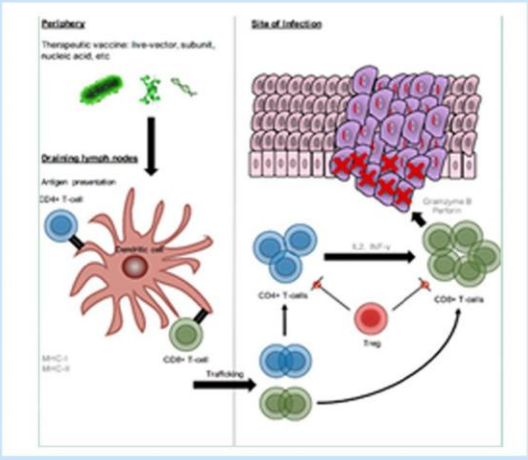
e-Newsletter

ISCCP

Member International Federation of Cervical Pathology and Colposcopy

Newsletter of Indian Society of Colposcopy & Cervical Pathology (Reg.)

Therapeutic HPV Vaccines



Truescreen Ultra

Index of newsletter

President's Message

Dear ISCCP Members,

With all your support and trust, I took the reins of our society from Dr. Saritha Shamsunder, the past president of par excellence. She did exemplary work in the past three years, making our society known to both the national and international community.

My strength lies in my team who have joined me as office bearers, executive members and members of various committees. With their relentless support and dedication, I aim to take our society to greater heights

All of us are going through difficult times due to waves of the Covid Pandemic that is causing a lot of uncertainty in our lives and to our activities. However, we need to utilize every possible opportunity to reach our goals. For this, we need innovative ideas that can be scaled up to local, regional and national programs.

The Newsletter is our means of throwing ideas into action : do write in with whatever thoughts that you wish to share with others. You can ask questions, provide answers or just think aloud! With this short message, I extend my wishes to you and your family members for a happy and healthy
New Year 2022 and Makara Sankranti!

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From the Editor's Pen

Hello to every esteemed member, 🙏
It is a privilege to be in this meritorious group of gynecologists as the Editor for this News Letter

My vision of this newsletter is to use it is a platform for knowledge sharing, express warm appreciation of colleagues who are doing remarkable work in this profession, a forum to share their experiences, out of box ideas, innovations as well as 'things to ponder', in a lighter sense.

There is a column for queries and quick answers too. My special thanks to Dr Leela for giving me one of my favorite jobs to do. I would also like to thank Dr Saritha Shyamsunder, Dr Priya Ganesh, Prof Shalini Rajaram, Dr Aruna Nigam, Dr Jyothi and all other office bearers for their unconditional warm support.

I request all the seniors and friends to join and contribute to this forum to grow and become an academic landmark.

With warm wishes

Yours truly,

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Therapeutic HPV Vaccines

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A therapeutic vaccine is a vaccine which is administered after a disease or infection has already occurred. It works by activating the immune system of a patient to fight an infection. It differs from a prophylactic vaccine in that prophylactic vaccines are administered to individuals as a precautionary measure to avoid the infection or disease, while therapeutic vaccines are administered after the individual is already affected by the disease or infection.

A therapeutic vaccine fights an existing infection in the body rather than immunizing the body for protection against future diseases and infections. Therapeutic vaccines are mostly used against viral infections. Patients affected with chronic viral infections are administered therapeutic vaccines, as their immune system is not able to produce enough efficient antibodies.

Human Papilloma Virus (HPV): HPV related cancers account for 5% of all cancers worldwide. HPV association is seen in more than 80% of cervical cancers. HPV also contributes to penile, vulvar and anal cancers and over 40% of oropharyngeal cancers.

The three commercially available prophylactic vaccines effectively prevent HPV infection of targeted argeted types by eliciting the production of neutralizing antibodies that bind to viral particles and block their entrance to host cells. These vaccines are not effective at eliminating pre-existing infections since the target antigens L1 capsid proteins are not expressed in infected basal epithelial cells.

There is a need to develop nonsurgical and non-ablative treatment modalities for treating HPV infection and HPV pre-invasive conditions for reducing the progression to invasive cancers and cancer burden. Therapeutic vaccines fall into such investigational strategies.

Therapeutic HPV vaccines: These can be used to treat established HPV infections and could therefore have an immediate effect on the prevalence of HPV-associated malignancies. Therapeutic vaccine strategies aim to eliminate pre-existing lesions and even malignant tumors by generating T cell-mediated immunity against . HPV-infected cells.

Mechanism of Action: To eliminate existing lesions, a therapeutic vaccine should target HPV antigens that are continuously expressed in the infected and cancer cells. Thus, the choice of target antigen is extremely important for therapeutic HPV vaccine design. The early proteins of HPV are potential target antigens as they are expressed throughout the life cycle and help regulate progression of the disease. In particular, the HPV-encoded proteins E6 and E7 represent ideal targets for the development of

Firstly, E6 and E7 proteins are constitutively expressed by HPV-associated tumors.

Firstly, E6 and E7 proteins are constitutively expressed by HPV-associated tumors.

Secondly, because E6 and E7 are critical for the induction and maintenance of cellular transformation in HPV-infected cells, it is unlikely that the tumor cells can escape immune attack through antigen loss.

Thirdly, as E6 and E7 are foreign proteins, immunization against HPV-associated tumors circumvents some common cancer-vaccine-associated problems such as immune tolerance.

