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Recent development and further prospects of vaccine

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HPV vaccine: designed to prevent cancer

- ~ 18% of worldwide cancer cases are related to infections: parasites, bacteria, viruses (EBV, HBV, HCV, HPV) and thus theoretically preventable
- anti-HBV vaccine appears to be active against liver cancer but was primarily developed to prevent hepatitis
- HPV-specific vaccine designed solely for prevention of cancer

Prevention of cervical cancer

abstinence

condoms

prophylaxis

pre- post-exposure

VLPs chimeric particles?

immune therapy

early HPV proteins?

PAP screening

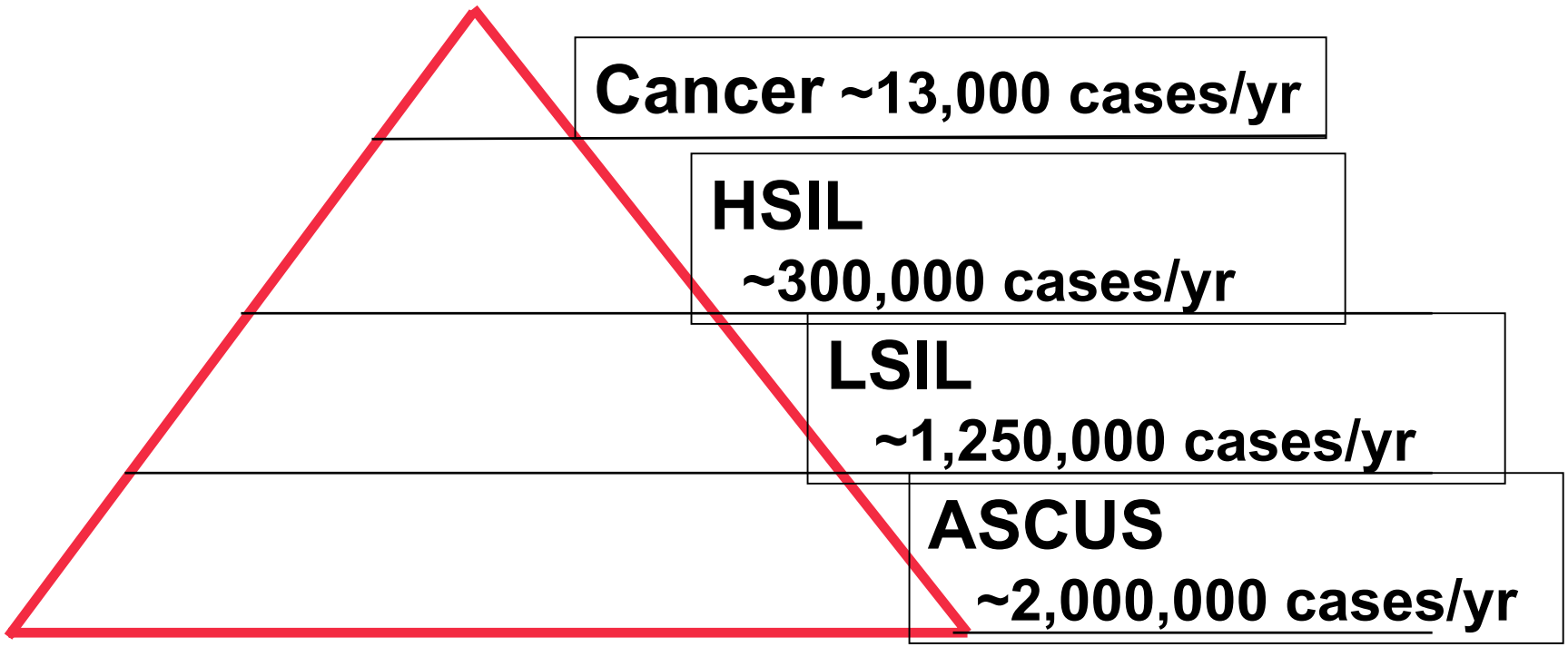
cytology, HPV?, p16?

