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**Board Members**

**Inaugural President**  
Suzanne Garland  
Australia

**President**  
Jong Sup Park  
Korea

**President Elect**  
Hextan Ngan  
Hong Kong

**Permanent Secretary**  
Jeffrey Tan  
Australia

**Vice President**  
Neerja Bhatla  
India

**Secretary General**  
Efren Domingo  
Philippines

**Treasurer**  
Eng Hseon Tay  
Singapore

**Education Committee**  
You Lin Qiao  
China

**Website**  
TY Chu  
Taiwan

**Liaison**  
Young Tak Kim  
South Korea

**Membership Committee**  
Wisit Suparakarapongkul  
Thailand

**Research Committee Chair**  
Hiroyuki Yoshihikawa  
Japan
Committees & Faculty

Conference Committee

Patron
Suneeta Mittal

Honorary Chairperson
Alka Kriplani

Organising Chairperson
Neerja Bhatla

Organising Secretary
Shalini Rajaram

Organising Secretary
Partha Basu

Treasurer
Sabhya Gupta

Workshop Coordinators

COLPOSCOPY & HANDS - ON LEEP

Swee Chong Quek
Singapore

Vijay Zutshi
India

CYTOLOGY & HPV TESTING

Annie NY Cheung
Hong Kong

Kusum Verma
India

ONCOSURGICAL VIDEO WORKSHOP

Eng Hseon Tay
Singapore

Shalini Rajaram
India
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**ORGANISING COMMITTEE**

- **Founder-President**: Neerja Bhatla
- **Vice-President**: Abraham Peedicayil
- **Honorary Secretary**: Partha Basu
- **Joint Secretaries**: Ranajit Mandal, Gauri Gandhi
- **Advisors**: R Shankaranarayanan, BC Das, M Siddiqui
- **Members**: Vijay K Ahuja, Lalit Dar, K Uma Devi, Veena Jain, Amita Maheshwari
- **Treasurer**: Shalini Rajaram

**AOGIN INDIA EXECUTIVE MEMBERS**

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<td>Jerome L Belinson</td>
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<td>Jose Jeronimo</td>
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<td>Kamal Buckshee</td>
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<td>KD Bakshi</td>
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<td>Kelvin YK Chan</td>
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<td>Kishore Chaudhry</td>
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<td>Kusum Verma</td>
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**FACULTY**

- A Kurian Joseph India
- Aisha O Jumaan USA
- Albert Singer UK
- Aika Kripiani India
- Amita Maheshwari India
- Annie NY Cheung Hong Kong
- Aruna Batra India
- Arvind Rajwanshi India
- Asha Jain India
- Ashok Sehgal India
- Ashrafat Nessa Bangladesh
- Attila Lorincz UK
- Bharti Bhariari India
- Bhudev C Das India
- Cecilia Llave Philippines
- Christopher Fairley Australia
- DK Vijaykumar India
- DN Sharma India
- Efren Domingo Philippines
- Elizabeth Vallikad India
- Eng Hsoon Tay Singapore
- Esmy PO India
- Gauri Gandhi India
- GK Rath India
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- Hema Divakar India
- Hemant Tongaonkar India
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- Ian Frazer Australia
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- Jose Jeronimo USA
- Kamal Buckshee India
- Kavita Singh India
- KD Bakshi India
- Keerti V Shah USA
- Kelvin YK Chan Hong Kong
- Kishore Chaudhry India
- Kusum Verma India

**AOGIN ASIA OCEANIA RESEARCH ORGANISATION ON GENITAL INFECTIONS & NEOPLASIA**

- AOGIN India Executive Members
- Founder-President: Neerja Bhatla
- Vice-President: Abraham Peedicayil
- Honorary Secretary: Partha Basu
- Joint Secretaries: Ranajit Mandal, Gauri Gandhi
- Advisors: R Shankaranarayanan, BC Das, M Siddiqui
- Members: Vijay K Ahuja, Lalit Dar, K Uma Devi, Veena Jain, Amita Maheshwari
- Treasurer: Shalini Rajaram
Dear Friends and Colleagues,

The Organising Committee of AOGIN 2010 welcomes you to the 4th Biennial Conference of the Asia Oceania research organization on Genital Infections and Neoplasia and to India. This is the moment we have been waiting for nearly 2 years now and it is indeed a pleasure to see old friends and new, from not only Asia Oceania but from 40 countries and indeed from different specialties on one platform. India and its neighbouring countries carry the major burden of disease due to genital infections, especially cervical cancer and for long we have lamented – Preventable but not yet prevented. The scope of secondary prevention has now widened with the development of new diagnostic tests, which include HPV tests as well as improved cytology methods; the role of simple visual inspection methods has been better defined; a new era has dawned with the advent of primary prevention through HPV vaccines. Truly we have many reasons to rejoice in this new era of immense possibilities, of the hope that we can finally get rid of the scourge of cervical cancer especially, in spite of all the logistic difficulties, financial constraints and cultural differences we face in most of the Asia Oceania region. The theme of the meeting “Agenda 2010: Towards eradication of cervical cancer” reflects this hope.

