



AOGIN INDIA

The newsletter of Asia Oceania research organization on Genital Infections and Neoplasia - India

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From the Secretary's desk

Dear AOGIN members,

The world has changed in an unrecognisable manner since the last newsletter. Masks, lockdowns and social distancing have come into our everyday vocabulary. But then, life has to go on for us- the medical & paramedical people. To make sure that we do not forget what is important while dealing with what is urgent during covid times, AOGIN has organised a research methodology lecture series, a clinical practice lecture series followed by talks for paramedical people.

Our AOGIN website is also being updated and we hope that our members will be able to turn to it for recent and relevant updates. Please do ensure that we have your recent email and contact numbers so that we can be in touch with you.

Looking forward to seeing many of you on zoom during the lecture series.

Lets wear our masks, be safe and remember this too shall pass.

With all best wishes,

Latha Balasubramani



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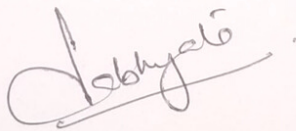
Forthcoming Events 12-13

MESSAGE FROM THE PRESIDENT

Dear colleagues,

With immense pleasure, I take this opportunity to make my first address as the President of AOGIN India. At the outset, I thank everyone for reposing in me their faith to lead this society for the next two years. With utmost humility, I assure you that my approach shall be all-inclusive, driven by participative decision-making. Despite the hardship brought upon us by the current pandemic, I am certain we will learn and relearn so that we can continue to inch closer to the mission of AOGIN India. To begin with, we shall strive to disseminate information by increasing our reach and online presence by enriching the website and conducting online CMEs. Especially in these compelling times, where gaining access to health care facilities has become challenging, it is of utmost importance that we continue to spread awareness and conduct screening when feasible. I solicit your wholehearted support in taking this esteemed society to greater heights and making it more meaningful in the day to day professional activities of researchers and caregivers engaged in the field of prevention, early detection and management of genital infections and neoplasia.

Warm Regards,



Dr Sabhyata Gupta
President, AOGIN (India).
Chairperson, Department of
Gynaecology&Gynaec Oncology,
Medanta - The Medicity, Gurugram (Delhi
NCR), India.



HPV VACCINE-AN UPDATE

Prof Nisha Singh
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King George Medical University, Lucknow



WHO call for Cervical cancer elimination 2030 states that the elimination is possible through three strong tools. This includes HPV vaccination of 90% of eligible population, screening with treatment of 70% of eligible population and treatment of 90% of women with pre invasive disease (WHO 2019).

High risk HPV prevalence in Asia is approximately 12% and Cervical cancer is the second most common cancer in Indian women. India contributes to one fifth of the global cervical cancer burden with annual diagnosis of 122,000 and annual deaths of 67477.

HPV vaccination is the most cost effective tool for control of cervical cancer in both high income and low income countries, more so in the latter.

HPV vaccine was introduced in 2006 by Merck as a quadrivalent vaccine (HPV4) effective in preventing infection with HPV types 6, 11, 16 and 18. HPV types 16 and 18 are the high risk types and are associated with more than 80% of cervical cancers all over the world. The vaccine in addition protects against genital warts and condylomas caused by low risk HPV types 6 and 11. In 2009, GSK introduced its bivalent vaccine effective against HPV types 16 and 18. The two vaccines underwent extensive trials before their launch that showed high efficacy through 100% seroconversion rates. Both vaccines have about 60 months followup data among vaccinated cohorts showing persistence of high antibody titres and significant reduction in incidence of CIN 2+ cases in these populations.

Both vaccines were initially introduced with a dosage schedule of three doses. The quadrivalent vaccine was recommended at 0, 2 and 6 months while the bivalent vaccine was recommended at 0,1 and 6 months.

The seroconversion rates in those vaccinated with one dose, two dose and three doses were compared with unvaccinated women. The data showed that efficacy was comparable in two dose and three dose regimens. Hence, WHO in 2014 recommended the use of only two doses (0 & 6 months) for adolescents aged below 15 years. Three doses are now recommended for those above 15 years or for immunocompromised individuals. There is more evidence to show that a single HPV vaccine dose is as effective in preventing HPV infection as multi dose schedules in healthy young women.

