zoster incidence would occur predominantly in middle-aged adults too young to be targeted for herpes zoster vaccination. An increase in varicella infection in adulthood might also be expected. This would include women of childbearing age, potentially increasing the risk to unborn children or neonate should infections occur during pregnancy.

[†] Minutes of these meetings can be found on the JCVI website or down loaded here: Download varicella/herpes zoster minutes 2007 ; Download varicella minutes 2008; Download varicella minutes 2009; Download JCVI minutes 13 Feb 2008; Download JCVI minutes 17 June 2008; Download JCVI minutes 14 October 2009

11. Cost-effectiveness modelling indicates that a two-dose childhood vaccination programme or a combined childhood and adult vaccination programme could be cost-effective but only after 80-100+ years of vaccination at an assumed cost of vaccine. Before this time, the combined programme would be unlikely to be cost-effective and for the first 30-50 years of a programme would have a high probability of being cost ineffective. In light of the epidemiological and cost effectiveness modelling, neither a universal childhood nor a combined vaccination programme is recommended. This recommendation will be kept under review in light of emerging data on herpes zoster epidemiology. This recommendation does not override the previous advice on the use of varicella vaccine in children as outlined in the Varicella 'Green Book' chapter.

12. Cost-effectiveness modelling of a herpes zoster only vaccination programme[4] suggests that a universal herpes zoster vaccination for those aged 70 years and up to and including 79 years is cost effective provided that a licensed vaccine is available at a cost effective price. The impact of vaccination is greatest in this age group due to a combination of factors. These include:

    - an increase in the burden of shingles disease with age,
    - a decrease in the effectiveness of the vaccine with age,
    - the duration of protection of the vaccine, and
    - the lack of knowledge about the effectiveness of a second dose of vaccine.

    Vaccination of people aged 60 to 69 years could be cost-effective. However, based on current evidence, the vaccine may not provide long lasting protection and there is a lack of knowledge about the effectiveness of a second dose of vaccine. Therefore, vaccinating this age group could leave them unprotected when they are older and herpes zoster is more severe. Vaccination of older age groups would not be cost-effective because the effectiveness of the vaccine declines with age in older age groups. However, should clinical data show that protection from the vaccine lasts for longer than currently estimated (at least 7.5 years) and / or that a second dose of vaccine would be effective, this recommendation would be reviewed.

Recommendation

13. JCVI reviewed medical, epidemiological, and economic evidence as well as vaccine safety and efficacy data relevant to a herpes zoster (shingles) vaccination programme. Based on the evidence, a universal herpes zoster vaccination programme for adults aged 70 years up to and including 79 years is recommended provided that a licensed vaccine is available at a cost effective price. A universal varicella vaccination for children is not recommended. These recommendations will be kept under review in light of emerging data on the epidemiology of varicella and herpes zoster infections and the cost-effectiveness of vaccines against these infections.

Appendix A
Published papers considered by JCVI

Vaccine efficacy and safety

Apuzzio, Ganesh, et al. 2002[20]
Brisson, Edmunds, et al. 2000[21]
Chaves, Gargiullo, et al. 2007[22]
Gershon, LaRussa, et al. 2006[17]
Hambleton, Steinberg, et al. 2008[23]
Jumaan, Yu, et al. 2005[24]
Lau, Vessey, et al. 2002[10]
Levin, Gershon, et al. 2006[25]
Levin, Oxman, et al. 2008[12]
Macartney & Burgess 2008[26]
Meurice, De Bouver, et al. 1996[27]
Nguyen, Jumaan, et al. 2005[28]
Oxman, Levin, et al. 2005 [11]
Reynolds, Chaves, et al. 2008[29]
Sadzot-Delvaux, Rentier, et al. 2008[30]
Seward, Marin, et al. 2008[31]
Sheffer, Segal, et al. 2005[32]
Shinefield, Black, et al. 2002[33]
Vazquez, LaRussa, et al. 2001[9]
White, Kuter, et al. 1991[34]
Wise, Salive, et al. 2000[35]
Yih, Brooks, et al. 2005[36]

PHN

Daniel, Narewska, et al. 2008[37]
Dworkin, O'Connor, et al. 2007[38]
Hempenstall, Nurmikko, et al. 2005[39]

Epidemiology and burden of disease

Baba, Yabuuchi, et al. 1982[40]
Brisson, Edmunds, et al. 2002[41]
Brisson & Edmunds 2003[42]
Brisson, Gay, et al. 2002[18]
Cameron, Allan, et al. 2007[43]
Chapman, Cross, et al. 2003[44]
Daniel, Narewska, et al. 2008[37]
Diez-Domingo, Gil, et al. 2005[45]
Dworkin, O'Connor, et al. 2007[38]
Edgar, Galanis, et al. 2007[46]
Edmunds & Brisson 2002[47]
Fairley & Miller 1996[48]
Hempenstall, Nurmikko, et al. 2005[39]
Holmes 2005[49]
Holmes, Iglar, et al. 2004[50]
Jumaan, Yu, et al. 2005[24]
Kanra, Yalcin, et al. 2003[51]
Miller, Marshall, et al. 1993[52]
Mullooly, Riedlinger, et al. 2005[53]
Plourd & Austin 2005[54]
Rawson, Crampin, et al. 2001[55]
Reynolds, Chaves, et al. 2008[29]
Ronan & Wallace 2001[56]
Ross & Fleming 2000[1]
Russell, Schopflocher, et al. 2007[57]
Scott, Johnson, et al. 2006[58]
Solomon, Kaporis, et al. 1998[19]
Thomas, Wheeler, et al. 2002[16]
Yawn, Saddier, et al. 2007[59]
Yih, Brooks, et al. 2005[36]

Modelling - disease

Brisson, Edmunds, et al. 2000[60]
Brisson, Edmunds, et al. 2000[21]
Brisson, Edmunds, et al. 2003[61]
Brisson, Gay, et al. 2002[18]
Brisson, Pellissier, et al. 2008[62]
Edmunds, Brisson, et al. 2001[63]
Gauthier, Breuer, et al. 2009[3]
Levin, Oxman, et al. 2008[12]
Oxman, Levin, et al. 2005[11]

Modelling - Cost effectiveness

Ahnn 2005[64]
Banz, Wagenpfeil, et al. 2003[65]
Bonanni, Boccalini, et al. 2008[66]
Brisson & Edmunds 2002[67]
Brisson & Edmunds 2003[68]
Brisson, Pellissier, et al. 2007[69]
Coudeville, Brunot, et al. 2004[70]
Edmunds, Brisson, et al. 2001[63]
Ginsberg & Somekh 2004[71]
Hammerschmidt, Bisanz, et al. 2007[72]
Hornberger & Robertus 2006[73]
Hsu, Lin, et al. 2003[74]
Lenne, Diez Domingo, et al. 2006[75]
Pellissier, Brisson, et al. 2007 [76]
Pinot de Moira, Edmunds, et al. 2006[77]
Rothberg, Virapongse, et al. 2007[78]
Rozenbaum, van Hoek, et al. 2008[79]
Scuffham, Devlin, et al. 1999[80]
Scuffham, Lowin, et al. 1999[81]
Valentim, Sartori, et al. 2008[82]
van Hoek, Gay, et al. 2009[4]
Zhou, Ortega-Sanchez, et al. 2008[83]

Appendix B
References

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