CERVICAL CANCER CONTROL PROGRAM IMPLEMENTATION BY USING THE "SPICE" STRATEGY OF RAJ ©

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I. INTRODUCTION

Cervical cancer is responsible for about 500000 cases and 270000 deaths per year, worldwide. Cervical cancer is a Preventable Cancer and is targeted for Elimination by 2030. Screening by HPV testing, Pap smear, VIA would result in the identification of CIN lesions which are precursors for cervical cancer. Specific treatment like Cryotherapy, LEEP, Cold coagulation and Laser ablation are effective. Follow up studies, world over have indicated that screening and effective management of pre cancer stages result in reduction of incidence of Cervical Cancer and mortality due to Cervical Cancer.

The Editor / Author has a proof of concept of a model which has resulted in successful screening and reduction of invasive cancer by 25% and mortality by 35% in a period of about 7 years. The author served as PI for this project during 2000-2004, especially in the phase of conception , planning and implementation.

With added experience from several other projects during 2000-2018, the author has developed Screening Protocols. He is advocating them in the chapter for the benefit of Health Planners in developing Countries.

II. "SPICE" STRATEGY

S- SCREENING - 3 tools
P- PRECANCER - 3 treatments
I- IMMUNISATION - 3 types of HPV Vaccines
C- COMMITMENT - 3 levels - global, regional, local
E - ELIMINATION - 3 levels of prevention - Primary, Secondary, Tertiary

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S – Screening: Screening is a process in which, apparently normal individuals are subjected for simple tests to detect abnormalities. Also, the management of the abnormal conditions is included in the process of Screening.

III. SCREENING FOR CERVICAL CANCER

Women in the age group of 25-65 years,who are with or without symptoms, are invited to undergo screening tests,

Types of Screening Tests

1. **PAP Smear Test:** This is also called the conventional cytology test. This test is used worldwide for many years, Pap Smear is a simple test in which the cervical cells are collected from the squamo-columnar junction of the uterine cervix, by using a wooden spatula and this is fixed in a glass side and sent for histo-pathological evaluation.

   According to the cytology results, the case is diagnosed and if found to be positive for Dysplasia or CIN, pre cancer management is done. The Pap smear Sensitivity is about 45% and Specificity around 65%. (1)

2. **Liquid based Cytology – LBC:** In this test, the cells are collected and kept into ethanol or methanol ,later a single layer of cells are prepared and examined under light microscope LBC has the sensitivity of 82.8% (specificity 62%) in one study; in the other study, the sensitivity ranged from 41.7% (specificity 90.2%) to 82.6% (specificity 52.2%) and the specificity from 52.2% (sensitivity 81.9% or 82.6%) to 90.2% (sensitivity 41.7%), (2)

3. **HPV- DNA Test:** This is an advanced technology test, where the cells are examined for HPV –The high risk strains of HPV -16,18,31,45.The positive ones are subjected for pap smear test .

Table 1: Management Protocol for Test Positives

Recommended Management of Combined HPV Test and Pap Test		
HPV Test	**PAP Test**	**Management**
Negative	Negative	Repeat testing in 5 years
Any	Negative	Repeat testing in 3 years
Negative	Atypical squamous cells of undetermined significance (ASC-US)	Repeat testing in 3 years
Negative	Low grade squamous intraepithelial lesion (LSIL)	Repeat testing in 6–12 months
Not performed	Atypical squamous cells of undetermined significance (ASC-US)	Repeat testing in 6–12 months
Positive	Negative	Repeat testing in 6–12 months
Not performed	Low grade squamous intraepithelial lesion (LSIL)	Immediate colposcopy
Positive	Low grade squamous intraepithelial	Immediate colposcopy

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	lesion (LSIL)	
Any	Atypical squamous cells – cannot rule out high grade lesion (ASH-H)	Immediate colposcopy
Positive	Atypical squamous cells of undetermined significance (ASC-US)	Immediate colposcopy
Any	High-grade squamous intraepithelial lesion (HSIL)	Immediate colposcopy
Any	Squamous cell carcinoma (SCC)	Immediate colposcopy
Any	Atypical glandular cells (AGC)	Immediate colposcopy