Merck launched the nona valent vaccine (HPV 9) in 2014 after clinical trials on more than 15000 women showing comparable efficacy with HPV2 and HPV4 vaccines against HPV type 16 and 18. It is effective against 5 more high risk HPV types (31,33,45,52,58). The nonavalent vaccine is not yet available in India.

The HPV vaccination is ideally recommended for adolescents aged between 9-14 years. Vaccination at this age showed the highest efficacy because the The Geometric Mean Titres (GMTs) induced by both vaccines were two times higher in girls aged 10-15 than older girls aged 16-26. The vaccine is not licensed for males in India. If there is a shortage of HPV vaccine, vaccinating boys and men will obviously not be given the same priority as vaccinating adolescent girls.

Catch-up vaccination through age 26 years was recommended for all women, men who have sex with men, transgender persons, and immunocompromised persons. Vaccination for males was recommended from 13 to 21 years.

Recent ACIP guidelines (2019) have recommended catchup vaccination for both girls and boys from 15 through 26 years with a three dose schedule (0, 1-2, 6) if they have not received it at the recommended age of 10-12 years.

This guideline also recommends shared decision making for HPV vaccination to adults aged 27 to 45 years who have not started or completed the vaccination series based on individual risk factors and likelihood of benefit. age. Thus, selective vaccination of adults aged 27 to 45 years is advised, both for cost-effectiveness and given the public policy concern that indiscriminate vaccination of adults older than 26 years could divert focus and vaccine supply from effective adolescent vaccination programs. Persons who are in a long-term, mutually monogamous sexual partnership are not likely to acquire a new HPV infection or benefit from vaccination.

The vaccine may be more beneficial for persons who have had few prior sex partners and who are at greater risk of acquiring unencountered strains of HPV from new sex partners. Individuals with multiple prior sex partners are likely to have been exposed to the vaccine serotypes in the past, reducing usefulness. The other recommendations about HPV vaccination schedule and 3 dose schedule for persons with HIV and other immunocompromising conditions remain unchanged. HPV vaccination can be offered to persons who are breastfeeding or lactating. It should not be given during pregnancy, but a pregnancy test is not required before vaccination.

It is heartening to know that the indigenous Serum Institute HPV vaccine has entered phase III clinical trial and showing promising results thus far. The Serum Institute Vaccine, if successful will play a very important role in the elimination of cervical cancer in India.

References

1. Canfell, Kim, Brisson et al. Mortality impact of achieving WHO cervical cancer elimination targets: a comparative modelling analysis in 78 low-income and lower-middle-income countries. January 30, 2020
[https://doi.org/10.1016/S0140-6736\(20\)30157-4](https://doi.org/10.1016/S0140-6736(20)30157-4)
2. Lauren D Oshman et al. Human Papillomavirus Vaccination for Adults Updated Recommendations of the Advisory Committee on Immunization Practices (ACIP) JAMA January 13, 2020.
[doi:10.1001/jama.2019.18411](https://doi.org/10.1001/jama.2019.18411)

E6 ONCOPROTEIN ASSAY IN CERVICAL CANCER SCREENING

Dr Anupama Rajanbabu, Dr. Madhavi P
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Background:

Cervical cancer is potentially preventable with screening. A paradigm shift noted on screening methods from cytology to HPV DNA based tests, they however fail to distinguish transforming infections from transient ones.

The mechanism of HPV induced oncogenesis show that E6 and E7 oncoproteins are essential for the development of cervical cancer. This is based on their interaction with tumor suppressors p53 and pRb, leading to inhibition of apoptosis and uncontrolled cell proliferation respectively. Detection of these proteins is indirect evidence of viral genome integration with that of host genome, which is paramount for expression of E6 and E7 proteins, persistence of virus and for progression to cancer. Hence, research for detection of these new molecular biomarkers led to introduction Onco E6 Cervical Test (Arbor Vita Corporation).