age 15 20 30 50

Need for Cervical Cancer (anti-HPV) Vaccines

- CxCa is the 2nd most frequent cancer in women worldwide.
- 80% of cases in Third World Countries where screening programs for early detection don't exist.
- In industrialized areas, Pap-screening programs have substantially reduced the incidence but cause
  - discomfort and anxiety to women
  - morbidity by (unnecessary) treatment of cancer precursors
  - substantial costs for medicare

Burden of disease (US): cervical neoplasia



The ASCUS/LSIL Triage Study Newsletter, Vol 1, Issue 1
Janicek MF & Averette HE, 2001; Greenlee RT et al., 2001
http://www.fda.gov/ohrms/dockets/ac/01/slides/3805S1_01%20Goldenthal/sld001.htm

Prevention/treatment of cervical neoplasia: Annual costs US (Mio USD)

	costs x cases	total costs (million USD)
screening	75 x 50 mio	3,500
treatment ASCUS	300 x 2 Mio	600
treatment LSIL	1250 x 1.25 Mio	1,560
treatment HSIL	1500 x 270,000	400
	3500 x 30,000	100
treatment cancer	10,000 x 13,000	130
		6,290

source: BancAmerica Robertson Stephens 1998

Prevention/treatment of cervical neoplasia: Annual costs US (Mio USD)

	costs x cases	total costs (million USD)	savings by vaccination
screening	75 x 50 mio		
treatment ASCUS	300 x 2 Mio	600	360
treatment LSIL	1250 x 1.25 Mio	1,560	936
treatment HSIL	1500 x 270,000	400	240
	3500 x 30,000	100	60
treatment cancer	10,000 x 13,000	130	78
		2,790	1,674

source: BancAmerica Robertson Stephens 1998

Clinical Development

therapeutic trials: results of 27 phase I/II studies (n=772)

- **no major side effects**
- **Immune response (IR) in some patients: abs, CTL, cytokines**
- **clinical response (CR) variable in cancer patients**
- **CIN, VIN and AIN patients showed promising clinical results**
- **poor correlation between IR and CR**

Clinical development: results

prophylactic trials (phase I/II): HPV 16/18 L1 VLPs (n=4466)

- well tolerated
- highly immunogenic: neutralizing antibodies
- sustained ab response with appropriate adjuvant
- protection (type-specific?) against persistent infection and high grade dysplasia
- clinical efficacy data (cancer) not yet available
- early licensing expected

HPV-specific cervical cancer vaccine: marketing is shortly ahead

People In Life Sciences P.I.L.S. Home

New report on cervical cancer vaccine gets media jumping

April 21, 2005

Mark Terry

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A media and industry buzz was created with the publication of a paper in *The Lancet Oncology* by researchers at Merck & Company, Inc., about results from a Phase II clinical study comparing their new human papillomavirus (HPV) vaccine, [redacted], against a placebo. There are currently two major clinical trials underway for an HPV vaccine, the other for a vaccine called [redacted] by GlaxoSmithKline.

