

HPV Vaccine In The UIP: Is it a Sound Move?

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Talking Points

- What is Cervical Cancer?
- Risk factors for cervical cancer/
- Incidence & trends in India.
- HPV as a risk factor for cervical cancer
- Precancerous lesions and their course.
- Evidence on HPV Vaccines
 - Past misadventures
- Gaps in the evidence.
- Recommendations for policy makers.

CERVICAL CANCER



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Risk factors for Cervical Cancer

- **Multiple Sex Partners (either partner)**
- **Poor Genital Hygiene**
- **Early Age of Marriage**
- **Repeated Pregnancies**
- **Human Papilloma Virus**

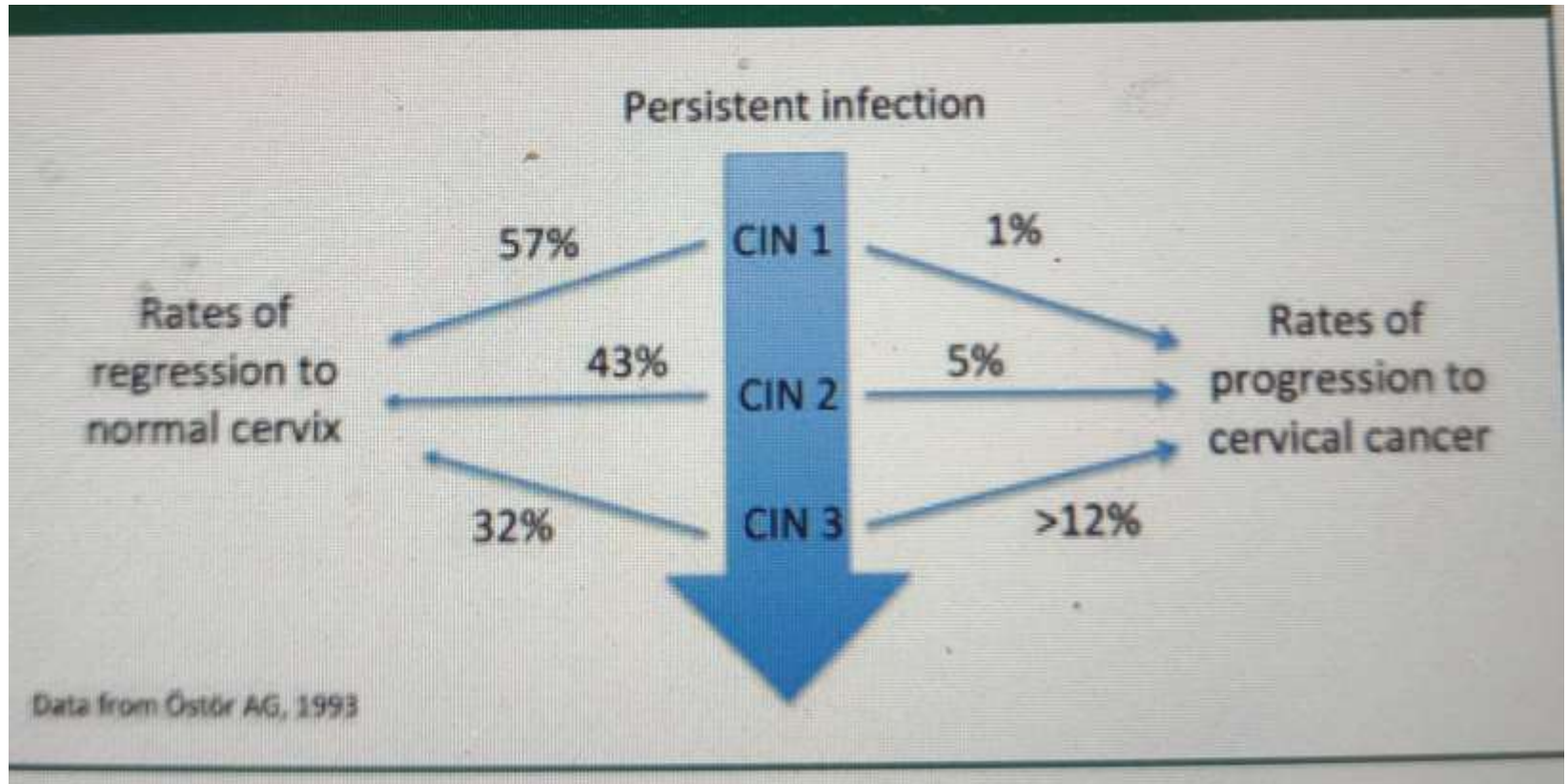
Incidence and trends in India vis-a-vis MMR