Source: Wikipedia

The sensitivity of HPV testing was 94.6%, whereas that of Pap testing was 55.4%. The specificity was 94.1% for HPV testing and 96.8% for Pap smears. (3)

4. Visual Inspection with Acetic Acid –VIA

Visual Inspection with Lugol's Iodine - VILI

This test is most suited for low and limited resource settings. The age group ideal for the VIA/VILI tests is 30-60 years .even a single test is good enough to detect pre cancer lesions. In many studies ,single round of VIA has shown a reduction in the incident rate of Cervical Cancer and also reduction in the mortality rate due to cervical cancer. The author**,** has served as principal investigator of such a project, which he quotes below as the Proof of Concept. The project was in collaboration with the IARC /WHO during 2002-2007. (4)

- **Background of VIA Project (4):** The Effect of VIA, as a Screening tool, was tested in a RCT, in Dindigul district, Tamil Nadu, during 2000-2007

- **Methods:** From 114 study clusters, 57 were randomised to Single Round of VIA by trained nurses, and 57 to a control group. Apparently normal woman aged 30 - 59 years, were enrolled for the study. The VIA Positive had Colposcopy directed Biopsy, and, Cryotherapy, in the same visit. Advanced lesions were referred, for higher treatment., Incidence rate of Cervical Cancer and Mortality rate due to Cervical Cancer, were analyzed as the Primary Outcome of the study.

- **Results**
  Eligible women : 49 311.
  Screened: 31 343 (63.6%)
  Screene Positives: 3088 (9.9%)
  Colposopy: 3052
  Colposcopy directed Biopsy: 2539
  Pre Cancer: 1874
  Treated with Cryotherapy / LEEP : 1349
  In the intervention group, 274 430 person years, 167 cervical cancer cases, and 83 cervical cancer deaths were accrued compared with 178 781 person-years, 158 cases, and 92 deaths and in the control group during 2000–06 (incidence hazard ratio 0·75 [95% CI 0·55–0·95] and mortality hazard ratio 0·65 [0·47–0·89]). (4)

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- **Discussion:** VIA screening, in the presence of good training and sustained quality assurance, is an effective method to prevent cervical cancer in developing countries (4)

- **Challenges in Screening:** In most of the cervical cancer screening projects across the world, there is low participation of women. this may be due to the following reasons. The solutions are also given in the form of screening protocol

Challenge	**Screening Protocol**
1. Accessibility	The screening clinics have to be arranged in mobile vans or nearby health posts .the woman should not be referred to far away places.
2. Cost is an inhibitory factor	The cost of Pap is about 10-15 USD, and HPV-DNA test is about 40 USD, but VIA/VILI is cost effective and the cost is around 5 USD This cost could be managed by the health care providers by mobilizing source from internal/external sources
3. Functional Barrier	Only Female Nurses /.Doctors to provide services like screening and treatment
4. Multiple visits are difficult	Single visit - See & Treat Policy
5. Referrals for Treatment - Logistics	Screening & Treatment under the same roof
6. Followup Services - Regular & Complete	Volunteers & Health workers , to be engaged

IV. P - PRECANCER

Treatment of pre cancers is by different modalities to suit the specific clinical situations.

1. **Cryotherapy:** A highly effective method for the treatment of CIN 2,CIN2 lesion ,which are small involving less than 75% of transformation zone –TZ .

   Highly pressurized Nitrogen di oxide is used to coagulate the tissues by using "single or double freeze technique". the whole procedure lasts for less than 1 hour .no anesthesia is needed and it can be done by well trained nurses. The technology is low cost and a cryotherapy procedure costs around 20-30 USD

2. **Cold Coagulation / Laser Ablation:** The other ablative modality of pre cancer treatment are Cold Coagulation Laser Ablation ,they are well suited for the treatment of CIN I,II,III lesions .the cost factor in low resource settings is still under study.