Basic principle of the test:

Onco E6 Cervical Test is a dip stick test, using immunochromatographic principle for qualitative assessment E6 oncoprotein expressed by HPV types 16 and 18. Cell lysates generated from the cervical swab specimen are incubated with alkaline phosphate (AP) conjugated with high affinity monoclonal antibodies (mAbs) to E6 oncoprotein. Nitrocellulose test strip with two capture lines having immobilized mAbs to E6 is placed in lysate mix. In the presence of E6 oncoprotein in the mix, a tertiary complex is formed which creates purple lines in the corresponding capture lines of the strip.

A cross-sectional study was conducted by Rifa et al. (1) on 99 women with CIN or cervical cancer on cervical biopsy and not taken any treatment. A cervical swab specimen collected from them was sent to virology lab for Onco E6 Cervical Test assay.

Results reported E6 positivity in 36/99 women and 4.44%, 28.57%, 50%, 77.78% for CIN I, II, III and cervical cancer respectively. Among E6 positive cases, 83.33%, 13.89%, 2.78% were positive for HPV type 16, 18 and both respectively. Multi-nominal logistic regression analysis produced Odds ratio with 95% confidence interval was 6.95 ($p = 0.052$), 18.10 ($p = 0.026$) and 43.57 (p value < 0.001) for CIN II, III and cervical cancer respectively.

The results proved a significant association between E6 oncoprotein expression and cervical disease severity, which increased with increasing severity of disease. Thus the onco E6 test can be used as a triage method for primary HPV screen positive cases to detect true cancer precursors which have high risk of progression to cancer.

Reference:

1. Rifat Ara, et al. Low-Cost Molecular Biomarker HPV-16/18 E6 Oncoprotein Expression in Cervical Intraepithelial Neoplasia (CIN) and Cervical Cancer with Its Relation with Severity of Neoplastic State. *Indian Journal of Gynecologic Oncology* (2020)18:73.

<https://doi.org/10.1007/s40944-020-00416-5>

PRIMARY HPV SCREENING FOR CERVICAL CANCER

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Cervical cancer continues to be a major health concern worldwide, especially in low- and middle-income countries, which lack universal screening programmes. Even though cytology was considered the gold standard, the need for a repeated test due to poor sensitivity makes it cumbersome. This recent comprehensive report by Neerja Bhatla and Seema Singhal summarises various methods and screening strategies for cervical cancer. Recognition of persistent HPV infection as an important risk factor for cervical cancer and pre-cancerous lesions was the rationale to consider HPV test as the primary screening modality. It typically yielded a higher sensitivity compared to cytology (96.1% versus 53.%) but lower specificity (90.7% versus 96.3%).

The HPV tests include DNA based HPV assays by (i) Direct genome detection (Hybrid capture2 and CareHPV), (ii) amplification of HPV L1 fragment (Cervista HPV-HR, BD Onclarity HPV assay), and (iii) amplification and genotyping of HPV 16 and 18 (Cervista HPV 16/18, Cobas HPV test, Xpert HPV Cepheid, Realtime high-risk HPV assay and papilloCheck). The RNA based HPV assays include amplification of E6/E7 proteins (Aptima HPV assay, PerTect HPV-Proofer assay) and Monoclonal antibodies (Avantage HPV E6 test). Cobas4800, HC2, Aptima, and BD Onclarity are clinically validated tests for primary cervical cancer screening. The practical concerns associated with HPV tests are the need for a dedicated laboratory facility, affordability, and the processing time (which also challenges the feasibility of Single Visit Approach).

For HPV-positive women, it is essential to adopt an appropriate triage strategy (Cytology triage, HPV genotyping triage, or VIA triage) to segregate clinically unimportant lesions that do not require colposcopy. There exists only a mild rise in the sensitivity for CIN 2 as well as CIN 3 on addition of cytology to HPV, with the expense of specificity and cost..

In the vaccinated cohort, screening can be started at an older age and can be done at longer intervals since there is mounting evidence that there is a fall in prevalence of CIN among the vaccinated cohorts. However, it is worth noting that the currently available vaccines do not offer complete protection against high-risk HPV.