Many therapeutic HPV vaccine strategies have focused primarily on stimulating the production and activation of T cells by targeting E6 and/or E7 proteins. Usually, a DNA sequence that encodes a fusion protein of E6 and E7 is inserted into a vector, and, mutations are introduced into the regions that are responsible for the E6 interactions with p53, and the E7 interactions with pRB, to eliminate their oncogenic potential. The E1 and E2 viral proteins are also attractive candidates for therapeutic vaccines that target early viral infections, as they are highly expressed before viral genome integration.

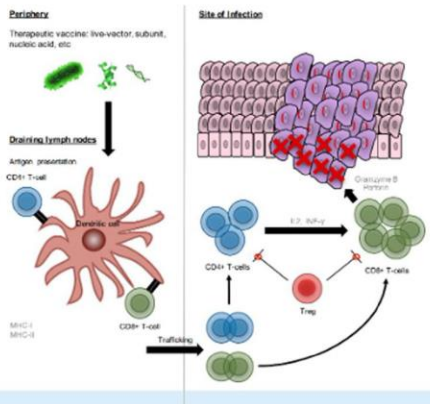

Fig 1. An ideal HPV therapeutic vaccine would elicit a strong cell-mediated immune response where CD4+ T-cells would provide support to CD8+ T-cells by secreting cytokines such as IFN-γ and IL2 labelling in malignant cells. Cytotoxic CD8+ T-cells would eliminate infected cells by secreting high amounts of granzyme B and perforin which lead to cell death.

The response would be effective even in the presence of immunosuppressive cells (Adapted from A. Chabeda et al. Papillomavirus Research 5 (2018) 46–58)Fig 1. An ideal HPV therapeutic vaccine would elicit a strong cell-mediated immune response where CD4+ T-cells would provide support to CD8+ T-cells by secreting cytokines such as IFN-γ and IL2 labelling infected and malignant cells. Cytotoxic CD8+ T-cells would eliminate infected cells by secreting high amounts of granzyme B and perforin which lead to cell death. The response would be effective even in the presence of immunosuppressive cells (Adapted from A. Chabeda et al. Papillomavirus Research 5 (2018) 46–58)

Types of Vaccines:

1. Live vector-based vaccines: Bacterial vectors and viral vectors
2. Peptide/Protein based vaccines: Peptide based and protein based
3. Nucleic acid-based vaccines: DNA based and RNA replication vaccines
4. Whole cell vaccines: Dendritic cell based and Tumour cell based

Combined approach: Prime-boost regimens are perhaps the most effective treatment strategy for vaccination against HPV. Because nucleic acid vaccines often generate relatively weak cytotoxic T lymphocyte (CTL) response, combinatorial vaccination approaches are used to circumvent this limitation. Priming with a DNA or RNA vaccine and then boosting with a viral-vector vaccine has been shown to result in enhanced immune responses relative to single modality vaccinations.

Therapeutic vaccines trials: Currently, there is no therapeutic vaccine approved by US FDA. Vaccines are at different stages of development, as well as potential combinations of vaccines with other immunotherapy modalities. Immune checkpoint inhibitors can potentiate an existing immune response, while other agents can help increase an immune response by decreasing immune-suppressive elements in the tumor microenvironment (TME). Both these mechanisms may be useful to potentiate the efficacy of a therapeutic vaccine. Current clinical trials for therapeutic HPV vaccines when queried at the NIH ClinicalTrials.gov database utilizing "HPV Vaccine" as the search string, yield over 60 studies that involve therapeutic HPV vaccines as monotherapy or in combination with other immunotherapeutics.

Clinical trails :

A phase I study with DNA vaccine VGX-3100: It consists of a mixture of two plasmids that encode the optimized consensus of the E6 and E7 genes of HPV genotypes 16 and 18. These were delivered via intramuscular injection, followed by electroporation, with 18 patients who had been previously treated for cervical intraepithelial neoplasia (CIN2/3). This study showed that 78% of the patients developed CD8+ T-cell responses, and 100% showed antibody positivity to at least two vaccine antigens. Notably, the peripheral blood T-cell responses elicited by VGX-3100 were an order of manitude greater than naturally occurring responses, and a log unit greater than those previously reported for HPV therapeutic vaccines.

A Phase II study of VGX-3100 in patients with CIN2/3: In the per-protocol analysis, 30.6% of the placebo recipients and 49.5% of the VGX-3100 recipients showed histological regression. Concomitant histopathological regression and viral clearance occurred in 14.3% of placebo recipients compared with 40.2% of vaccinated recipients. Post-hoc immunological analysis here demonstrated that VGX-3100 elicited significantly increased frequency of T-cell responses against HPV16/18 E6 and E7, and that the magnitude of the T-cell response against E6 was associated with clinical outcome.

A Phase III clinical trial of VGX-3100 for women with CIN was initiated in 2017, and it is expected to end in 2021 (NCT03185013).

A Phase II Modified Vaccinia Ankara Virus trial: A MVA vector was used to produce the Tipapkinogen Sovacivec vaccine, which includes three exogenous genes that encode the human cytokine interleukin-2, and non-oncogenic E6 and E7. This vaccinia virus can induce interferon-α production and expression of HPV16 E6 and E7 antigens, which are presented by dendritic cells to activate naïve T cells in lymph nodes. At a follow-up of 2.5 years, compared to the placebo cohort at 10% viral clearance, the administration of Tipapkinogen Sovacivec vaccine provided complete resolution for 24% of patients with CIN2/3, irrespective of their HR-HPV baseline infection (i.e., HPV16, 18, 31, 33, 35, 39, 45, 52, 56, 58, 59, or 68). It needs to be evaluated through a Phase III . study.