AOGIN was born in 2005, modelled on the European organisation, EUROGIN, with the basic goals of research and education in the field of HPV-related diseases. In 2008, we launched the Indian wing of this organisation, AOGIN-India – an association without borders that brings together people from different disciplines with one common goal – to eliminate cervical cancer from India - clinicians and basic scientists, epidemiologists and public health experts, each of whom contribute in different ways to surmount this problem. The AOGIN 2010 conference will help us to consolidate the work that has been going on already and give a direction to our efforts for the future. We have had a record number of proffered papers this year. The active participation of the delegates will ensure that the mission of AOGIN goes forward, not just in the scientific community, but also among the lay public, so that women come forward and demand that they be protected from this highly preventable cancer. At this meeting, we also introduce the concept of WACC, Women Against Cervical Cancer, a movement started at Eurogin in 2008 to increase awareness among women.

We welcome all of you from far and near. The Organizing Committee members have done their very best to put together an excellent scientific and social program. I hope that this three day meet will be as memorable as previous ones have been.

I conclude my welcome with a quotation from Prof. Fathallah, the former President of FIGO:

“Women are not dying because of disease we cannot treat. They are dying because societies yet have to make the decision that their lives are worth saving.”

At this AOGIN meeting we pledge to save every life that we can.

Sincerely

Neerja Bhatla
Organizing Chairperson
**IF YOU ARE A CHAIRPERSON**

Locate your session room as soon as possible.

Arrive in your session room 15 minutes before beginning of the session.

We remind you that:
- The room must be cleared exactly in accordance with the program schedule.
- Discussion time must comply with the allowed timing.
- Discussants should clearly state their name, institution and country.
- Participants should not speak without permission from their chairperson.
- Time allocated to presentations includes discussion.

**IF YOU ARE A SPEAKER**

Locate your session room in due time.

Speakers are requested to hand in their slides at the **preview room**.

You should be in your session room 10 minutes before the beginning of the session and meet with the chairperson. Please comply strictly with the instructions given by the chairperson, especially with regard to your time allowance.

**PRESENTATION REQUIREMENTS AND FORMATS**

Only files compatible with PCs can be accepted (no MAC and UNIX). Please prepare your presentation using Power Point 2007 or prior versions, Open Office, PDF.

If you have video files attached to your power point presentation, these must be in one of the following formats:
- .mpeg, .avi or .wmv. We recommend to avoid the .mov (quicktime) format. Should you have .mov files, please export them to .avi format. When saving your final presentation to a CD or a USB memory stick, make sure you include your video files (if any) and all the links to these multimedia files.

Please use the common PC fonts (Arial, Times…) with your PowerPoint presentation and the Wingdings symbols for any special characters.

- The Preview System supports presentations prepared with the following tools (latest versions):
  - MS Office
  - Adobe PDF
  - Open Office
  - Keynote

- Presentations prepared on a Macintosh: these need to be converted to be compatible with the Preview System:
  - Allow enough time when you go to the Preview room as the conversion of the files may be lengthy.
  - We do not guarantee that after conversion of documents prepared with Keynote, the presentation will be completely identical, in particular animations.

- The Preview System supports the Standard Western European fonts. If the presentation contains special characters or needs other fonts, they have to be provided by the speaker in the Preview room.

- Slides must be sized for an on-screen show of 4:3 and NOT 16:9.

- The video files attached to the presentation must be located in the same folder as the presentation files.

**HOLDING IN YOUR FILES**

Your computer file must be handed in to the personnel in the preview room either as a CD, a ZIP (100 or 250 Mbyte) or on USB memory stick, **as early as possible**:
- In the morning for the afternoon sessions
- The day before the presentations for the sessions scheduled for the morning.

In any case, presentations must be handed in at the **Preview Room two hours before the beginning of the session at the latest**

Sessions are tightly scheduled and strict compliance with the allotted time frame is essential.

**PREVIEW ROOM/SPEAKERS ROOM**

The preview room is located at Wazir Hall. The preview room is fully equipped for slide and computer projections. Qualified personnel are available for receiving the slides/files which will be checked before being forwarded to the projectionists at the appropriate time. Speakers will not have access to projectionists; therefore, they must hand in their slides 2 hours before the beginning of the session at the latest. Slides for the early morning sessions must be handed in on the previous day.

Speakers will be able to check their presentations and, if needed, to make slight modifications.

A team is available in the preview room to assist the speakers with these different steps.

The following mass storage devices are accepted:
- CDROM/DVDROM - USB memory stick - Laptop
PLEASE NOTE
No presentation can be directly downloaded on the conference room computer.

IN THE CONFERENCE ROOM
The equipment in the conference room is exactly the same as in the preview room.
The files downloaded in the preview room are automatically backed up and transferred without any modification to the conference room.
A technician is available before and during the presentation in the conference room, to assist the speaker if required.

PRIVACY OF PRESENTATIONS
At the end of the Congress, we systematically remove and delete all the presentations and associated files.
We do not keep or transfer files to the third parties unless requested and authorized by the author or the member of the organization committee.