The cost-effectiveness of primary HPV test has been demonstrated by various studies comparing multiple screening modalities. It detects more CIN lesions at a lower/affordable cost and offers better reassurance once the test turns negative. On balance, a clinically validated HPV test (as the primary screening modality) along with HPV vaccination can be considered as an efficient and currently the best option for prevention of cervical cancer and pre-cancerous conditions. With 70% of HPV screening coverage along with treatment for 90% detected lesions by 2030 would potentially help eradicate the clinical and socioeconomic burden associated with cervical cancer.

Reference:

1. Neerja Bhatla, Seema Singhal. Primary HPV screening for cervical cancer. Best Practice & Research Clinical Obstetrics & Gynaecology

<https://doi.org/10.1016/j.bpobgyn.2020.02.008>

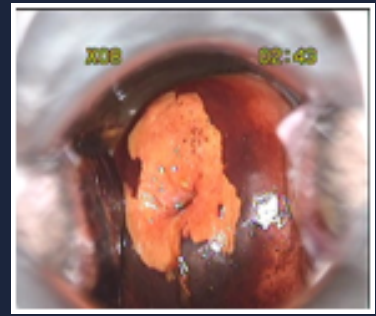
CLINICAL PEARLS

Dr. Premalatha
Gynaecologist, Colposcopist
Ratna Medical Centre, Coimbatore



Q1- Mrs P a 29yr old lady, presented with history of one month duration of increased vaginal discharge accompanying irritation and itchiness of vagina and vulva

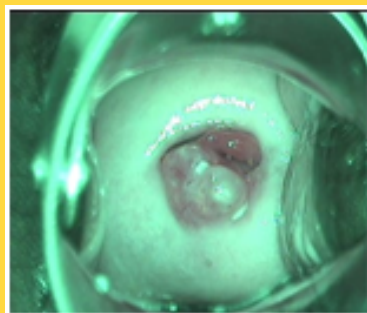
Following are her vulval and colposcopy pictures



1. What is the interpretation
2. How can you manage her?



Q2- Mrs A, 43 yr old lady was referred for colposcopy for abnormal growth in cervix and one year history of inter-menstrual bleeds. Her recent LBC reported as – NILM, moderate inflammation.



1. What are the features seen in the pictures?
2. What further management is needed?

WATCH THIS SPACE..

With HPV as primary screening, the potential for self-collection has increased. In women with high-grade disease, the viral load in self-collected vaginal specimens is significantly lower than in direct endocervical samples, thereby requiring PCR to amplify the specimen.

The novel platform of AmpFire HPV assays is a technology developed by the California-based Atila Biosystems. AmpFire has regulatory approval from CE-IVD, China, Indonesia, Israel and Belgium. It is in use in eight African countries, plus regions of several other LMIC's

- There are two platforms:
- i) A screening assay for 16, 18, with a pool of thirteen high-risk HPV types
 - ii) a genotyping assay for 15 specific types

The AmpFire assay uses isothermal amplification to amplify the specimens. This methodology results in a constellation of assays addressing not only HPV, but all common STDs as well as COVID-19 in a simple, fast, versatile platform. Specifically the assay detects HPV from raw samples and no DNA extraction is needed. Turn around times are less than one hour.

No special labs or air flow management are needed, just a simple room. The AmpFire assay requires only 1 tube for its screening assay and four tubes are used for the full genotyping assay, which also takes less than 1hour and can be run individually, sequentially or simultaneously. Samples do not require batch processing, and the equipment is inexpensive and portable

A pilot study to test the AmpFire HPV screening assay using CIN2 or worse as the endpoint was conducted. For self and direct testing the Kappas ranged from 0.86 – 0.90 and there was only 1 discordant case >CIN3 (a non-16/18 AmpFire self-test positive, Cobas self-test negative). The AmpFire assay demonstrated equal sensitivity and significantly better specificity than the Cobas assay

The amplification works beautifully for self-collected samples and the technologies' acceptance of dry-brush transport and resistance to enzyme inhibition makes the "system" simple, inexpensive and adaptable to large population-based screening programs.