The following are the highlights of the trial:

The vaccine completely resolves CIN 3 lesions significantly more frequently than placebo.

It completely clears HPV16 viral DNA associated with CIN 2/3 significantly more often than placebo.

It has significantly greater complete resolution rates of CIN 2/3 regardless of HR HPV type

It offers 36% complete resolution or partial response of CIN2/3 associated with all HR HPV types.

Conclusions:

There is an urgent need for therapeutic HPV vaccines to reduce the burden of HPV related cancers.

Ongoing clinical trials using several vaccine trials are showing promising results.

A therapeutic vaccine may be available for clinical use in near future.

https://en.wikipedia.org/wiki/Therapeutic vaccines

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Diane M. Harper a, ⁎,1, Pekka Nieminen b, Gilbert Donders c, Mark H. Einstein d,2, Francisco Garcia e,3 Warner K. Huh f, Mark H. Stoler g, Katerina Glavini h, Gemma Attley i, Jean-Marc Limacher j,4, Berangere Bastien k, Elizabeth Calleja The efficacy and safety of Tipapkinogen Sovacivec therapeutic HPV vaccine in cervical intraepithelial neoplasia grades 2 and 3: Randomized controlled phase II trial with 2.5 years of follow-up. Gynecologic Oncology 153 (2019) 521–529.

Truscreen

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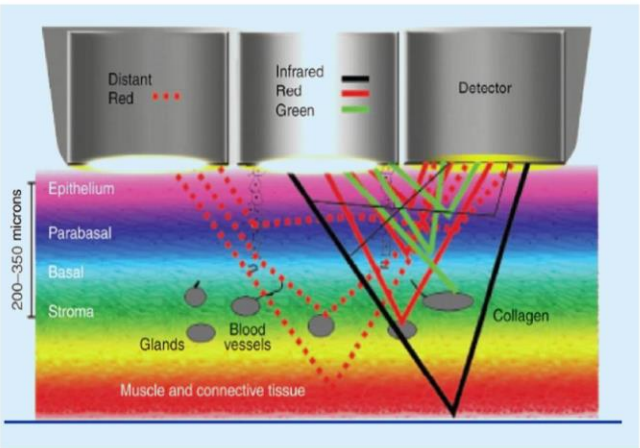
Martin Dillon said that the technology worked by emitting light and an electric current to stimulate the cervix which "creates a tissue signature and reports whether it is normal or abnormal. Since cervical cancer is one of the most common cancers among women, attempts have been made to design cost-effective devices capable of making distinction between normal and abnormal cervical epithelium. Pap smear, colposcopy and HPV DNA testing each have their own strengths and weaknesses. This study is based on the hypothesis that combination of an optoelectronic screening device and Pap smear increases the sensitivity and specificity of diagnosing cervical epithelial cell abnormalities. TruScreen is one of these devices with advantages of being cost-effective, non-invasive,safe and simple.[2]

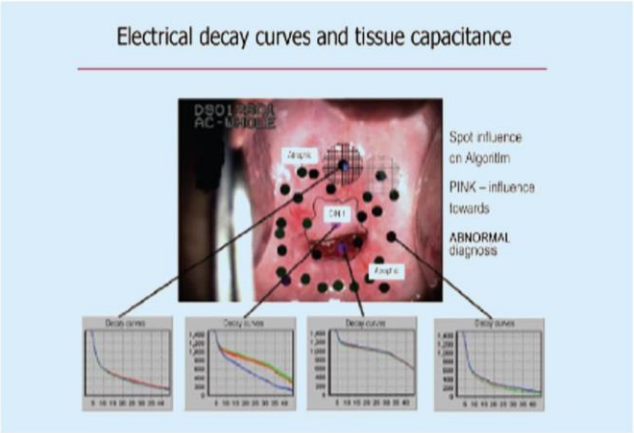
Principle of the technique: Light at specific frequencies is transmitted through cervical tissue for identifying changes in the basal and stromal layers. This includes increases in blood circulation and variations in blood vessels that occur with pre-cancerous change.



How does it work: The console has a microcomputer to calculate these tissue differences, and the results are compared with an integrated database of thousands of patients from wide geographic and ethnic backgrounds with differing histological diagnoses.

A sophisticated algorithm framework has been developed to distinguish between normal and abnormal (cancerous and precancerous) tissue. In a multicentre study, TruScreen was shown to detect precursors of cervical cancer (CIN 1-3) at an equivalent sensitivity to a standard Pap smear. The distal tip of the hand-piece is covered with a 5-mm-diameter single use sensor element designed disposable to protect against cross-infection. The information is filtered and processed by a microcomputer within a portable console to extract the parameters of greatest value for tissue discrimination as normal or abnormal[2]

As determined in study of TruScreen by Ozugu et al.[1] with a sensitivity of 86.1% can be used as a screening test with instant and not professional dependent results for cervical cancer screening. Avoiding from subjectivity in interpretation of Pap smears and requirement for pathologists, TruScreen can be a used for cervical cancer screening especially in countries with a low socio-economic status. The combination of TruScreen and HPV screening was not able to demonstrate a significant rise of effectiveness in screening.



