La prevenzione delle infezioni da HPV in Europa

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Chi li riconosce?

Harald zur Hausen

Premio Nobel per la Medicina 2008

Motivazione:
“Per la scoperta che il virus del papilloma umano causa il cancro della cervice uterina”
Two prophylactic HPV vaccines have been licensed in Europe: the quadrivalent vaccine, Gardasil® (Sanofi Pasteur MSD) and the bivalent vaccine, Cervarix® (GlaxoSmithKline Biologicals).

Both vaccines protect against the high-risk HPV types 16 and 18, responsible for an estimated 73% of cervical cancer cases in Europe. Gardasil also protects against HPV 6 and 11, which cause most cases of genital warts.

In large phase III trials both vaccines have been shown to prevent more than 90% of precancerous lesions associated with types 16 or 18 among HPV-naive women.
Stato dell’introduzione della vaccinazione HPV in UE (2007)

EU + EEA countries

- Program implemented (5)
- Recommendation (7)
- not yet (17)

source: VENICE
Stato dell’introduzione della vaccinazione HPV in UE (2008)

EU + EEA countries

- Program implemented (7)
- Recommendation (8)
- not yet (14)

source: VENICE
Stato dell’introduzione della vaccinazione HPV in UE (2009)

EU + EEA countries

- Program implemented (9)
- Recommendation (6)
- not yet (14)

source: VENICE
Stato dell’introduzione della vaccinazione HPV in UE (2010)

**EU + EEA countries**

- **Blue**: Program implemented (14)
- **Light Blue**: Recommendation (3)
- **Red**: not yet (12)

*source: ECDC*
Stato dell’introduzione della vaccinazione HPV in UE (2012)

EU + EEA countries

- Program implemented (20)
- Recommendation (3)
- not yet (6)

source: ECDC
Raccomandato in 23 Stati Membri (3 a pagamento)
HPV e ineguaglianze

Mortalità standard per cancro della cervice in donne 0-64 anni

Human Development Index
HPV e ineguaglianze

Mortalità standard per cancro della cervice in donne 0-64 anni

Human Development Index
Costo della vaccinazione HPV

Il prezzo per una dose da 10/15 € a >100 €!

In un Paese Europeo di medie dimensioni, come la Polonia, significherebbe risparmiare circa 17 milioni € l’anno per coorte vaccinale (2 milioni invece di 19 milioni!)
La costo-efficacia dei 2 vaccini, confrontata in diversi modelli – se pur pieni di limiti – non è sovrapponibile, soprattutto per le nuove evidenze relative al burden dei condilomi anogenitali: il **vaccino bivalente dovrebbe costare 20-42 euro in meno.**

La vaccinazione anti-HPV è costosa e difficile da completare: spiega in parte le basse CV. Possibilità che **schedule ad 1 o 2 dosi** siano ugualmente efficaci di quella raccomandata a tre dosi: se risultati confermati, grande impatto sui costi e le strategie per i programmi di vaccinazione HPV.

Evidenze di non-inferiorità di programmi alternativi, in cui il ciclo di tre dosi è completato in >6 mesi (es. 3° dose a 12 mesi)
“Coverage rates, when available, range from 17-84% and are generally lower than expected”
Campagna vaccinale HPV in UK

- Quasi 300.000 ragazze in ogni coorte di età
- Copertura superiore a 90% per la prima dose
- Coperture >85% per la terza dose
Come demolire un successo

Morte improvvisa di una adolescente dopo vaccinazione HPV
La potenza della “a”

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Adverse event YES and Vaccination NO have the case b. Adverse event NO and Vaccination NO have the case d.
Schoolgirl dies after cervical cancer vaccination

- HPV vaccine batch quarantined as 'precautionary measure'
- Vaccination part of national immunisation programme