Table 1
Comparison of AmpFire's and Cobas' sensitivity and specificity for cervical CIN2 lesions or worse, using clinician-collected and self-collected samples.
Adapted from Zhang et al.⁵

High-Risk HPV Test Sample	Sensitivity for ≤CIN2 (%) (n) (CI)	Specificity for ≤CIN 2 (%) (n) (CI)
AmpFire Clinician-collected samples	95.74% (90/94) (88.85-98.63)	90.77% (5399/5948) (90.00-91.49)
AmpFire Self-collected samples	96.81% (91/94) (90.29-99.17)	89.81%* (5342/5948) (89.01-90.56)
Cobas Clinician-collected samples	92.55% (87/94) (84.75-96.70)	91.04% (5415/5948) (90.28-91.75)
Cobas Self-collected samples	95.74% (90/94) (88.85-98.63)	88.48%* (5263/5948) (87.64-89.28)

*p= <0.05

The sensitivity for CIN2 or worse was similar between AmpFire and Cobas tests. Specificity was significantly better for AmpFire than Cobas.

POORNAM (COMPLETE)

Sharda Jayaraman
Psychotherapist
GKNMH, Coimbatore

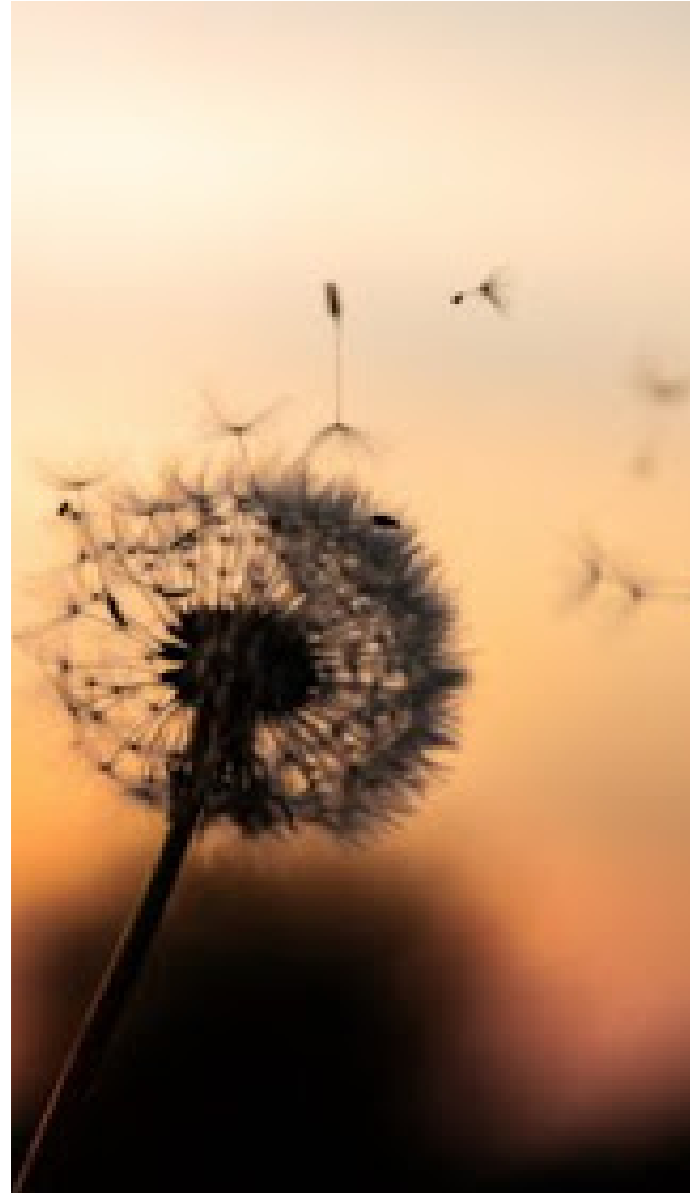


Medical professionals are expected by patients to be all-knowing, strong, powerful, God-like protectors and are placed on a high pedestal. While on one hand, this helps patients unload their fears and get continuous reassurance in their path of getting well, it does not seem to give doctors the opportunity to live out their vulnerable and human sides. Constantly having to assume this larger, all-knowing role can cause stress and the more doctors ignore acknowledging their own vulnerable selves, the more the pressure accumulates.