POSTER PRESENTATIONS
All posters are displayed in Jehangir Hall, Taj Palace Hotel. Only one board side will be allocated to each participant. Authors are requested to ensure installation and removal of the posters on the designated boards, in accordance with the following time schedules:
Dismantling: Any posters that are not collected by 1700 hours on Sunday, March 28, 2010 will be discarded.
The Organizing Committee will not be responsible for any loss or damage to the posters.
Fixing devices can be obtained from the Poster Assistance desk.
Poster boards are numbered according to the program.
The Organizing Committee declines liability for any loss or damage incurred to posters left on their board beyond the indicated time.
Authors are requested to stay close to their poster during the allotted presentation timings. (Coffee and lunchtime breaks).

Disclosure of potential conflicts of interest
Poster presenters of AOGIN 2010 are required to disclose their potential conflicts of interest. Consequently, a conflict of interest statement should be included in the poster.

GENERAL INFORMATION

CONGRESS SECRETARIAT/REGISTRATION
Opening Hours
The registration desk will open on March 26-28, 2010 from 0730 till 1730 hrs, delegates are required to collect their delegate bag, personalized badge and abstract/program book for AOGIN 2010.

ON SITE REGISTRATION
Persons who have not preregistered for the Congress will be able to register onsite at the on-spot counter.

CLOAKROOM
The Cloakroom facility is located at the Registration Area. Cloakroom service is free of charge.

BADGES
All delegates are required to wear their badge at all times throughout their presence at the conference venue, including social events.

CERTIFICATE OF ATTENDANCE
A certificate of attendance will be included with the documents handed out after registration. Participants who register on the spot should request their certificate of attendance from the registration desk.

FOOD AND BEVERAGES
The general registration fee includes lunch and tea/coffee on Workshop/Conference days and during the Social Program on 26th and 27th March 2010.
Vouchers are enclosed in your registration kit for lunch and dinner.

SOCIAL PROGRAM
Inauguration Ceremony
Friday, March 26, 2010, 1800 hrs.
At Durbar Hall, The Taj Palace Hotel, New Delhi
The Inaugural is open to all the delegates and accompanying persons.

Conference Banquet
Saturday, March 27, 2010 at 1930 hrs
At Randhawa Garden, Rangpuri, New Delhi
Delegates and accompanying persons who have registered for the conference will have the opportunity to socialize with their international colleagues. Entertainment program followed by drinks and dinner.
ABBOTT MOLECULAR

Abbott is a global, broad based health care company devoted to the discovery, development, manufacture and marketing of pharmaceuticals and medical products, including nutritional devices and diagnostics. The company employs more than 72,000 people and markets its product in more than 130 countries.

Women’s health has been gaining a lot of importance in the last decade resulting in introduction of new preventive and diagnostic methods particular for cervical, ovarian and breast cancer. Please visit our booth for more information.

Contact Person: Gurprit Singh
Company: ABBOTT MOLECULAR
Address: V-5, Virenser Nagar, Street No 3, New Delhi -110058
Telephone: +91-9560188788
Email: gurprit.singh@abbott.com, Website: www.abbottmolecular.com

AIMIL Limited, New Delhi

AIMIL is a multifunction, multiservice organization providing total solution to a spectrum of industries with presence in 12 cities across India. AIMIL has diversified business interest with focus on distribution, software development & services. In the healthcare arena, AIMIL markets HPV RT PCR & GENO TYPING KITS for Hybridra Innovation autoanalyzer for early detection of diabetes from Impenta Medical, Hospital Information Systems for NextGen eSolutions etc.

At AOGIN, AIMIL launches Home Health Education and Testing for women, combating 5 major diseases, under the brand “Hygea”.

Contact: Dr. Mallika Kapur (mallika@aimil.com) Website: (www.aimil.com)

GSK

GlaxoSmithKline Biologicals (GSK Biologicals), GlaxoSmithKline’s vaccines business, is one of the world’s leading vaccine companies and a leader in innovation. The company is active in vaccine research, development and production with over 30 vaccines approved for marketing and 20 more in development - both in the prophylactic and therapeutic fields. Headquartered in Belgium, GSK Biologicals has 15 manufacturing sites strategically positioned around the globe. In 2008, GSK Biologicals distributed 1.4 billion doses of vaccines – of which 130 million H1N1 vaccine doses - to 182 countries in both the developed and the developing world. Through its accomplished and dedicated workforce, GSK Biologicals applies its expertise to the discovery of innovative vaccines that contribute to the health and well-being of people of all generations around the world.

GlaxoSmithKline – one of the world’s leading research-based pharmaceutical and healthcare companies – is committed to improving the quality of human life by enabling people to do more, feel better and live longer. For further information, please visit www.gsk.com

HOLOGIC, INC

Hologic has grown to become a leading developer, manufacturer and supplier of premium diagnostic products, medical imaging systems, and surgical products created specifically to address the healthcare needs of women throughout the world. The complex health issues facing women today deserve and demand the singular dedication of a passionate company committed to doing everything in its power to help women live longer, stronger, healthier lives. We are proud of the difference we have made in women’s lives for nearly 25 years

Contact Person: Mr. Girish Subramanian
Company address: 250 Campus Drive, Marlborough, MA 01752 USA
Email: intsales@hologic.com, Website: www.hologic.com

MAXCARE MEDICAL SYSTEMS PVT. LTD.