3. **LEEP (Loop Electro Excision Procedure):** This is a surgical modality in which the pre cancer lesion is excised as a cone and removed .this is ideally suited and remove large lesions of CIN I-III, Which involve more than 7-5 Transformation Zone –TZ.

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The settings are like that in a surgical room and the procedure requires more equipments, instruments .this can be performed only by a highly competent, well trained person good in surgical skills. the cost is at higher than other modalities.

V. I - IMMUNISATION

In India, there are about 511.4 million women, aged more than 15 years to 60 years, who are at risk of developing cervical cancer, with HPV 16 & 18, accounting for, about 80% of all Cervical Cancers. Every year, there are about 123,907 new cases of Cervical Cancer with 77,348 Deaths due to Cervical Cancer - Globocan 2020. (5)

Types of Vaccines presently aActs against b4 vStvailable in India (5)

1. **Gardasil :** Acts against 4 Strains of HPV - 6,11, 16 &18, which account for about 85 % of all Cervical Cancers.
   - **Gardasil – 9:** Nonovalent vaccine, licensed from 2018, in India. Addresses the 9 Oncogenic strains - 6,11,16, 18 and 32,33,45,52 and 58

   - **Cervavac – Acts against 4 strains - HPV 6,11, 16 &18**. Made in India and available from 2023. A cost effective Vaccinre for India.

Vaccination Guidelines: Quadrivalent & Nonovalaent HPV Vaccines
Girls: 9 to 14 years. 2 doses. 0 & 6 months (IM)
Catch up Vaccination: 15 - 26 years. 3 doses. 0, 2, 6 months (IM)
- Later age Vaccination : (27 - 45 years) . 3 doses. 0 - 2- 6 months,. (IM)

Best Method is to Vaccinate before the starting of Marred Life

WHO Recommendation - 2022 (5)
- **A one or two-dose schedule** for girls aged **9-14 years**
- **A one or two-dose schedule** for girls and women aged **15-20 years**
- **Two doses with a 6-month interval** for women **older than 21 years**

VI. C – COMMITMENT

1. Global Level

Cervical Cancer Elimination By 2030 - The Commitment at Global level (6) b**y** WHO. The WHO call for Elimination of Cervical Cancer in- May, 2018. The Global strategy was framed in 2020 at the World Health Assembly

2. Regional Level

Commitment by 190 Countries - Regional level
The target set by all countries, is to achieve the Incidence rate, of < 4/100 000.
90% Vaccination - 70% Screening - 90 % Treatment (Precancers & Cancers)

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To eliminate cervical cancer, all countries must reach and maintain an incidence rate of below 4 per 100 000 women. Achieving that goal rests on three key pillars and their corresponding targets:

3. Local level

The Teal Ribbon Movement - many Public places all over the World, were illuminated with TEAL light, on 17th Niovembert, to symbolize the Global efforts for Elimination of Cervical Cancer by 2030

17 November marks the Cervical Cancer Elimination Day of Action and the anniversary of the launch of the World Health Organization's (WHO) Global strategy to accelerate the elimination of cervical cancer as a public health problem.

Each country should meet the 90–70–90 targets by 2030 to get on the path to Eliminate Cervical Cancer within the next century. (6)

Committment Goals

- **Vaccination:** 90% of girls fully vaccinated with the HPV vaccine by the age of 15
- **Screening:** 70% of women screened using a high-performance test by the age of 35, and again by the age of 45
- **Treatment:** 90% of women with pre-cancer treated and 90% of women with invasive cancer managed

There is a long way to go to meet the 2030 elimination target of 90% in India as presently less than 1% of our girls are vaccinated and less than 2% of Indian women have ever been screened according to NFHS-5.(5)

VII. E – ELIMINATION

Level 1

1. Primordial Prevention

- **Human Papilloma Virus: HPV** is the known caused factor for cervical cancer .Prevention of HPV infection is the very ambitious goal of HPV vaccination programs, in girls who are not yet exposed to sexual activity. The policy for **HPV vaccine** differs from country to country and the readers are requested to make appropriate references.

