Papillomavirussen en vaccinatie
Virologie en classificatie van papillomavirussen
circulair dsDNA
Early proteins

Late proteins

HPV-16
7904 bp

Long control region
TATA Signal 1, 2

PolyA Signal 2

PolyA Signal 1

L1

L2

E1

E2

E4

E5

E6

E7
PHYLOGENETIC CLASSIFICATION OF HUMAN PAPILLOMAVIRUSES

Van Ranst et al., J Gen Virol. 1992
CUTANEOUS BENIGN PAPILLOMAVIRUSES: WARTS (VERRUCA)
PHYLOGENETIC CLASSIFICATION OF HUMAN PAPILLOMAVIRUSES

CUTANEOUS TROPISM

HPV-1
  - HPV-25
  - HPV-20
  - HPV-14
  - HPV-21
  - HPV-5
  - HPV-47
  - HPV-8
  - HPV-2
  - HPV-57

HPV-6
  - HPV-11
  - HPV-13
  - HPV-44
  - HPV-43
  - HPV-42

HPV-16
  - HPV-35
  - HPV-31
  - HPV-52
  - HPV-33
  - HPV-58

HPV-51
  - HPV-56

HPV-18
  - HPV-45
  - HPV-39
  - MF180

Van Ranst et al., J Gen Virol. 1992
VERRUCA VULGARIS: HPV
CUTANEOUS MALIGNANT PAPILLOMAVIRUSES: EPIDERMODYSPLASIA VERRUCIFORMIS (EV)
PHYLOGENETIC CLASSIFICATION OF HUMAN PAPILLOMAVIRUSES

CUTANEOUS TROPISM

Van Ranst et al., J Gen Virol. 1992
EPIDERMODYSPLASIA VERRUCIFORMIS

MUCOSAL LOW-RISK PAPILLOMAVIRUSES

GENITAL WARTS (CONDYLOMATA)
PHYLOGENETIC CLASSIFICATION OF HUMAN PAPILLOMAVIRUSES

CUTANEOUS TROPISM

LOW-RISK MUCOSAL

HIGH-RISK MUCOSAL

Van Ranst et al., J Gen Virol. 1992
MUCOSAL HIGH-RISK PAPILLOMAVIRUSES

CERVICAL INTRAEPITHELIAL NEOPLASIA (CIN) AND CERVICAL CANCER
PHYLOGENETIC CLASSIFICATION OF HUMAN PAPILLOMAVIRUSES

CUTANEOUS TROPISM

LOW-RISK MUCOSAL

HIGH-RISK MUCOSAL

Van Ranst et al., J Gen Virol. 1992
HPV vaccinatie
IMMUNOLOGIE VAN HPV

- Infectie is beperkt tot mucosa: geen viremie
- Weinig contact met immuunsysteem!
- Natuurlijke infectie geeft slechts lage antistoftiters tegen L1
- T-cel immuniteit verantwoordelijk voor natuurlijke regressie van letsels: andere antigenen dan L1
IMMUNOLOGIE VAN HPV

• IgG-gemedieerde humorale immuniteit verantwoordelijk voor preventie van letsels: vooral tegen L1 antigeen
• IgG belangrijker dan locale IgA productie
• Transudatie van IgG in cervicale mucosa na intramusculaire injectie van L1 VLPs
• Goeie correlatie tussen serum IgG levels en mucosale IgG levels
<table>
<thead>
<tr>
<th>Comparison</th>
<th>Gardasil®</th>
<th>Cervarix®</th>
</tr>
</thead>
<tbody>
<tr>
<td>Company</td>
<td>Sanofi Pasteur &amp; MSD</td>
<td>GlaxoSmithKline</td>
</tr>
<tr>
<td>Recombinant production</td>
<td><em>Saccharomyces cerevisiae</em> CANADE 3C-5 (strain 1895) yeast</td>
<td><em>Spodoptera frugiperda</em> Sf-9, <em>Trichoplusia ni</em> Hi-5 insect cells</td>
</tr>
</tbody>
</table>
| Antigen composition                | 20 µg HPV 6 L1 VLP  
40 µg HPV 11 L1 VLP  
40 µg HPV 16 L1 VLP  
20 µg HPV 18 L1 VLP                  | 20 µg HPV 16 L1 VLP  
20 µg HPV 18 L1 VLP                  |
| Adjuvants                          | AAHS:  
225 µg amorphous Aluminum-hydroxy-phosphat-sulfat | AS04:  
500 µg Aluminumhydroxid  
50 µg 3-deacylated monophosphoryl lipid A |
| Vaccination schedule (within 1 year) | Month 0, 2, 6                                    | Month 0, 1, 6                                 |
LONG-TERM IMMUNITY?