Analysis of studies: The results of study show that combination of TruScreen and Pap smear compared to Pap smear alone increases the sensitivity and specificity and reduces false negative rate of the screening program. However, this combination increases the rate of false positive results. Moreover, the combination has lower positive and negative predictive values compared to Pap smear alone.

In a study by Allameh,T., Khanjani,S. et.al [2] the use of this combination provides a very high degree of assurance about the absence of a significant cervical epithelial cell abnormality when both tests yield negative results. On the other hand, the significant increase in false positive rate of the combination in comparison to Pap smear alone leads to unnecessary additional evaluations. However, this burden would be negligible when the benefits resulted from higher sensitivity and specificity of the combined tests is considered.

In an another study Wei Y, wang M et al. stated that to select a reasonable cervical cancer screening method, it is important to consider not only the screening indices (such as sensitivity and specificity) of the method, but also the applicability of the method (including cost, efficiency, and patient experience) [3]. Patient experience is improved because TruScreen is more acceptable to women than a cytological test because no cervical tissue needs to be taken during the test, meaning minimal to no discomfort. Furthermore, real-time results are provided, so instead of patients needing to wait for test results to come back and make another appointment, they can ask their doctor right away if they need further treatment. To some extent, this can also avoid the anxiety that can arise while waiting for the report.

Another major multicentric comparative study with large number of cases with a total of 9972 woman who received cervical cancer screening services of National Cervical Cancer Screening Program in Rural Areas (NCCSPRA) in 8 project counties participated. TruScreen, HPV test and LBC test were performed in all participants. A total of 1945women had one or more than one positive or abnormal screening results of the above three screening tests subsequently received colposcopy. The detection rate of CIN2+ between the three tests were compared. [4]

The total detection rate of CIN2+ in HPV group was highest (0.73%), following in LBC group (0.44%) and TS group (0.31%). There was no statistical difference in the total detection rate of CIN2+ between TS and LBC screening groups. Moreover, except for the eastern regions, there was no statistical difference in the detection rate of CIN2+ between TS group and the other two groups in central and western regions.

Conclusion: The quest for ideal screening test for Cancer cervix will continue to give various possibilities which are high sensitivity with less false negative results. One such invention is Truescreen with dual principle application with light reflection as well as electrical potential transmission and resistance in normal and abnormal tissues. In future Artificial Intelligence incorporation into these devices is going to give more precise results to us there by the screening programmes become much more effective and rewarding

Negativity is contagious. Unhappiness is contagious. Fear is contagious. But so is happiness. So is optimism. So is love. Surround yourself with people who bring out the best in you. And strive to be a reflection of what you want to receive.

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Comparison of the detection rate of cervical lesion with TruScreen, LBC test and HPV test: A Real-world study based on population screening of cervical cancer in rural areas of China. Yu Ma, Jiangli Di ,Hui Bi, Qingping Zhao, Tianhua Qin, Wen Xu, et.al https://doi.org/10.1371/journal.pone.0233986

Case study: Postcoital Bleeding

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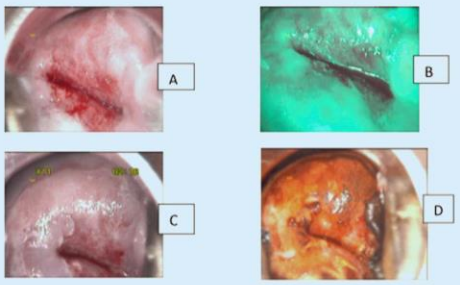
Mrs X, 40-year-old P3L3 presented to the gynaecological OPD with the complaints of discharge per vaginum for the past one year and post coital bleeding for the past six months. She had 3-4 such episodes with significant amount of bleeding. Her periods were regular 4-5/28-30 day interval. She had three vaginal deliveries, LCB 20 yrs. No cervical cancer screening test was done in the past. Past history and family history were nil contributory. The gynaecologist did Pap test and VI acetic acid and a pelvic examination. It was normal.VIA was positive and the Pap test was reported as LSIL(low grade squamous intraepithelial neoplasia). In view of the post-coital bleeding and abnormal Pap report Colposcopy was performed it showed TZ 1 with a major lesion - dense aceto whitening with sharp margins occupying 3 quadrants of the cervix as given below with patchy mustard yellow appearance of lesion on applying Lugol's iodine. (Figure 1, A-D)



Colposcopy findings (Figure 1)
A. No magnification
B. green filter
C After acetic acid application
D Lugol's iodine application

SWEDE 7	0	1	2
Uptake of acetic acid	0 or transparent	Shady, milky	Distinct, stearin-like
Margins and surface	0 or diffuse	Sharp, but irregular, jagged, "geographical" satellites	Sharp and even, difference in surface level such as "cutting"
Vessels	Fine, regular	Absent	Coarse or atypical
Lesion size	< 5mm	5-15 or spanning 2 quadrants	>15mm or spanning 3-4 quadrants or endocervically undefined
Iodine staining	Brown	Faintly or patchy yellow	Distinct yellow

Swede's score was 7 and a punch biopsy with Kervokian punch biopsy Histopathology reported CIN 1 with koilocytic changes. Since most CIN 1 lesions are known to regress she was asked to follow-up after one year. One year later the Pap report was NILM. Colposcopy was repeated and there was regression of the lesion. She was advised to follow-up with an HPV DNA test and Pap test after one year and to report any symptoms