A partner of B’ORZE Inc., America for South Asia, deals in Digital Video colposcope which is head-quartered in Delhi with regional offices all over India. We have a maximum market share in India for Digital video colposcope in a short span of 5 years which includes Medical Collages, Corporate hospitals, Individual Hospital and Private Practitioners.

We always strives for the maximization of customer satisfaction, by providing rapid, professional, efficient and low cost after sales services. We are also committed to provide the highest quality medical equipments and services at the most competitive prices. Its products have the best performance/Price ratio in the market.

Since its inception, the policy of Maxcare Medical Systems has been focus on Customer as Customers are the most valuable asset. Quality and safety have priority in everything we do. For any assistance, you can call on 0091-9319003030 & 011-32842271 or log on to maxcaremedicalsystem.com

MSD PHARMACEUTICALS PVT. LTD.

MSD, which operates in India via three separate legal entities MSD Pharmaceuticals Pvt. Ltd., Organon India Limited and Fulford India Limited, is the subsidiary of Merck & Co. Inc. USA. Today’s MSD is working to help the world be well. Through our medicines, vaccines, biologic therapies, and consumer and animal products, we work with customers and operate in more than 140 countries to deliver innovative health solutions. We also demonstrate our commitment to increasing access to healthcare through far-reaching programs that donate and deliver our products to the people who need them. MSD. Be well. For more information, visit www.msd.com.

Company address: MSD Pharmaceuticals Pvt. Ltd.
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Tel: +91 124 4647300 Fax: +91 124 4375581/64
Email: contactmdindia@merck.com Website: www.msd.com; www.msdindia.in

DIAGEN

DIAGEN is the leading global provider of sample and assay technologies, used to isolate and process DNA, RNA and proteins from biological samples such as blood or tissue. Assay technologies are used to make such isolated biomolecules, visible. DIAGEN has developed and markets more than 500 sample and assay products as well as automated solutions for such consumables. The company provides its products to molecular diagnostics laboratories, academic researchers, pharmaceutical and biotechnology companies, and applied testing customers for purposes such as forensics, animal or food testing and pharmaceutical process control. DIAGEN’s assay technologies include one of the broadest panels of molecular diagnostic tests available worldwide. This panel includes the digene HPV Test, which is regarded as the “gold standard” in testing for high-risk types of human papillomavirus (HPV), the primary cause of cervical cancer. DIAGEN is publicly listed on the NASDAQ and Frankfurt stock exchanges and has more than 3,000 employees in over 30 countries worldwide, including more than 400 employees across 10 offices in Asia.

SHENZHEN GOLDWAY INDUSTRIAL, INC

Founded in 1995, Goldway has been focusing on the patient monitor, fetal monitors and digital video colposcope. With the 15 years development, Goldway has established a strong position in China healthcare market. Goldway has a strong distribution networks with more than 20 sales offices and service centers in China. The products have been exported to more than 70 countries worldwide.

After joining Philips in 2008, Goldway are taking both brand and technology advantages of Philips to improve marketing competitiveness and provide better reliable and affordable medical equipment.

Base on the principle of win-win cooperation, Goldway is willing to work with its partners to provide the best possible products and services.

Tel: +86 755 26980999 Fax: +86 755 26980222 Email: jeff.zzz.zhang@philips.com; Xiaolan.ren@philips.com
Website: www.goldwayhealthcare.com

THE GLOBAL COMPANY KARL STORZ

Since the KARL STORZ company was founded in 1945, more than half a century has passed - a period of time during which the enterprise has written a significant chapter of medical and technological history. Karl Storz had a vision which was transformed into reality and has been extended through to this very day thanks to pioneering discoveries and inventions.

Since its beginnings in 1945, KARL STORZ has established itself worldwide as an international and highly regarded company in the production and sale of medical instruments and devices. Not a giant on an international scale, but leaders in matters that count: creativity, versatility and competence.

Today KARL STORZ is internationally acclaimed as the World Leader with its Endoscopic product ranges for Human Medicine, Veterinary Medicine & Industrial Endoscopy.

Future and Tradition

The future has tradition, but tradition too has a future! KARL STORZ will maintain and extend even further its leading position in technological development. However, genuine progress is rarely spectacular – it is the result of countless individual steps that are subjected to repeated scrutiny.

For more details please visit the company website: www.karlstorz.de
## PRE-CONGRESS COLPOSCOPY AND HANDS-ON LEEP WORKSHOP

**co-sponsored by the International Federation of Cervical Pathology and Colposcopy (IFCPC)**

March 26, 2010, 8.00 a.m.- 4.00 p.m.