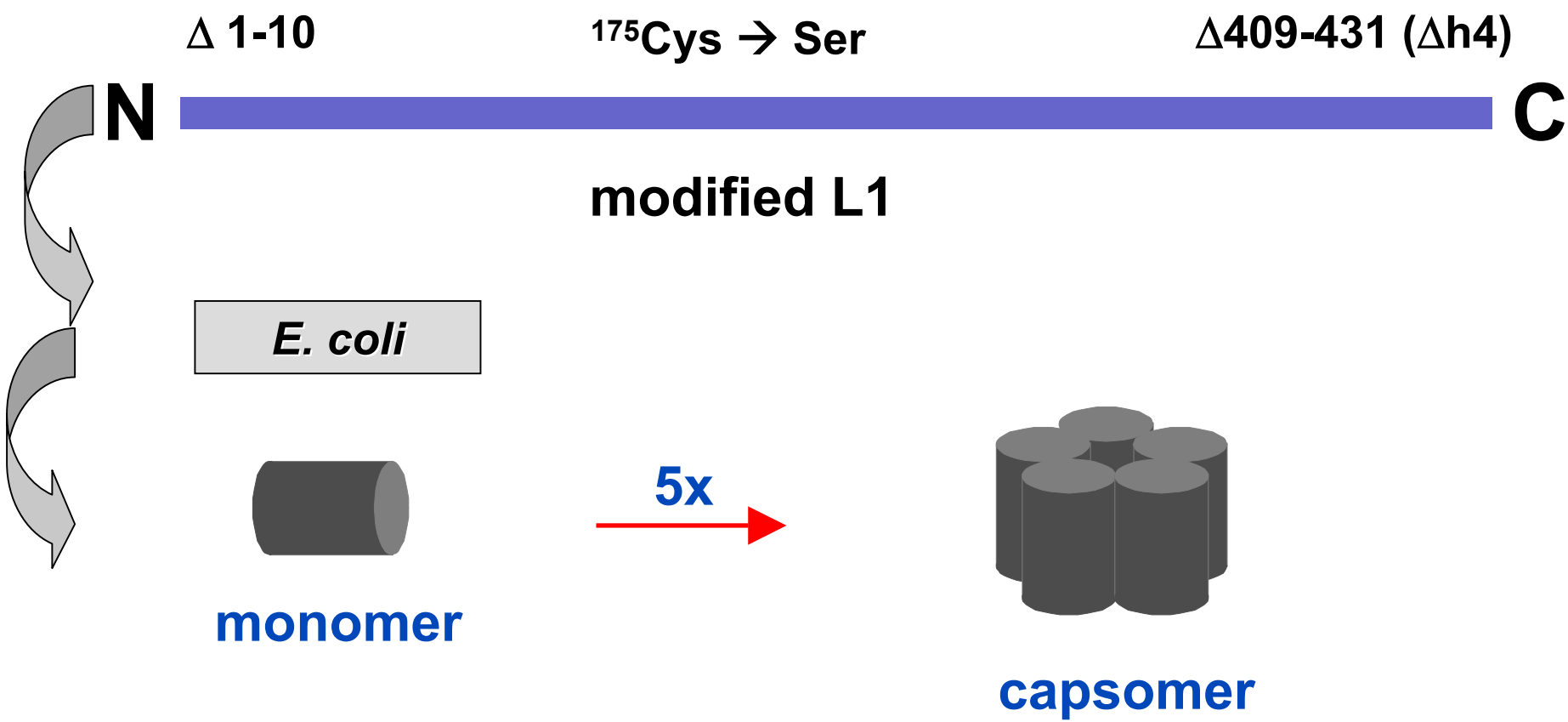
HPV-specific cervical cancer vaccine: some challenges

- HPV plurality
- duration of protection ?
- long-term effect of prophylactic vaccine
  → need for immune therapy
- public acceptance of vaccination (male factor) ?
- impact on screening, compliance after vaccination ?
- biological balance between HPV types ?
- special needs for developing countries