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Level 2

1. Primary Prevention

- **Health Promotion And Specific Protection:** The HPV infection which occur in women should get cleared in a couple of months. This largely depends on the nutritional status of women.Good nutritional status ensures recovery of the women from prolonged infection which may lead to development of pre cancer lesions.

2. Specific protection

- **Menstrual Hygiene:** In many communities, the use of sanitary napkins,during menstrual periods may not be in practice due to ignorance, illiteracy, poverty and sociocultural factors. Non availability of napkins, also to be considered.

Solution – Prevention protocol

The women in the needy societies should have educational sessions about menstrual hygiene and the importance of prevention of HPV infections. In some countries the government supplies sanitary pads in schools.The NGOs – Non government organizations, also play a big role in education about menstrual hygiene and they also supply the sanitary pads, free of cost, or at subsidies rates.

- **Sexual Hygiene:** Use of condoms can be encouraged to prevent HPV infection and reinfections, during sexual activity. Multiple sex partners is a definite risk factor for HPV transmission . Education and counseling play an important role in cultivating safe sex culture.

- **HPV Vaccination:** HPV vaccines are available in bivalent , quadrivalent and multivalent forms they claim to have immune prophylactic or immuno therapeutic values which authenticity needs to be established through vaccine trials for efficiency and effectiveness.

The cost of HPV vaccine are high and the health planners in different countries , resource settings needs to take policy decision on introduction of HPV vaccine in their immunization programs.

Level 3

1. **Early Diagnosis and Treatment:** Screening programs, as discussed above should follow recommended protocol and become successful in getting large number of women screened.

The 'yield' in the screening programs is the detection of pre cancer lesion of CIN I ,II and III. Early diagnosis thus made leads to 'treatment' of pre cancer lesions to prevent the occurrence of invasive cancers.

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Thus,the intervention through the Three Tier Protocol of primordial ,primary and secondary prevention play the sheet anchor role in the prevention of Cervical Cancer.

VIII. CONCLUSION

The author envisages that **"Systemized Screening"** should be a new concept at planning level, of cervical cancer screening programs. The program should have a system in place as follows. The eligible women who are invited for screening should be well educated about the available " Screening Tools", their prospects and consequences. The women should have the right to choose their screening procedure - The Cafeteria Approach.

They should be referred appropriately. The next important aspect is Treatment of Precancers, and availability of methods like Cryotherapy, LEEP, Cold coagulation and Laser ablation. The merits and limitations should be well explained to the women.

The final aspect is "Prevention", at Primary, Secondary and Tertiary levels, in which "Heath Education and HPV Vacciation", are included as vital strategies. Thus, the concept of **Systemized Screening** will have fully functional and well equipped strategies in place for 1.Health Education 2.HPV Vaccination 3. Screening protocols 4.Precancer treatment 5. Five year regular followup services with biopsy for confirmation of disease status.

IX. RECOMMENDATION

Thus, the advocacy of 5 pronged strategy "SPICE": Screening – **P**recancer treatment – Immunization – **C**ommitment, **E**limination, are the 5 prongs, termed "**SPICE strategy of Raj© ".** These are the recommended and strongly advocated strategies, for GLOBAL ELIMIUNATUIN OIF CERVICAL CANCER BY 2030. These strategies are proven, by the success of the program, which is widely quoted in this chapter, as "Proof of Concept - POC project", and, the Author, had the privilege and honour of being the Principal Investigator, of this largest Cervical Cancer Screening Program, in Tamil Nadu, India, during 2000 - 2007, which was financially supported by The Bill & Melinda Gates Foundation, and with technical guidance from IARC / WHO (4)

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