**Venue:** Maulana Azad Medical College, New Delhi

**Coordinators:** Swee Chong Quek, Singapore; Vijay Zutshi, India

### Programme

#### 0800-0830 hrs - Registration & Inauguration

#### 0830-1030 hrs - Colposcopy Course

**Chairpersons:** Jeffrey Tan, Swaraj Batra

1. Objectives of the Course
2. Anatomical and histological basis of colposcopy
3. Colposcopy of the normal cervix
4. Colposcopy of the abnormal cervix
5. Pitfalls of colposcopy
6. The role of cold coagulation in the treatment of CIN

Swee Chong Quek, Singapore
Patrick Walker, UK
Albert Singer, UK
Jeffrey Tan, Australia
Swee Chong Quek, Singapore
R Sankaranarayanan, France

#### 1030 - 1100 hrs - Coffee Break

#### 1100-1300 hrs : Practical Case Demonstration (Live):

Patrick Walker, Swee Chong Quek, Jeffrey Tan, R Sankaranarayanan

**Coordinators:** Partha Basu, Saritha Shamsunder, Neha Gami

1. Colposcopy
2. Cryotherapy
3. Cold Coagulation
4. LEEP

#### 1300 - 1400 hrs - Lunch

#### 1400-1600 hrs - Breakout Groups

(I) Practical Hands-on cryotherapy and LEEP exercises (six stations, two groups):

(II) Interactive Case Discussions - 60 mins - Albert Singer, Patrick Walker, Swaraj Batra

#### 1600 hrs - Close of Workshop

#### 1600 - 1700 hrs - Training of Trainers (By invitation only)

**Introduction:** Vijay Zutshi

- IFCPC role in colposcopy training and experience of ToT in BSCCP
- QA in colposcopy including web based education
- Colposcopy training in developing countries
- Collaboration of ToT in India - Model for consideration
- Open discussion chaired by nominee from India host

Patrick Walker
Jeffrey Tan
Swee Chong Quek
Veena Acharya
Swaraj Batra
Panel discussion, focused on the Asia-Pacific world region, with the following objectives:

1. WHO recommendations for HPV vaccines
   - Neerja Bhatla

2. Monitoring of outcomes for different cervical cancer prevention strategies including vaccination in the Asia/Pacific region
   - You Lin Qiao

3. Feasibility and challenges of integrating HPV vaccines into existing cervical cancer prevention strategies in the Asia/Pacific region
   - Partha Basu

4. Feasibility and challenges of integrating HPV vaccines into existing cervical cancer prevention strategies and adolescent health programs in the Asia/Pacific region
   - Suzanne Garland

5. Review data about HPV vaccine safety in Asia/Pacific region and globally, to review safety monitoring systems, and to discuss effective ways to address concerns about vaccine safety
   - Manju Rani

6. Discuss the efficacy, feasibility, and cost considerations of vaccinating boys against HPV
   - Manju Rani

7. Discuss PATH’s demonstration projects in the Asia-Pacific region
   - Martha Jacob

Proceedings of this WHO Webcast can be viewed for 6 months on our website
www.aoginindia.org/webcast
or
http://wstech.wstream.net/aogin/100327
**PRE-CONGRESS WORKSHOP ON CYTOLOGY & HPV TESTING**

March 26, 2010, Time: 9.30 a.m. - 4.00 p.m.
Venue: Durbar Hall, The Taj Palace Hotel, New Delhi