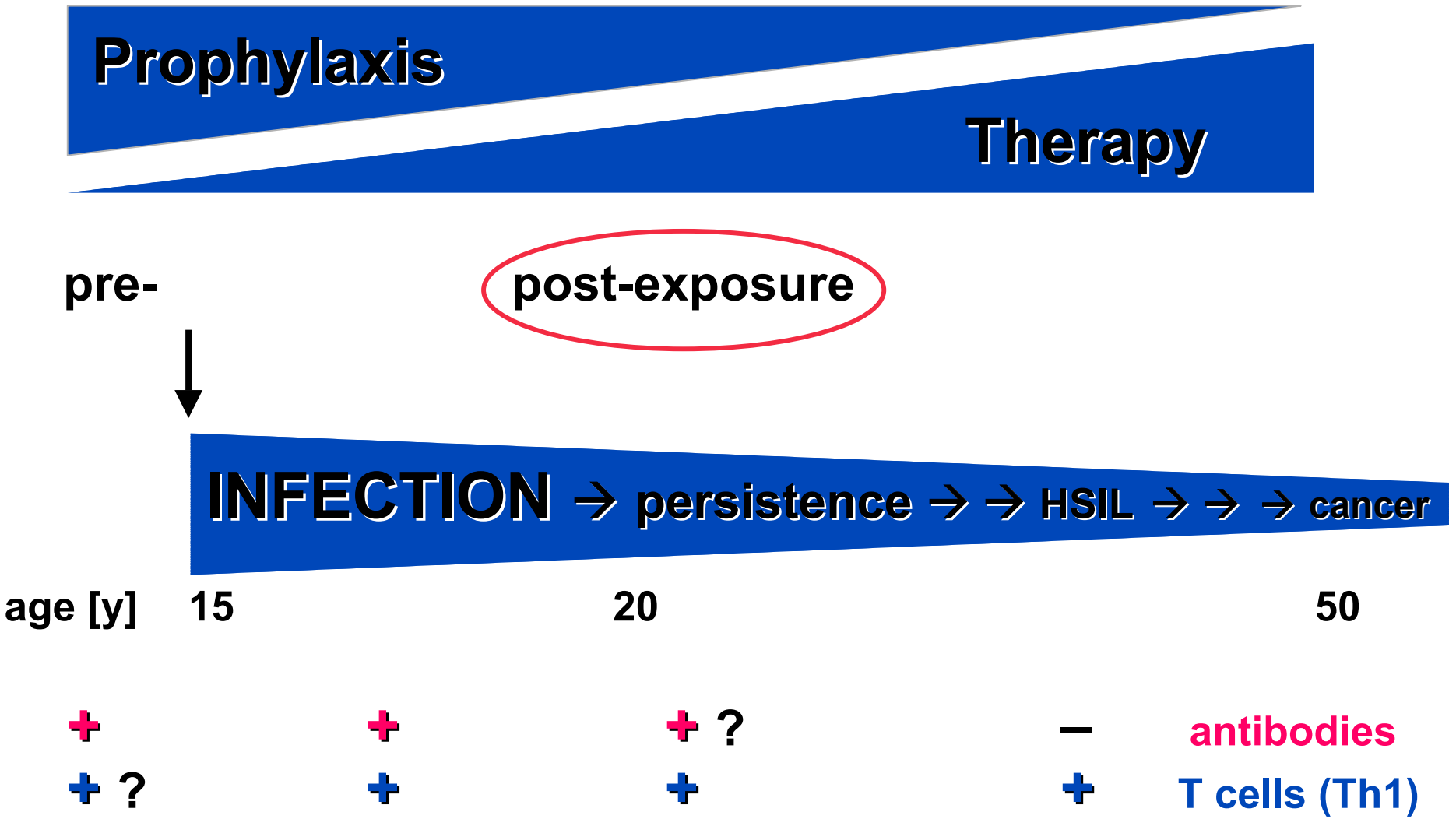
2nd generation HPV vaccines: needs and feasibility

- cross-protecting vaccines — industry
- therapeutic vaccines (DNA, peptides) — academia
- vaccines for low-budget countries — public
  - economical production
  - stable vaccine
  - non-invasive immunization
  - post-exposure prophylaxis

HPV 16 L1 capsomeres: more stable and less costly



HPV-Specific Cervical Cancer Vaccines



HPV chimeric capsomeres

- prophylactic and therapeutic features
- treating persistent infections and preventing re-infection in a post-exposure scenario
- suitable for developing countries

HPV chimeric capsomeres

- generation of expression plasmids (E6, E7)
- production of chimeric capsomeres
- characterization
  - size, structure, activation of DCs
  - antibodies, CTL, tumor rejection
- selection of vaccine candidate
- GMP production
- phase I clinical trial

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Grand Challenges in Global Health