Cervarix against HPV-16: >8 years (and counting)
LONG-TERM IMMUNITY?

Cervarix against HPV-18: >8 years (and counting)
LONG-TERM IMMUNITY?

Gardasil against HPV-16: >5 years (and counting)
LONG-TERM IMMUNITY?

Gardasil against HPV-18: >5 years (and counting)
LONG-TERM IMMUNITY?

COMPARISON CERVARIX/GARDASIL
(2 years after vaccination)

*the clinical relevance of the antibody difference between the two vaccines in relation to long term protection and prevention of disease has to be evaluated by long term observation*
LONG-TERM IMMUNITY?

COMPARISON CERVARIX/GARDASIL
(2 years after vaccination)

Einstein et al., Human Vaccines, 2010
LONG-TERM PROTECTION?

Cervarix efficacy (%) after 4.5 years

- Initial efficacy study (001)
  - ATP: 92%
  - ATP: 100%
  - ATP: 100%
  - ITT: 93%
  - 0/6

- 001 / 007 combined analysis
  - ATP: 95%
  - ATP: 96%
  - ATP: 100%
  - ITT: 96%
  - ITT: 100%

HPV-16/18 associated

Incident Infection
6M Persistent Infection
12M Persistent Infection (post hoc analysis 001 Initial efficacy study)
Cytology
CIN

LONG-TERM PROTECTION?

Demonstration of Long Term (up to 9.5 yrs) Prophylactic Efficacy of HPV-16 monovalent Vaccine (Extension of the initial Merck efficacy trial)

Prophylactic efficacy against HPV-16 infections and cervical lesions

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>Vaccine (N = 114)</th>
<th>Placebo (N = 118)</th>
<th>Efficacy against HPV 16</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cases</td>
<td>Cases</td>
<td>(%)</td>
</tr>
<tr>
<td>Infection</td>
<td>1</td>
<td>21</td>
<td>96</td>
</tr>
<tr>
<td>CIN 1+</td>
<td>0</td>
<td>8</td>
<td>100</td>
</tr>
<tr>
<td>CIN 2+</td>
<td>0</td>
<td>7</td>
<td>100</td>
</tr>
</tbody>
</table>

* Extension study of Protocol 005 with a gap period of 2 years between the end of the original study and the beginning of the extension study

N.B. this is NOT Gardasil but only HPV16 VLP experimental vaccine potentially proving the principle

Rowhani-Rahbar et al., Vaccine 2009
LONG-TERM PROTECTION?

Years After Vaccination

GMT (mMU/ml)

>30 years?
CROSS-PROTECTION?

HPV-16
HPV-35
HPV-31
HPV-52
HPV-33
HPV-58
HPV-51
HPV-56
HPV-18
HPV-45
HPV-39
MF180

CROSS-PROTECTION?
<table>
<thead>
<tr>
<th></th>
<th>6 month persistence</th>
<th>CIN2+</th>
</tr>
</thead>
<tbody>
<tr>
<td>HPV 31</td>
<td>77% (66-85)</td>
<td>100% (78-100)</td>
</tr>
<tr>
<td>HPV 33</td>
<td>43% (19-61)</td>
<td>72% (19-92)</td>
</tr>
<tr>
<td>HPV 45</td>
<td>81% (64-91)</td>
<td>100% (-19-100)</td>
</tr>
</tbody>
</table>

Cervarix: Skinner et al., 2009 (Malmö Conference)
## CROSS-PROTECTION?