Discussion

There are several causes of post coital bleeding (PCB) but every effort must be made to rule out malignancy. Prevalence varies from 0.7 to 9 % .Various causes are cervical ectropion (34%), CIN (7-17 %),cervical or uterine polyps, fibroids, OCPs, atrophic vulvo-vaginal changes, vulvar dermatitis, vulvar lichen sclerosus, lichen planus etc (1). Malignancy as a cause of postcoital bleeding occurs in less than 5 %. 11-39% of women with cervical malignancy have PCB (2). Trauma/foreign body may be seen in a few cases and in many no cause maybe identified. In our study of PCB majority of women had a vascular ectopy (35/110) on colposcopy and histopathology showed chronic cervicitis (16%), tuberculosis (1.8%), CIN 1-3 (9.2%) and invasive cancer (5.6%) (3). A complete diagnostic evaluation is mandatory in a woman with PCB and not mere screening(4)

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"NCPCC- THE NEED OF THE HOUR"

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Chairperson gyaecologic oncology committee fogsi

Introduction: WHO Mission statement of Cervical cancer Elimination by 2030 has been a historic moment and has created an impactful global awareness regarding this deadly disease. The triple formula of 90-70-90 has been designed to have a 30% reduction in mortality from cervical cancer to be achieved by 2030. The goal of Cervical cancer elimination is to bring down the cases of cervical cancer below 4 per 100,000 women.

Indian scenario: Unfortunately, India leads the globe next to China in Cervical cancer deaths with a lady succumbing to this disease every 8 minutes. Albeit the fact, that much has been advocated for Cervical Cancer prevention, the basic truth of its implementation at the grass root level is still very disheartening. In a survey conducted amongst HCP, it was noted that the importance and need for Cervical cancer prevention with vaccination and screening were acknowledged by all, but the nuances of adopting different screening methods and integrating it with diagnostic methods like colposcopy with biopsy and further treating the cases were less understood. Thus, reiterating the fact, that there is a strong need to improve the skill sets in HCP, encouraging them to adopt In India, the art and science of Colposcopy has been in practise since 1980s. Colposcopy with directed biopsy has been the Gold Standard for diagnosis of precancerous lesions with enhanced case management.

What are the limitations faced by doctors for adopting Colposcopy? A quick key point as below:

- Lack of adequate talent & skill in Colposcopy Science
- Lack of adequate knowledge in Biomolecular diagnosis and consolidating reports
- Lack of confidence in reporting and fear of missing out any major concerns
- Lack of availability of well-trained cytopathol ogists in most parts of our country
- Where to send the samples grey zone

Understanding the limitations faced by practising gynaecologist in the private sector across the nation, Sainiwas Health Care has adopted the novel approach and methodology through its NATIONAL CONTROL AND PREVENTION OF CERVICAL CANCER (NCPCC) movement empowering the private practitioners to practise preventive oncology for cervical cancers prevention in the distantremote places of the nation.

Through the chain of franchise centres. support is rendered for reporting of Colposcopy images, with a one-stop solution for laboratory testing (LBC, HP and HPV). Thus, the doctors are enabled to manage Precancer and cervical cancer patients with confidence, adopting a unified call/recall system of the patients.

In this digital era and a good web connectivity electronic data reporting is the key for efficient reporting and enabling support on guided case management techniques. So far, this novel NCPCC centres are functioning at 29 cities Pan India mainly in tier 2/3 cities where the health care facility for comprehensive case management of cervical lesions is not up to the mark. Through this NCPCC SNHC has so far helped more than 1 lakh women with appropriate case management with call recall surveillance system & proper maintenance of records of all the cases in a standardised manner.

Mission : is "To Provide Quality Education, Support & Services to Doctors and Empower them through Technology, ensuring Preventive Oncology.

Report of AOGD 2021 Pre-Conference Workshop on 18 th November, 2021.

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A Precongress workshop on "Protocols and Procedures for Cervical Cancer Prevention (videoworkshop) was organised on 18 th November 2021 between 2:00-7:00pm by department of obstetrics & gynaecology, VMMC and Safdarjung hospital under aegis of AOGD Gynae oncology Sub- Committee, Indian Society of colposcopy and cervical pathology. The Workshop was well attended by gynaecologists, medical officers, staff nurses and nursing students from many states of country. The Scientific program was inaugurated by Dr. R.Sankarnarayanan; Dr.Partha Basu from IARC, WHO; Dr. Anjali Dabral HOD Dept. Of Obst.& Gynae,VMMC & Safdarjung Hospital; Dr.Achla Batra President AOGD and Dr. Archana Vice President FOGSI.

Dr. Sankarnarayanan underlined the importance of these workshops for sensitization and skill building of doctors and nurses essential for Elimination of Cervical cancer by 2030. Dr. Partha Basu said that the WHO-IARC is developing the IARC Academy which will be a repository of lectures and videos of the various procedures for

Cervical Cancer Prevention. Highlights of the workshop were video sessions on pap smear, visual methods of cervical screening, colposcopic procedure , cervical biopsy , cryotherapy , thermal ablation, large loop excision of the transformation zone and cold knife conization. The faculty consisted of eminent experts working for cervical cancer prevention from various parts of India, including the National Health Mission. Dr. Sunita Malik, the organising chairperson updated the audience on the WHO recommendations for screening and treatment of precancerous lesion of cervix, Dr. Neerja Bhatla elaborated the various algorithms for screen & treat and screen-triage and treat. Attendees actively participated in question and answer session and were benefitted by inputs from all the experts.