**Coordinators:** Kusum Verma, India; Annie Cheung, Hong Kong

**PROGRAMME**

<table>
<thead>
<tr>
<th>Time</th>
<th>Session</th>
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<tr>
<td>0800-0930 hrs</td>
<td>REGISTRATION</td>
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<td>0930-1030 hrs</td>
<td>CYTOPATHOLOGY</td>
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<tr>
<td><strong>Chairpersons:</strong></td>
<td>Kusum Verma, Manjula Jain</td>
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<tr>
<td>1.</td>
<td>Introduction to the course, Cytology for</td>
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<td></td>
<td>screening: scope and limitations</td>
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<tr>
<td></td>
<td>(Kusum Verma, India)</td>
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<tr>
<td>2.</td>
<td>HPV/Pap triage in routine primary cervical</td>
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<td>cancer screening</td>
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<td>(Kelvin YK Chan, Hong Kong)</td>
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<td>3.</td>
<td>Liquid based cytology and reflex HPV testing</td>
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<td>(Venkateswaran K Iyer, India)</td>
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<tr>
<td>1030 -1100 hrs</td>
<td>TEA/COFFEE BREAK</td>
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<tr>
<td>1100-1300 hrs</td>
<td>HPV DIAGNOSTICS</td>
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<tr>
<td><strong>Chairpersons:</strong></td>
<td>BC Das, Neeta Singh</td>
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<td>4.</td>
<td>Types of HPV DNA tests: Role of HPV</td>
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<td>Genotyping</td>
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<td>(Lalit Dar, India)</td>
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<td>5.</td>
<td>Role of HPV m-RNA testing</td>
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<td>(Sam Ratnam, Canada)</td>
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<td>6.</td>
<td>Biomarkers: Role of p16 and other cell</td>
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<td>cycle markers in triage</td>
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<td>(Annie Cheung, Hong Kong)</td>
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<td>7.</td>
<td>Pitfalls of HPV testing and How to run a</td>
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<td>QA program: WHO Labnet</td>
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<td>(Heather Cubie, UK)</td>
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<td>1300-1400 hrs</td>
<td>LUNCH</td>
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<td>1400-1500 hrs</td>
<td>HISTOPATHOLOGY</td>
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<td><strong>Chairpersons:</strong></td>
<td>Sarla Agarwal, Shyama Jain</td>
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<tr>
<td>8.</td>
<td>CIN: conventional vs. two-tiered reporting</td>
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<td>(Sandeep R Mathur, India)</td>
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<td>9.</td>
<td>HPV carcinogenesis and glandular lesions</td>
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<td>(Arvind Rajwanshi, India)</td>
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<td>10.</td>
<td>Pre-neoplastic lesions of vulva &amp; vagina</td>
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<td>(Manoj K Singh, India)</td>
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<td>11.</td>
<td>Role of immunohistochemistry in problematic</td>
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<td>cervical biopsies</td>
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<td>(Annie Cheung, Hong Kong)</td>
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<tr>
<td>1500-1530 hrs</td>
<td>TEA/COFFEE BREAK</td>
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<tr>
<td>1530-1600 hrs</td>
<td>SCREENING IN SPECIAL SITUATIONS</td>
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<td><strong>Chairpersons:</strong></td>
<td>NK Chaturvedi, Suresh Bhambhani</td>
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<td>12.</td>
<td>Screening in low resource settings</td>
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<td>(Lynette Denny, RSA)</td>
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<td>13.</td>
<td>Screening in the post vaccine era</td>
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<td>(Attila Lorincz, UK)</td>
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<tr>
<td>1600 hrs</td>
<td>CLOSING REMARKS</td>
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<td>(Annie NY Cheung, Hong Kong)</td>
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</tbody>
</table>
**PRE-Congress Oncosurgical Video Workshop**

**co-sponsored by IGCS**

**March 26 2010, Time: 8.00 a.m. - 4.00 p.m.**

**Venue: Jehangir Hall, The Taj Palace Hotel, New Delhi**

**Coordinators:** Eng Hseon Tay, Singapore; Shalini Rajaram, India

### Programme

**0800-0830 hrs - REGISTRATION**

**0830-1030 hrs - SESSION I**

**Chairpersons:** SK Giri, Sunesh Kumar

1. Objectives of the Workshop, Understanding surgical anatomy and pelvic spaces
   - EH Tay, Singapore
2. Abdominal Radical Hysterectomy
   - EH Tay, Singapore
3. Nerve sparing radical hysterectomy
   - Shingo Fujii, Japan
4. Laparoscopic radical hysterectomy
   - Alka Kriplani, India

**1030-1100 hrs - COFFEE BREAK**

**1100-1300 HRS: SESSION II**

**Chairpersons:** Lynette Denny, Amita Maheshwari

1. Vaginal Radical Hysterectomy
   - KD Bakshi, India
2. Extraperitoneal lymphadenectomy
   - Ranajit Mandal, India
3. Vaginal Radical trachelectomy
   - Vito Chiantera, Germany
4. LEEP with Harmonic Scalpel
   - Ryo Konno, Japan
5. Single port laparoscopic radical hysterectomy; Ovarian transposition
   - Shailesh Puntambekar, India

**1300-1400 hrs - LUNCH**

**1400-1500 HRS - SESSION III**

**Chairpersons:** DK Vijaykumar, Vijay Ahuja

1. Sentinel node evaluation in cervical & vulvar cancers
   - SP Somasekhar, India
2. Radical vulvectomy with groin dissection
   - K Uma Devi, India
3. Laparoscopic groin dissection
   - Rupinder Sekhon, India
4. IMRT
   - DN Sharma, India

**1500-1530 hrs - COFFEE BREAK**

**1530-1600 HRS - SESSION IV**

**Chairpersons:** Veena Jain, UD Bafna

1. Pelvic exenteration
   - Kavita Singh, UK
2. Robotic radical hysterectomy
   - Hextan Ngan, Hong Kong

**1600 hrs - CLOSE OF WORKSHOP**

**Shalini Rajaram, India**

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**Quiz on Lower Genital Tract Infections and Neoplasia**

**March 26 2010, Time: 4.00 p.m. – 5.00 p.m.**

**Venue: Jehangir Hall, The Taj Palace Hotel, New Delhi**

**Quiz Masters:** Aruna Batra, Shalini Rajaram, Sumita Mehta
The Organising Committee of “AOGIN 2010” cordially invites you to the

INAUGURATION

of

The 4th Biennial Conference of the Asia Oceania Research Organisation on Genital Infections and Neoplasia

by

Chief Guest Shri Prithviraj Chavan, Hon’ble Minister of State (IC) for Science & Technology and Earth Sciences, Government of India

&

Guest of Honor Smt Jayanthi Natarajan, MP, Rajya Sabha and National Spokesperson, Indian National Congress

on March 26, 2010 at 6.00 pm

at Durbar Hall, Taj Palace Hotel, New Delhi

7.00 pm. Keynote Address:

Beyond the Nobel Prize: Reducing the burden of cervical cancer

Prof Keerti V Shah

Chairpersons: Prof Jong Sup Park, Prof Suneeta Mittal

7.30 pm. Cultural Programme by Manipuri Nrityasharam, Delhi

(presented by Indian Council for Cultural Relations)

8.15 pm. Welcome Reception at Rani Bagh, Taj Palace Hotel, New Delhi
### Session 1: Plenary - Natural History & Epidemiology

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<thead>
<tr>
<th>Session</th>
<th>Title</th>
<th>Speaker</th>
<th>Country</th>
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<tbody>
<tr>
<td>I-1.1</td>
<td>Natural history of HPV infections: epidemiological &amp; clinical perspectives</td>
<td>R Sankaranarayanan</td>
<td>France</td>
</tr>
<tr>
<td>I-1.2</td>
<td>Global HPV epidemiology update</td>
<td>Xavier Bosch</td>
<td>Spain</td>
</tr>
<tr>
<td>I-1.3</td>
<td>Asia Oceania HPV Update</td>
<td>Jihong Liu</td>
<td>China</td>
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<tr>
<td>I-1.4</td>
<td>Burden of cervical cancer in Asia Oceania</td>
<td>Kishore Chaudhry</td>
<td>India</td>
</tr>
<tr>
<td>I-1.5</td>
<td>Male genital HPV infections</td>
<td>Suzanne Garland</td>
<td>Australia</td>
</tr>
<tr>
<td>O-1.1</td>
<td>HPV burden and genotype distribution in anogenital cancers from Asia-Pacific and Middle East region</td>
<td>Xavier Bosch</td>
<td>Spain</td>
</tr>
<tr>
<td>O-1.2</td>
<td>Population prevalence of high risk human papilloma virus (HPV) infection in semi-urban and rural areas adjoining Chennai, India</td>
<td>Malliga J Subramanian</td>
<td>India</td>
</tr>
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</table>

### Session 2: Plenary - Eradication of Cervical Cancer: New Horizons

<table>
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<tr>
<th>Session</th>
<th>Title</th>
<th>Speaker</th>
<th>Country</th>
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<tbody>
<tr>
<td>I-2.1</td>
<td>Cross talk of NKT cells and CD4+CD25+ Regulatory T cells in cervical cancer patients</td>
<td>Shubhada Chiplunkar</td>
<td>India</td>
</tr>
<tr>
<td>I-2.2</td>
<td>Novel cellular/molecular mechanisms of HPV infections &amp; cervical carcinogenesis - Role of epigenetics</td>
<td>Sharmila Sengupta</td>
<td>India</td>
</tr>
<tr>
<td>I-2.3</td>
<td>Sequence variation within HPV16 isolates implicated in cervical cancer pathogenesis</td>
<td>Neeta Singh</td>
<td>India</td>
</tr>
<tr>
<td>I-2.4</td>
<td>New molecular markers in prediction of high grade disease</td>
<td>Sandeep R Mathur</td>
<td>India</td>
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<tr>
<td>I-2.5</td>
<td>Second generation vaccines - a suitable alternative?</td>
<td>Mausumi Bharadwaj</td>
<td>India</td>
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<tr>
<td>I-2.6</td>
<td>Natural antivirus &amp; immunomodulators</td>
<td>Bhudev C Das</td>
<td>India</td>
</tr>
<tr>
<td>I-2.7</td>
<td>HPV and progression to cancer in the immunosuppressed</td>
<td>Priya Abraham</td>
<td>India</td>
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</table>

### Session 3: Plenary - Screening for Cervical Neoplasia

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<th>Session</th>
<th>Title</th>
<th>Speaker</th>
<th>Country</th>
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<tbody>
<tr>
<td>I-3.1</td>
<td>Recent advances in cervical cancer prevention in low-and medium resource countries</td>
<td>R Sankaranarayanan</td>
<td>France</td>
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<tr>
<td>I-3.2</td>
<td>START - UP program results</td>
<td>Jose A Jeronimo</td>
<td>USA</td>
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<tr>
<td>I-3.3</td>
<td>Self sampling- Empowering women to screen themselves</td>
<td>Neerja Bhatla</td>
<td>India</td>
</tr>
</tbody>
</table>
## Session 4: Proffered Papers – New Techniques & Molecular Markers