<table>
<thead>
<tr>
<th>CIN 2/3 or AIS by type</th>
<th>GARDASIL (N = 4616) Cases</th>
<th>Placebo (N = 4675) Cases</th>
<th>% Efficacy (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HPV 6, 11, 16 or 18</td>
<td>0</td>
<td>52</td>
<td>100 (93, 100)</td>
</tr>
<tr>
<td>HPV 31 or 45</td>
<td>8</td>
<td>21</td>
<td>62 (10, 85)</td>
</tr>
<tr>
<td>HPV 31, 33, 45, 52 or 58</td>
<td>27</td>
<td>48</td>
<td>43 (7, 66)</td>
</tr>
<tr>
<td>10 Non-Vaccine Oncogenic Types: HPV 31, 33, 35, 39, 45, 51, 52, 56, 58, or 59</td>
<td>38</td>
<td>62</td>
<td>38 (6, 60)</td>
</tr>
<tr>
<td>Non-Vaccine HPV A9 Species</td>
<td>26</td>
<td>48</td>
<td>45 (10, 68)</td>
</tr>
<tr>
<td>HPV 31</td>
<td>5</td>
<td>21</td>
<td>—</td>
</tr>
<tr>
<td>HPV 33</td>
<td>7</td>
<td>13</td>
<td>—</td>
</tr>
<tr>
<td>HPV 35</td>
<td>2</td>
<td>1</td>
<td>—</td>
</tr>
<tr>
<td>HPV 52</td>
<td>12</td>
<td>16</td>
<td>—</td>
</tr>
<tr>
<td>HPV 58</td>
<td>9</td>
<td>13</td>
<td>—</td>
</tr>
<tr>
<td>Non-Vaccine HPV A7 Species</td>
<td>8</td>
<td>15</td>
<td>46 (-35, 80)</td>
</tr>
<tr>
<td>HPV 39</td>
<td>2</td>
<td>6</td>
<td>—</td>
</tr>
<tr>
<td>HPV 45</td>
<td>3</td>
<td>2</td>
<td>—</td>
</tr>
<tr>
<td>HPV 59</td>
<td>4</td>
<td>7</td>
<td>—</td>
</tr>
<tr>
<td>HPV 51</td>
<td>8</td>
<td>10</td>
<td>—</td>
</tr>
<tr>
<td>HPV 56</td>
<td>5</td>
<td>10</td>
<td>—</td>
</tr>
</tbody>
</table>
Countries Using HPV Vaccine in National Immunization Schedule, 2008

Source: WHO/IVB database, 193 WHO Member States. Data as of July 2009
Date of slide: 12 August 2009
• Na introductie van vaccin toch blijvende cervixscreening!
• Algemene vaccinatie meisjes 10-13j via schoolgezondheidszorg
• Vrouwen tussen 14 en 26 jaar die nog geen seksueel contact hebben gehad
• Vrouwen tussen 14 en 26 jaar die reeds sexuele betrekkingen gehad hebben
GARDASIL™
[Quadrivalent Human Papillomavirus (Types 6, 11, 16, 18) Recombinant Vaccine]

1 x 0.5 mL Single-dose Syringe with Separate Needle
Suspension for Injection

Each 0.5 mL dose contains approximately 20 mcg HPV 6 L1, 40 mcg HPV 11 L1, 40 mcg HPV 16 L1 and 20 mcg HPV 18 L1 proteins

FOR INTRAMUSCULAR INJECTION ONLY.
IMPACT OF VACCINATION ON CERVICAL CANCER

Elamin H. Elbasha
IMPACT OF VACCINATION ON HPV16/18 CIN 2/3

- No Vaccination
- 12-yo females
- 12-yo females+females catch up
- 12-yo females&males
- 12-yo females&males+females catch up
- 12-yo females&males+females and males catch up

Elamin H. Elbasha
IMPACT OF VACCINATION ON GENITAL WARTS

Elamin H. Elbasha
IMPACT OF VACCINATION ON GENITAL WARTS

Vaccination program commences

<table>
<thead>
<tr>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Q1 04</td>
</tr>
<tr>
<td>Q3 04</td>
</tr>
<tr>
<td>Q1 05</td>
</tr>
<tr>
<td>Q3 05</td>
</tr>
<tr>
<td>Q1 06</td>
</tr>
<tr>
<td>Q3 06</td>
</tr>
<tr>
<td>Q1 07</td>
</tr>
<tr>
<td>Q3 07</td>
</tr>
<tr>
<td>Q1 08</td>
</tr>
<tr>
<td>Q3 08</td>
</tr>
<tr>
<td>Q1 09</td>
</tr>
<tr>
<td>Q3 09</td>
</tr>
</tbody>
</table>

Quarters since 2004

Women<28
Women ≥28
MSM
MSW
HSV
WHAT CHRISTIAN CONSERVATIVE GROUPS CONSIDER A FORM OF FOREPLAY

HPV VACCINE
AHA! THE SURE SIGN OF PROMISCUITY!!

HPV VACCINE

CHRISTIAN RIGHT
I'm very sorry to tell you this... but your daughter has... sex???
Rogue cervical cancer jab fears after girl, 14, dies
Authorities seize suspect vaccine batch

A GIRL of 14 died yesterday hours after being given the cervical cancer vaccine at her school.
The pupil, who attended the Blue Coat Church of England School in Coventry, died in hospital after receiving the Cervarix jab.
The tragedy is the first reported death in Britain since the national vaccination programme began last September, with more than 1.5 million doses given to girls.
Last night an urgent investigation began to establish the exact cause of the death. It is not yet known whether the girl had an extreme - and very rare - reaction to a standard vaccine, or whether the particular dose she was given was from a rogue contaminated batch.

By Daniel Martin
Health Reporter

A post mortem will take place to determine the exact cause of her death.
The vaccine batch used at the school has been quarantined to test whether it is faulty or was contaminated during production or distribution.