Role of office colposcopy in State - Kerala

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Aim: To study the applicability of Office colposcopy as a part of standard gynecological examination in a state like Kerala.

Materials and methods: This is Colposcopic study was conducted in 1000 women between the ages of 30 to 60yrs as OP clinic at Vatakara, Kozhikode dist. Kerala. Study duration was five years from 1/6/2011.The importance of cervical screening was discussed with all married gynecological patients. 1000 subjects accepted colposcopic examination of cervix. (Only 17 (1.7%) of them had previous Pap smear). Office colposcopy was done using ASCON AC 3 with a fixed magnification of 6x. Colposcopic findings were graded with Ried's colposcopic index. Biopsy was taken if the Ried's index was taken if the Ried's index was 1 or more.

Results: Out of 1000women studied, colposcopic study was adequate in 897 subjects (89.7%) and inadequate in 105 subjects (10.5%). Normal colposcopic findings were seen in 254 women (25.4%). Colposcopicdiagnoses of precancerous lesions were made in 209 (20.9%) Subjects.

Out of this LSIL was diagnosed in 193 subjects (19.3%) and HSIL was seen in 16 (1.6%) women. Invasive carcinoma was diagnosed in 5(0.5%) subjects. Benign conditions of cervix seen in 34.4 %n(344) of subjects which are Cervicitis 187 (18.7%), Severe ectropion 96 (9.6%), cervical polyps 61 (6.1%). The incidence of infection was 18.8% (188) they are Candida infection 10.3% (103), Trichomoniasis 6.1% (61), Mixed bacterial infection 24 (2.4%) and subclinical HPV infection 8 (0.8%).

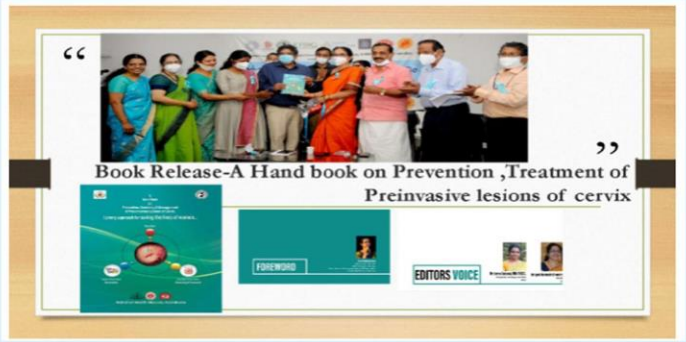
Conclusion: In a state like Kerala where people are educated and health concerned, unfortunately we have no organized screening program for cervical cancer. Including Colposcopic examination of cervix as a part of standard gynecological examination gynecologist can diagnose cervical pathology and can give necessary treatment in the same sitting. Normal Colposcopic findings confidently predicts cancer free cervix to the next 5-10 years

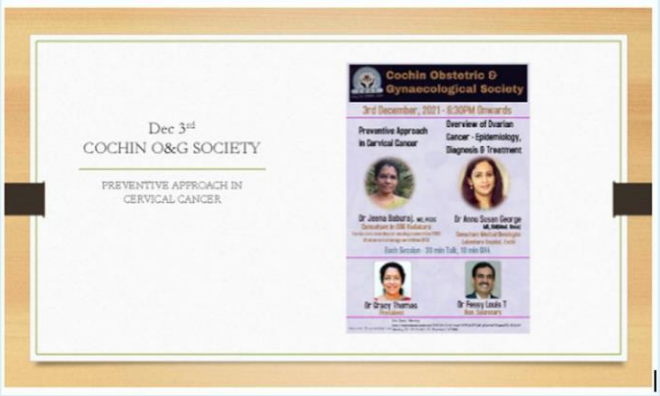
Programmes ISCCP members

PATH TO CERVICAL CANCER FREE KERALA

Dr Jeena Baburaj

MD DGO DNB FRCOG





Dr. Jyothi GS,

Current Vice President of BSOG &
Professor and Unit Chief of Obstetrics & Gynaecology at Ramaiah Medical College and Hospitals, Bengaluru 54 ,Karnataka.

4 activities in the month of November 21.

1.Coordinated the pledge taking ceremony for Nov 17th for the WHO call.

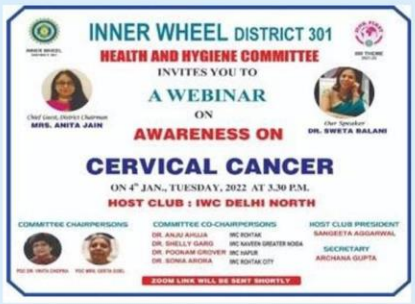
2. guest lecture for sensitising the issue of Cervical cancer elimination and stressed on primary prevention

3.Was invited for the expert input forum for Gardasil 9 held at Mumbai on Nov 21 st

4. screening camp for breast and cervical cancer, totally 47 were given awareness and counselled and screened

Dr Sweta Balani
Treasurer Indian Society of
Colposcopy and Cervical Pathology

Inner Wheel District 301- Health and Hygiene CommitteeA mega-event was organized by Inner Wheel District 301-Health and Hygiene Committee with Pink First IIW Theme 2021-22in the form of a Webinar on Awareness on Cervical Cancer on 4 th January 2022 on a virtual platform.