- New cases 14.7 per 1,00,000 women
- Deaths **9.2 per 100,000 women**
- Decline in incidence >21% and mortality >32% in 3 decades, 1990 – 2019
 - [Singh M, Jha RP, Shri N, Bhattacharyya K, Patel P, Dhamnetiya D. Secular trends in incidence and mortality of cervical cancer in India and its states, 1990-2019: data from the Global Burden of Disease 2019 Study. BMC Cancer. 2022 Feb 7;22(1):149. doi: 10.1186/s12885-022-09232-w. PMID: 35130853; PMCID: PMC8819855.]
- Deaths due to Child Births: **97 per 100,000 childbirths**
 - [<https://pib.gov.in/FeaturesDeatils.aspx?NoteId=151238&ModuleId%20=%202>]
- Deaths due to Child Birth in West: 12 per 100,000 childbirths

Human Papilloma Virus As Risk Factor

- **There are > 100 strains of HPV**
- **Out of these Type 16 and Type 18 considered risk factor for cervical cancer. (others 31,33,42,45,52,58.) 6 & 11 genital warts.**
- **Majority of HPV infections are asymptomatic & resolve spontaneously.**
- **Prevalence of HPV varies from 2% – 42%**
- **High prevalence found in patients with cancer.**
- **Women living with AIDS - 54%**

Natural History of Pre-Cancerous Lesions



What are the limitations in Evidence?

- We do not know how well HPV vaccination will protect against cervical cancer.
- Trials have not focused on the outcome of cervical cancer
- They had too few participants and did not follow them up for long enough:
- Cervical cancer may take decades to develop.

- Published numbers from randomised controlled trials may overstate efficacy because:
 - (a) testing occurred too frequently in the trials when, in real-world settings, lesions may regress spontaneously;
 - (b) trials used composite surrogate outcomes, some of which, such as HPV-infection and CIN1, occur more frequently than others and are very unlikely to progress to cancer; and
 - (c) subgroups were over-analysed.

- The trial populations have limited relevance and validity for real world settings:
 - for example, women in the trials were older than the target population;
 - we do not have enough data on the benefits in women who may have been exposed to HPV before they were vaccinated and who do not know their HPV status.

- We do not have enough data on the impact of the vaccine on CIN3, which is more likely than CIN1 and 2 to progress to cervical cancer. We also have less data on the impact on cervical disease due to any HPV type rather than just lesions due to HPV 16 and 18.

- Women should still attend regular cervical screening because efficacy in preventing cervical precursors is $<100\%$
- There are more oncogenic types than covered by the HPV Vaccine.
- There is good evidence that Cervical Cancer Screening reduces risk of death irrespective of vaccination status.
- Number of cervical cancer deaths have reduced drastically in the last three decades before vaccine rollout.

- Information from the trials can tell us what happens between five and nine years after vaccination, but we do not know if protection wanes after this time.
- A recent observational study provides some evidence of efficacy against CIN3 in girls vaccinated before sexual debut.
- Ongoing observational studies may tell us about the long-term effect on rates of cervical cancer, but it will take many years before we have the evidence.

Past Mishaps – The Indian Experience

- HPV vaccine trials among adolescent tribal girls, undertaken in a low-key manner in India, in 2009.
- PATH (Gates Foundation) conducted the trials in Andhra Pradesh and Gujarat from July 2009 to October 2010.
- Described it as an observational study instead of a formal clinical trial to circumvent thorny ethical issues.

Past Indian Misadventure contd...

- During the trial, a few girls died after receiving the vaccine.
- None reportedly had any prior illness.
- All were residents of a government-run hostel for tribal children.
- Stakeholders claimed that the deaths were unrelated to the impact of the jabs.
- But still, there was an outcry.

Mishaps...contd...

- The central government halted the trial.
- ICMR claimed the deaths were coincidental.
- People demanded an independent enquiry, even as the state government said the girls committed suicide.
- Other side effects included - symptoms such as epileptic fits, mood swings, and severe stomach illness

Past mishaps in India...contd...

- The tragedy was investigated by the Parliamentary Standing Committee on Health and Family Welfare. It submitted the 72nd Report – Alleged Irregularities in the Conduct of studies using human papilloma virus vaccine (HPV) by PATH in India – to both houses of Parliament on August 30, 2013.