Although other girls at the school, a mixed specialist music college with 1,400 pupils, suffered from dizziness and nausea after the jab it is understood that none were hospitalized.

Critics say the tragedy highlights the risks of mass vaccination because no testing regime can detect all the rare and potentially most lethal side effects.

Last night there were calls for the entire cervical cancer vaccination programme to be suspended. But the Department of Health refused to say whether it would go ahead for the tens of thousands of girls due to receive the jab in the months ahead.

The Cervarix vaccine is being given to all girls aged 12 and 13 in a nationwide programme. All under the age of 18 will have received it by 2016.
The injection is not compulsory but parents who do not wish their daughters to have it must opt out of the programme. Just 30 per cent have done so.

The vaccine guards against infection by the sexually transmitted disease HPV, which causes 70 per cent of all cases of cervical cancer. Although the disease does not usually strike severe adverse reactions do they need before they act?

The school vaccination programme followed clinical trials in 2005 on more than 18,000 women under 26.

Some schoolgirls have experienced health problems after being given the jab.

More than 2,000 have suffered side effects ranging from rashes to paralysis in the year since the vaccine was introduced in schools, according to the Medicine and Healthcare Regulatory Agency.

Around the world, Gardasil and another version, Cervarix, have been linked to 30 deaths as well as cases of Guillain-Barré syndrome - a little-understood immune disorder.

Last year the Daily Mail reported that a girl had been left partially paralysed. Ashley Cave collapsed shortly after having the jab.

And in January last year two schoolgirls died after being given the Gardasil jab in Germany and Austria.

Last night Dr Carol Grady, joint director for public health for NHS Coventry and Warwickshire, said: 'Sympathies are with the family and friends of the child who died.

The incident happened shortly after she received her HPV vaccine.

No link can be made between the death and the vaccine as all the facts are known post mortem takes place.'
Cancer jab girl 'died of tumour'

A girl who was vaccinated against cervical cancer died from a malignant tumour of the chest and not from a reaction to the jab, it has emerged.

Natalie Morton, 14, died after being given the injection at the Blue Coat Church of England School in Coventry.

Deputy coroner for Coventry Louise Hunt said the vaccine was not thought to have been a contributing factor.

A pathologist said her undiagnosed condition was "so severe that death could have arisen at any point".

Natalie collapsed less than two hours after being given the Cervarix vaccine on Monday and was pronounced dead at Coventry's University Hospital.

Her death sparked concern among pupils and parents and on Tuesday HPV1 Cervarix vaccinations were temporarily suspended by some schools and primary care trusts.

The deputy coroner, who opened and adjourned the hearing at Coventry Magistrates' Court, said: "It appears that Natalie died from a tumour in her chest involving her heart and her lungs."

The inquest was told that the tumour had "heavily infiltrated" her heart and extended into her left lung.
OMG... are you SERIOUS?! You think she died coincidentally from the vaccine? Yeah, she has a tumor in her chest, but THAT wasn't what killed her. You people will believe anything that the media tells you. So easily gullible and naive. Well, why don't you look up the 26 year old cheerleader who died is

**Blaming the girl, not the vaccine**

Today, the mainstream media is reporting an obviously-fabricated explanation for her death. A pathologist is declaring that Natalie died from a "malignant chest tumor" that just coincidentally and suddenly killed her within hours after she received the cervical cancer vaccine.

This explanation is obviously a cover story to protect the vaccine industry; and it's not even a convincing cover story at that. Natalie Morton had never been diagnosed with a chest tumor before, and she showed absolutely no symptoms of a cancer tumor. Chest tumors don't just "lash out" and attack their hosts all of a sudden, without warning. A typical death from a cancer tumor is more often a slow, painful wasting away that can take months or years. Natalie Morton was killed in hours, and the description of her symptoms exactly matches what might be expected from an inflammatory reaction to a chemical vaccine.

But why would a pathologist cover up the true cause of Natalie Morton's death? It's simple: **There are billions of dollars in profits at stake.** Natalie's death threatened to put the entire first-world cervical vaccination program on hold. "News of Morton's death came shortly before U.S. health regulators again delayed a decision on whether to allow Glaxo to sell Cervarix in the United States where a panel of specialists has recommended its use," reports Reuters.

The continuation of global cervical cancer vaccination programs -- which generate billions in profits -- absolutely required blaming Natalie's death on something other than the vaccine. Blaming it on cancer is very easy to do, since every person living today has cancerous micro-tumors in their body right now. All the pathologist had to do was locate such a micro-tumor in Natalie's body, then dismiss the vaccine altogether.
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Girly Fitted T-Shirt

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Medium

Body Color

Print Location
Front

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€19.66 each

Quantity
1

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