Jo Adetunji
The Guardian, Tuesday 29 September 2009 01.49 BST
Article History

Girl who died after cervical cancer injection had tumour in her chest

Death of Natalie Morton due to underlying medical condition, inquest hears

Owen Bowcott
guardian.co.uk, Thursday 1 October 2009 11.36 BST
Article history

Natalie Morton, aged 14, from Coventry. Photograph: Caters News Agency Ltd

Natalie Morton, aged 14, from Coventry. Photograph: Caters News Agency Ltd
Scienza vs Disinformazione
Gardasil is the HPV vaccine, touted to fight cervical cancer. What they are not telling you is that thousands of girls are having adverse reactions to the HPV Vaccines, some have even died—at last count, at least 103 lives have been lost. We have got to do something about this. These girls need our help! These girls are having reactions such as; seizures, strokes, dizziness, fatigue, weakness, headaches, stomach pains, vomiting, muscle pain and weakness,
Comunicazione emotiva
Nessun sito istituzionale nella prima pagina di risultati Google
Vaccino anti-HPV (papillomavirus umano) - VaccinarSi
www.vaccinarsi.org/vaccini-disponibili/vaccino-anti-hpv.html
22/apr/2013 - I vaccini anti HPV, somministrati prima dell’esposizione al virus, prevenendo le lesioni genitali .... Effetti indesiderati della vaccinazione.

Vaccinazione contro il Papilloma Virus - VACCINAZIONI ...
www.asl.milano.it › ... › VACCINAZIONI ›
17/ott/2013 - A chi chiedere la vaccinazione contro il virus HPV? ... Gli effetti collaterali più comuni sono rappresentati da reazioni nella sede di iniezione ...

VAERS: 371 gravi reazioni avverse dopo vaccinazioni con G...
www.disinformazione.it/gardasil.htm
gardasil, vaccino, vaccinazione, cancro, farmacovigilanza, farmacosorveglianza, effetti collaterali, danni collaterali, papilloma virus, merck, lobbies.

Il Ministero della salute giapponese ritira la raccomandazione...
www.comilva.org/.../ministero_della_salute_giapponese Ritira raccomand...
17/giu/2013 - Tuttavia, sono stati segnalati 1.968 casi di possibili effetti collaterali, tra cui il ... La raccomandazione attiva del vaccino HPV deve quindi essere ...

Vaccinazione Papilloma virus HPV | Vaccini pericolosi | Na...
www.naturopatia-blog.it/papilloma-virus-vaccinarsi-oppure-no/
02/apr/2013 - Papilloma virus: vaccinarsi oppure no? Tutto quello che dovresti sapere sul vaccino anti Papilloma virus. Rischio, effetti collaterali, sicurezza del ...
ECDC Guidance on HPV introduction in Europe - 2008

- The reviewed data covered local and systemic events in short-term and long-term events up to six years, including pregnancy events. They concluded that the current evidence on the safety of HPV vaccines is reassuring *

- During adolescent vaccine campaigns, some mass sociogenic illnesses such as postvaccination dizziness and syncope have been reported *

*Data review by the WHO’s Global Advisory Committee on Vaccine Safety
**ECDC update on 2008 Guidance published September 2012**

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- 7 randomised controlled trials selected
- 44,000 females
- Risk of serious adverse events equal between vaccinated and not vaccinated

EMA statements after vaccine scares with Gardasil

• January 2008. Two reports concerning the sudden and unexpected deaths of two young women in Austria and Germany. [...] On the basis of the currently available evidence, the EMEA’s Committee for Medicinal Products for Human Use (CHMP) is of the opinion that the **benefits of Gardasil continue to outweigh its risks** and that no changes to its product information are necessary.

• February 2009. Two cases of status epilepticus with myoclonus reported in two girls vaccinated with the cervical cancer vaccine Gardasil in Spain. The EMEA’s CHMP has concluded that the **cases are unlikely to be related to vaccination** with Gardasil and that the benefits of Gardasil continue to outweigh its risks.
EMA statements after vaccine scares with Gardasil (2)

- September 2011. Letter in response to concerns by Sane Vax Inc. The CHMP noted that the presence of recombinant DNA fragments does not represent a case of contamination and is not considered to be a risk to vaccine recipients. The information brought to the attention of the CHMP by Sane Vax Inc. is not considered to provide new information about the quality of the vaccine.