Thus, striking a balance between what physicians are expected to be (the larger than life image) and who they are, is the key to physical and mental health and the precursor to joy and happiness. This can and should happen as a day-to-day practice. A moment by moment movement from pressure to power.

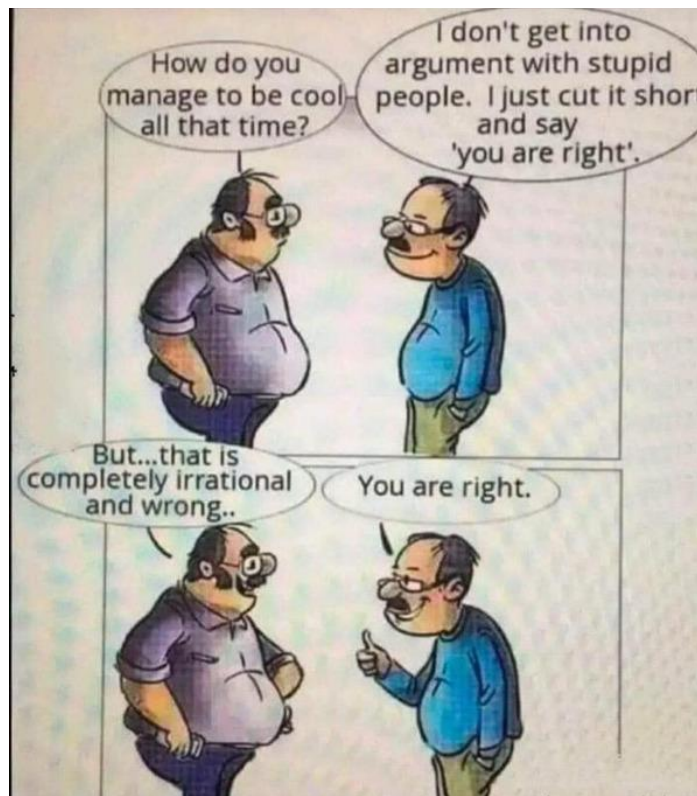
So, how does one identify this imbalance - By watching the subtle clues the body sends in the form of irritation, inappropriate emotional outbursts and so on. Once aware, shifting from stress to balance can be made by the allowing of 'living out from both polarities'. The first step is to acknowledge and to be kind to ourselves and to frequently stop and reflect on personal needs and wants.

In the course of our lives, all of us have gathered enough knowledge and information about taking care of ourselves. Like exercising, avoiding junk food, meditating, taking breaks and so on. Still most of us are unable to follow this consistently. So the question arises 'why'? An introspection as to "What is stopping us from following good advice?" can lead us to explore and unearth our resistance. We could start by exploring one simple behaviour which we are willing to change - NOW !



To make a start in the process of shifting towards becoming compassionate towards oneself, can we take a moment to check before we are compelled to say 'Yes' to a task. In other words, will this "yes" push us to include this task in our long to-do list where we have bitten off more than we can chew leading to pressure. It is important that we take the time to check and to practice saying "No". This can bring a shift from prioritising others and to start looking after ourselves. Thus starts the attempt to start living from both parts of ourselves.

IN A LIGHTER VEIN



ANSWERS

Answer- 1

1. Vulva shows multiple benign warts. These are caused by low risk HPV subtypes. They are generally multicentric. About one third of individuals have associated changes on cervix. Pap test is necessary and where feasible colposcopy can be done. Colposcopy shows a low grade CIN characterised by feathery indistinct AW areas, no vessel abnormal features and yellow staining on Lugol's application.

2. Topical Podophyllin application was suggested and it was explained that warts tend to recur. Podophyllin is once a week application only. Other modalities of treatment are cryotherapy, local 5FU, local excision and local Imiquimod. However it recurs in upto 20% of cases. LBC confirmed LSIL, HRHPV reported as negative and therefore follow up after a year for LBC and HRHPV has been recommended.

Answer- 2

1. Cluster of Nabothian follicles/ cysts are seen in the lower lip. There is a polyp seen coming through os. No abnormal vasculature is seen and there is no AW area after application of 3% acetic acid.