Futuristic options and recent developments in cervical cancer screening

Compiled by
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MD,DNB (O&G)
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1.Application of artificial intelligence in cervical cancer screening :

Medical field is very fascinating with always something new coming for better implementation and practice. Artificial intelligence will be a game changer in our lives including in our profession. In limited-resource areas and rural areas at the point of care (POC), a digital diagnostic system is setup in which Papanicolaou smears are collected and microscopy slides are digitized with a portable slide scanner, and whole-slide images were uploaded to a cloud platform using the local mobile data network for development and validation of a deep learning system (DLS). The diagnostic accuracy for the detection of common forms of cervical squamous cell atypia with the DLS by comparing them with the visual assessment of samples by independent pathologists achieved high accuracy for the detection of cervical squamous cell atypia, with sensitivities of 96% to 100%, compared with the visual interpretation of digitized and physical slides

Ref : Holmström O, Linder N, Kaingu H, et al. Point-of-Care Digital Cytology With Artificial Intelligence for Cervical Cancer Screening in a Resource-Limited Setting. JAMA Netw Open. 2021;4(3):e211740. doi:10.1001/jamanetworkopen.2021.1740

2.Electrochemical biosensors :

Among all of the available methods (ex. gold nanotubes, gold nanosheets, single-walled carbon nanotubes , etc) DNA hybridization biosensors or genosensors can be used for the detection of infectious diseases such as HPV

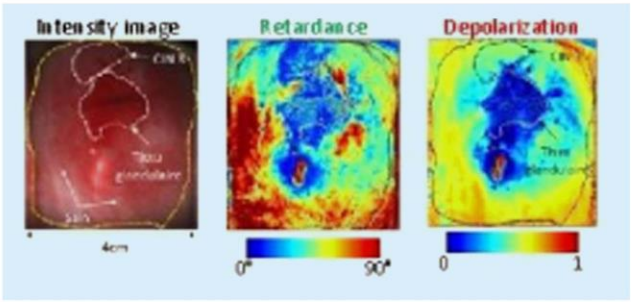
DNA biosensors revealed some advantages that includes fast detection of disease, ease of work, affordability, and sensitivity of the device Nanoplatforms based on carbon, chiefly graphene (GR) and its derivatives, are appropriate structures due to its owning characteristics including high mechanical strength (1.1 TPa) , high thermal conductivities(5000 W.m.K-1) and also the large surface area f(2630 m2.g -1) for use in electrochemical measurements.

Recently, in the literature, a large number of articles were published using Graphene derivatives for use in biosensors and medical fields: Huang et al. used ultrasensitive electrochemical DNA biosensors by using GR, Au nanorod (Au NR), and polythionine (PT) for HPV DNA detection. The DNA biosensor showed excellent function for the detection of HPV DNA. Farzin et al.

used an ultrasensitive electrochemical genosensor by using multiwalled carbon nanotubes by the amine-ionic liquid-functionalized reduced graphene oxide (MWCNTs/NH2-IL-rGO) nanoplatform for HPV detection. These Genosensors could detect very low amounts of HPV-16 DNA

Ref : H. Huang, W. Bai, C. Dong, R. Guo, and Z. Liu, "An ultrasensitive electrochemical DNA biosensor based on graphene/Aunanorod/polythionine for human papillomavirus detection," Biosensors and Bioelectronics, vol. 68, pp. 442–446, 2015
Ref : L. Farzin, S. Sadjadi, M. Shamsipur, and S. Sheibani, "Electrochemical genosensor based on carbon nanotube/amine-ionic liquid functionalized reduced graphene oxide nanoplatform for detection of human papillomavirus (HPV16)-related head and neck cancer,"Journal of Pharmaceutical and Biomedical Analysis, vol. 179, p. 112989, 2020

3.Mueller polarimetric imaging :

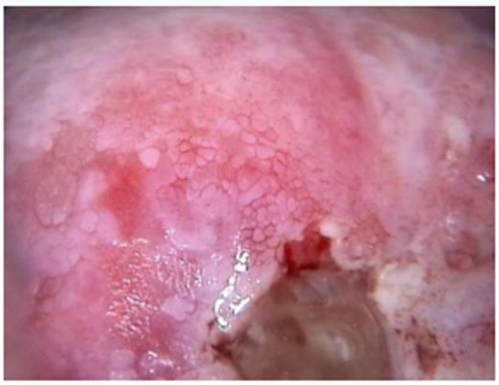


This polarimetric technique works on simple optical elements in the visible range (450 – 700 nm) and provides a macroscopic field of view (≈10 cm2) Different depths in the tissue can be reached using different wavelengths (due to different light absorption by hemoglobin, Hb being more absorbing for shorter wavelengths) Moreover the delineation of suspicious areas can be imaged without any tissue contact.

Mueller polarimetry has demonstrated high sensitivity to the structural and morphological microscopic transformations of biological tissue . These transformations are potentially related to the presence of pathology, and contrast between healthy versus cancerous tissues in Mueller imaging . studies

Through the integration of this technology into conventional instruments (e.g., colposcope, endoscope), polarimetric imaging is a promising tool for in vivo cancer detection and staging Application to cervical cancer In vivo measurements :A)Healthy zones are characterized by a strong Retardance (~80°) and Depolarization (~0. 8) B)Abnormal zones are characterized by a very low Retardance (< 10°) .Different degrees of Depolarization enable us to distinguish malignant lesions (CIN 3) from benign transformations of the cervix (glandular tissue) Ref : Meredith K et.al Polarimetric measurement utility for pre-cancer detection from uterine cervix specimens. BIOMEDI-

Spot diagnosis



Dear friends
See the Spot diagnosis of this picture and reply. The first received correct answer replied person will get a prize Good Luck

Yours friendly Fahmida Banu

Questions and quick answers

Question: Can LEETZ be performed as OP procedure?
Answer: Yes, it can be.