- Concerning the highlighted case of Juvenile Rheumatoid Arthritis observed in association with a third dose of Gardasil, the information is very limited. In view of the total number of doses of Gardasil distributed since launch in 2006, i.e. more than 79 million doses worldwide, this case might well be within the expected number of Juvenile Rheumatoid Arthritis cases in the vaccinated population but coinciding with vaccination.
Data on safety in males are indicating the same safety profile as in females:

Adverse event surveillance in the US

Vaccine Safety Datalink:

In 2011, VSD active looked at specific adverse events following more than 600,000 doses of Gardasil, such as Guillain–Barré Syndrome (GBS), stroke, venous thromboembolism, appendicitis, seizures, syncope, allergic reactions, and anaphylaxis.

No statistically significant increased risk for any of these adverse events was detected after vaccination.

• Attitudine dei Medici di Famiglia in Europa:

**Luttringer-Magnin et al. 2011:** A total of 80.8% of GPs reported a favourable opinion of HPV vaccination, 17.4% were uncertain and 1.8% were opposed. The main difficulties in providing HPV vaccination were patients' concerns about potential side effects (cited by 37% of the respondents)

**Piana et al. 2009:** In this study, 89.6% of family physicians answers were in favour of HPV. The family physicians most in favour of vaccination were those who were confident of the vaccine’s safety [...]

Nuove strategie delle lobby anti-vaccini

• 3 casi di insufficienza ovarica primitiva in seguito a vaccinazione HPV
• Suggerito il link con gli adiuvanti
• Espressione di ASIA: Autoimmune Syndrome Induced by Adjuvants

Cosa dicono i case reports

1. Tre casi sporadici di insufficienza ovarica primitiva
2. Due dei quali in due sorelle
3. Descrizione dei casi decisamente confusa ("the patient reported that her last period occurred shortly after the last injection of the HPV vaccine")
4. Le tre ragazze erano state vaccinate con Gardasil (adiuvante: alluminio)
5. Nessun tentativo di valutare l’associazione causale

ASIA: case definition

Major criteria:
1. Exposure to an external stimulus (infection, vaccine and/or immune adjuvants) prior to clinical manifestation
2. The appearance of ‘typical’ clinical manifestations: myalgia, muscle weakness, arthralgia and/or joint pain, chronic fatigue, sleep disturbances, neurologic manifestations, cognitive disturbances, pyrexia
3. Removal of inciting agents induces improvement
4. Typical biopsy of involved organs

Minor criteria:
1. The appearance of autoantibodies
2. Other clinical manifestations
3. Specific HLA
4. Evolvement of autoimmune disease

1 major + 2 minor criteria define ASIA

"ASIA or Shoenfeld syndrome" su Pubmed riporta 496 articoli!

Monitorare l’impatto della vaccinazione

- Nessuna sorveglianza delle infezioni da HPV a livello Europeo
- Registri tumori e programmi di screening limitati
- Pochi registri vaccinali

Registri vaccinali disponibili in 11 Paesi (5 hanno registri nazionali e 6 registri regionali). In aggiunta, 9 Paesi riferiscono l’intenzione di sviluppare registri nazionali.*

*VENICE II report on Vaccination coverage assessment in EU/EEA, 2011
HPV nell’UE
punti di forza e limiti

✅ Avvio rapido (in confronto ad altre vaccinazioni)
✅ La maggioranza dei programmi sono finanziati dal SSN
✅ Numerose “good practice” da poter diffondere

❌ Problemi nel monitoraggio delle AEFI
❌ Necessità di migliorare la comunicazione basata sulle evidenze (personale sanitario!)
❌ Lobby antivaccinali molto attive
❌ Politica dei prezzi da governare
❌ Monitoraggio dell’impatto al momento carente
Chi vincerà?
Grazie

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