- The Parliamentary Committee found that ICMR had signed an MoU with PATH in 2006 to support the trials before the Drug Controller General of India (DCGI) had approved the vaccine.
- It also questioned the ICMR's role in trying to promote the inclusion of the vaccine in the Universal Immunisation Programme (UIP) before any independent study about its efficacy.

Past mishaps contd...

- The committee noted that all seven deaths were dismissed as “unrelated to vaccinations without in-depth investigations”.
- According to the inquiry committee report, the speculative causes of death were suicides, accidental drowning, malaria, viral infections, subarachnoid haemorrhage (without autopsy) etc.
- The committee also noted that “suicidal ideation” is caused by many drugs.

Past mishaps...contd

- The Parliamentary Committee recommended that the matter be inquired into by a premier investigating agency. But it has almost been a decade since then. No such investigation has been carried out yet.
- Meanwhile, they seem to have built stronger alliances. While the MoU between the ICMR and PATH was looked at critically by the Parliamentary Committee a decade back, there seems to be scant respect for such censure.

Sleeping with the enemy...contd.

- Recently, the ICMR signed signed a Declaration of Intent (DoI) with BMGF and US-based (NIH) National Institutes of Health in research collaboration.
- And lobbying is underway to include the HPV vaccine in the UIP.

Medical Imperialism

- Well, the British ruled India by giving “sultanates” to petty Indian kings.
- These local satraps were effective at maintaining British rule and gained much from being loyal to the British.
- The British signed treaties and made military and trading alliances with many of the independent states that made up India.

Medical Empires contd...

- Today, are we witnessing the Era of Medical Imperialism where MoUs and grants for research are being offered by foreign donors as long as the recipients listen to their master's voice?

Class action lawsuits in USA

- New research has claimed that Gardasil can possibly induce and increase, in some cases, the risk of autoimmune diseases and other serious health complications, including Postural Orthostatic Tachycardia Syndrome, Neuropathy, and Fibromyalgia. Gardasil has also allegedly been linked to premature ovarian failure and infertility.
- However, the US CDC (Centers for Disease Control and Prevention) says on its website that “there is no relationship between Gardasil and autoimmune disorders”. The US NIH’s National Library of Medicine echoes the CDC’s view on the subject.

Lawsuits in USA contd...

- It is alleged that Merck could have obtained FDA approval for Gardasil in 2006 based on deceptive research and clinical trials, which seemingly misrepresented the efficacy of the vaccine while concealing its adverse effects.
- According to reports, some marketing campaigns for the HPV vaccine appear to have led to millions of parents opting to vaccinate their pre-teen daughters.
- These concerns eventually snowballed into the Gardasil Class Action Lawsuit in the US.

Present Medical Consensus

- The medical consensus favours adoption of HPV vaccination programmes for pre-adolescents girls (and also boys in some countries), but without adequate evidence of its efficacy.
- The WHO and standard textbooks recommend it.
- It is included in vaccination program of 125 countries.
- WHO says it will prevent 45 million deaths in the next 100 years.

2%
off

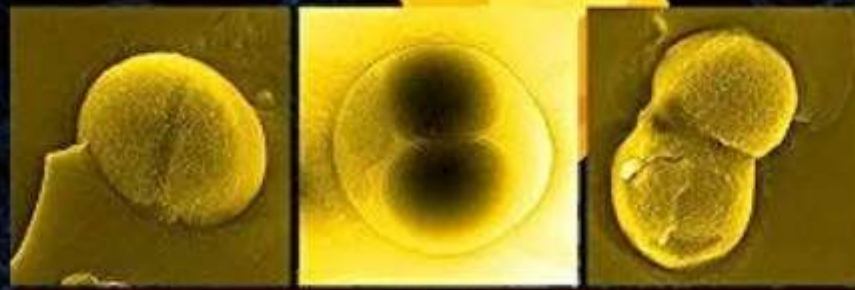
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Plotkin's **VACCINES**



Foreword by Bill Gates

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What our policy makers should suggest

- Establish national baseline data on
 - cancer incidence,
 - mortality, and
 - HPV subtype prevalence
- This will decide whether the vaccines will be cost effective and should be a priority.
- Ensure cancer surveillance and registration are in place before any mass rollout of vaccine
- Initiate national long term efficacy and effectiveness studies free from industry funding.
- AEFI reporting system should be in place.

References

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Thank You