Question: Does it need consent in writing.
Answer: Yes

Please write your replies, queries , thoughts,suggestions and experiences to the following email

write2youreditor@gmail.com

JOURNAL SCAN

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1) Vaccine efficacy against persistent human papillomavirus (HPV) 16/18 infection at 10 years after one, two, and three doses of quadrivalent HPV vaccine in girls in India : a prospective, cohort study

Basu. Petal , Lancet Oncol. 2021 Nov;22(11):1518-1529

Relevance: This Prospective cohort study highlights that single dose of HPV vaccination in girls provided 10-year protection against persistent infection HPV infection (serotype 16 &18) equal to 2 or 3 doses of vaccine This was a randomised trial designed to compare three and two doses of quadrivalent human papillomavirus (HPV) vaccine in adolescent girls in India which was converted to cohort study after suspension of vaccination trials in India and Aim was revised to compare vaccine efficacy of single dose to that of three and two doses in protecting against persistent HPV 16 and 18 infections at 10 years post vaccination

Methods: Unmarried 10- 18-Year-old girls from 9 centres in India were allocated to 4 cohorts based on no of quadrivalent HPV vaccine doses received and were longitudinally followed yearly. Unvaccinated women age-matched to the married vaccinated participants were recruited to serve as controls. Cervical specimens were collected from participants 18 months after marriage or 6 months after first childbirth, infections.

Married participants were screened for cervical cancer as they reached 25 years of age. Vaccine efficacy against persistent HPV 16 and 18 infections (the primary endpoint) was analysed after adjusting potential confounders among various cohorts.

Findings: Participants were followed over a median duration of 9 years. Vaccine efficacy against persistent HPV 16 and 18 infections was 95·4% in the single-dose default cohort (2135 women assessed), 93·1% in the two-dose cohort (1452 women assessed), and 93·3% in three-dose recipients (1460 women assessed).

This study shows a way to address the potential challenges of demand-supply deficit, affordability and logistic problems in vaccination programs.

2) Occupational Health

Prevalence of HPV infections in surgical smoke exposed Gynaecologists

Hu xiaoli et al, Int Arch Occup Environ Health. 2021 Jan;94(1):107-115

Relevance: Smoke-generating surgical procedures are commonly used for the treatment of human papillomavirus (HPV)-related lesions. Surgical smoke may represent a potential vehicle for the transmission of HPV to surgeons and other OT staff, leading to HPV infection and subsequent HPV-related disease. Most of the centres lack facilities to prevent Gynecologists from surgical smoke. This study highlights the de-

This study was designed to investigate prevalence of HPV in nasal swabs from gynecologists exposed to electrosurgical procedures eg LEEP

Methods: A self-administered questionaries related to procedures and exposure was taken and nasal swab samples of 700 Gynecologists were collected and those found positive were followed at 3 months,12 months and 24 months post exposure

Results: HPV DNA detection rate was higher in those doing electrosurgery (8.96 % versus 1.73 %) over whom didn't perform electrosurgery. The usage of N95 masks reduced the HPV DNA detection rate (0 % versus 13.8 %) over general masks

3) Relevance Cervical Pathology : New Frontiers

From Microbiome to Inflammation: The Key Drivers of Cervical Cancer

Zhou, Zi-Wei et al. Front Microbiol. 2021 Nov 15; 12:767931

Relevance: Hallmarks of cancer are a set of functional capabilities acquired by human cells as they transform from normal cells to malignant cells. With the inclusion of "polymorphic microbiomes "as an enabling characteristic in this hallmark framework, much light is shed on the capability of microbiomes in modulating cancer . phenotypes

This review article reviews the available evidence about the relationship between cervicovaginal microorganisms, inflammation and cervical cancer. Immunotherapy and probiotics have also been discussed.

Synopsis: When the microbial community of female reproductive tract is in dynamic balance, lactobacillus with high abundance will not only produce lactic acid, H2O2 and other products but also compete with anaerobic bacteria for vaginal epithelial cells. In addition, the complement system could be activated by lactobacillus. These features prevent the growth of pathogens and thus ensure the health of the host. When the balance of microbial environment of female reproductive tract is upset, the inflammatory response is activated. H2O2, the amount of lactic acid decreases because of the increase in the number of anaerobic bacteria. At the same time, the production of a large number of pro-inflammatory cytokines affects the protective ability of the mucosal epithelial barrier. These phenomena can increase the likelihood of persistent HPV infection, which can lead to cervical cancer. Abnormal expression of cytokines and abnormal activation of signal pathways also lead to the occurrence of cervical cancer. It is important to note that the presence of HPV could also influence microbial homeostasis and the activation of inflammation-related mechanisms.

Nevertheless, even gut microbes have been found to regulate the release of estrogen , tumour microenvironment and inflammatory modulation affecting cervical cancer pathogenesis

The role of probiotics and immunotherapeutic agents in warding off immune escape by tumour progenitors has been emphasise.