2. Polyp was avulsed and sent for HPE which confirmed benign endocervical polyp. Nabothian follicles/ cysts are benign mucous cysts formed when cervical gland crypts are covered by advancing squamous metaplasia. One or more can be seen commonly in women above 35 years of age and do not warrant any treatment. Very rarely larger ones need to be excised if they interfere with visualising cervix as a whole or with obtaining a Pap smear. This lady was reassured and referred back to her gynaecologist with suggestion of repeat Pap smears at regular intervals.

SHARE YOUR ACTIVITIES

1. Cervical Cancer prevention activities at Amrita Institute of Medical Sciences, Kochi in Jan 2020- Dr. Anupama Ranjanbabu



During the month of January Department of Gynecologic oncology at Amrita institute of medical Sciences conducted awareness classes among college students about cervical cancer focusing mainly on preventive strategies including vaccination. Over 1500 students studying in various colleges around Kochi were part of the program. Along with world cancer day on Feb4th ,2020, a poster competition was held for these students and best three posters were awarded prizes.



2. Health Camp organised by Medical Women's wing on 10 March, 2020 at Mumbai-Dr. Usha Saraiya



3. Cancer Screening and Awareness Camp Conducted in June 2020 at Coimbatore- Dr. Latha Balasubramani



FORTHCOMING EVENTS

AOGIN India & FOGSI Oncology Committee invite you to

AOGIN India ACADEMICS

1st August 2020-30th October 2020.

Every Saturday 1700-1800Hrs.



RESEARCH METHODOLOGY LECTURE SERIES

Date & Time	Topic	Speaker
01.08.2020 1700 - 1800	Use of evidence based medicine in clinical practice (Study designs , Phases of clinical trials, Evidence Pyramid)	Dr. Senthil Rajappa Basavataarakam Indo American Cancer Hospital and Research Institute, Hyderabad.
08.08.2020 1700 – 1720	1.Measures of Association – Odds, ratio. Relative risk correlation.	Dr.Kanhu Charan Patro Mahatma Gandhi Cancer Hospital and Research Institute, Visakhapatnam.
1725 - 1745	2.Interpretation of forest plot and its applications.	Dr.Sajjal Kakkar Max Superspeciality Hospital, Mohali, Punjab.
1750 -1800	3. Survival Curves – What do they tell us?	Dr.Anand Narayan, GKNM Hospital, Coimbatore.
15.08.2020 1700-1800	How to read a paper and incorporate it in our clinical practice ?	Dr.Santam Chakraborty, Tata Medical Center, Kolkata.
22.08.2020 1700 - 1800	How to write a paper and get it published?.	Dr.Peush Sahni, AIIMS, Editor, The National Medical Journal of India.

ICOG points applied for



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CLINICAL PRACTICE LECTURE SERIES

Date & Time	Topic	Speaker
29.08.2020 1700 - 1800	Global Strategies for cervical cancer elimination	Dr. Sankaranarayanan WHO-IARC, Lyon, France.
05.09.2020 1700 - 1720	1. Hereditary Breast and Ovarian Cancers – Indian data	Dr. Rajiv Sarin, Tata Memorial Centre, Mumbai.
1730 - 1750	2. "My mother is BRCA positive. What do I do now?"	Prof. Ranjit Manchanda Barts Health NHS Trust. Royal London Hospital, UK.
12.09.2020 1700 - 1800	Use of the HPV test in Primary Screening	Prof. Neerja Bhatla, AIIMS, New Delhi.
19.09.2020 1700 - 1800	Case based discussion on "Pre- invasive genital diseases".	Moderators- Dr. Shalini Rajaram, New Delhi. Dr. Dipanwita Bannerjee, Kolkata.
26.09.2020 1700 - 1800	Case based discussion on Cancer in pregnancy	Moderators- Dr. Shalini Rajaram, New Delhi. Dr. Dipanwita Bannerjee, Kolkata.
03.10.2020 & 10.10.2020	Webinar for Paramedical staff	Moderators- Dr. Uma Singh, Lucknow. Dr. Bindiya Gupta, New Delhi.

ICOG points applied for



ACKNOWLEDGEMENT

My sincere thanks to my research assistant Rithu Pushparaj, who has worked really hard to put this newsletter together.