**Chairpersons:** Annie Cheung, Hong Kong; Robin Mukhopadhyaya, India  
**Time:** 1100-1200 hrs

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<tr>
<th>Session O-4.1</th>
<th>Title</th>
<th>Presenter</th>
<th>Country</th>
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<tbody>
<tr>
<td>O-4.1</td>
<td>Assessment of a real-time computer-assistant imaging system for cervical cytology in China</td>
<td>Bin Yang</td>
<td>USA</td>
</tr>
<tr>
<td>O-4.2</td>
<td>Interleucin-10-1082 G/A polymorphism in HPV related cervical lesions</td>
<td>Mary Clarisse Bozzetti</td>
<td>Brazil</td>
</tr>
<tr>
<td>O-4.3</td>
<td>Comparing the Papanicolaou staining with a newer technique - Modified Ultra Fast Papanicolaou Staining (MUPS) in screening cervical cancer</td>
<td>Pushp Lata Sankhwar</td>
<td>India</td>
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<tr>
<td>O-4.4</td>
<td>A new generation of cervical cancer detection? The power and promise of DNA methylation biomarker</td>
<td>Hung-Cheng Lai</td>
<td>Taiwan</td>
</tr>
<tr>
<td>O-4.5</td>
<td>PCDH10 promoter methylation- a novel biomarker for cervical cancer detection</td>
<td>Deeksha Pandey</td>
<td>India</td>
</tr>
<tr>
<td>O-4.6</td>
<td>Evaluation of the Digene HPV genotyping Probeset Test (PS) relative to type-specific qPCR</td>
<td>Ha Thanh Thai</td>
<td>USA</td>
</tr>
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</table>

## Session 5: Plenary – Management of Cervical Neoplasia

**Chairpersons:** Wisit Supakarpongkul, Thailand; Sudha Salhan, India  
**Time:** 1200-1300 hrs

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<tr>
<th>Session I-5.1</th>
<th>Title</th>
<th>Presenter</th>
<th>Country</th>
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<tbody>
<tr>
<td>I-5.1</td>
<td>HPV positive test: What do you do?</td>
<td>Efren Domingo</td>
<td>Philippines</td>
</tr>
<tr>
<td>I-5.2</td>
<td>CIN management options &amp; post-treatment follow-up</td>
<td>Patrick Walker</td>
<td>UK</td>
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<tr>
<td>I-5.3</td>
<td>Long term complications of cryotherapy and LEEP</td>
<td>Swee Chong Quek</td>
<td>Singapore</td>
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## Session 6: Proffered Papers – HPV Prophylactic Vaccines: Basic & Clinical Aspects

**Chairpersons:** Indrani Ganguli, India; Renu Misra, India  
**Time:** 1200-1300 hrs

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<tr>
<th>Session O-6.1</th>
<th>Title</th>
<th>Presenter</th>
<th>Country</th>
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<tbody>
<tr>
<td>O-6.1</td>
<td>Baseline characteristics of women in Asia-Pacific region vaccinated with AS04-adjuvanted HPV-16/18 vaccine in the phase III PATRICIA trial</td>
<td>Unnop Jaisamrarn</td>
<td>India</td>
</tr>
<tr>
<td>O-6.2</td>
<td>Sustained immunogenicity and efficacy of HPV-16/18-adjuvanted vaccine up to 7.3 years</td>
<td>Cecilia Maria Roteli-Martins</td>
<td>Brazil</td>
</tr>
<tr>
<td>O-6.3</td>
<td>Long-term persistence of immune response to HPV-16/18 AS04-adjuvanted cervical cancer vaccine in women aged 15-55 years</td>
<td>Tino F Schwarz</td>
<td>Germany</td>
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<tr>
<td>O-6.4</td>
<td>Update on quadrivalent human papillomavirus [HPV] 6/11/16/18 vaccine clinical trial efficacy results</td>
<td>Suzanne Garland</td>
<td>Australia</td>
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<tr>
<td>O-6.5</td>
<td>Quadrivalent HPV (types 6/11/16/18) vaccine: End-of-study efficacy against HPV6/11/16/18-related persistent infection and disease in women aged 24 to 45</td>
<td>Ricardo Manalastas</td>
<td>Philippines</td>
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<tr>
<td>O-6.6</td>
<td>HPV genotyping and consequences for HPV vaccination in 500 healthy women attending a private women’s clinic in Tokyo</td>
<td>Sharon JB Hanley</td>
<td>Japan</td>
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**1300-1400 HRS : LUNCH BREAK**
GSK SPONSORED SYMPOSIUM - CERVARIX: AIMING TO MEET REGIONAL NEEDS FOR CERVICAL CANCER PREVENTION

Chairpersons: Neerja Bhatla, India; Hugues Bogaerts, Belgium

The burden of cervical cancer with a focus on Asia Oceania
S-G.1 The challenges of HPV immunology
S-G.2 Cervarix®: The clinician’s perspective
S-G.3 Impact of vaccination on treatment and colposcopy in the Asia Oceania region

GlaxoSmithKline’s initiatives to support access to vaccines across the globe

1400-1515 hrs

DURBAR HALL

1500-1530 HRS: COFFEE BREAK / POSTER SESSION II

WOMEN AGAINST CERVICAL CANCER (WACC) (By invitation only)

Chairpersons: Neerja Bhatla, India; Shalini Rajaram, India

1530-1700 hrs

SHEESH MAHAL

Welcome and Introductions
The WACC Movement
How cervical cancer develops, magnitude of the problem in India
What your doctor can do to prevent cervical cancer
What women want - Panel Discussion
Summary of the Recommendations

SESSION 7: PLENARY - CANCER TREATMENT UPDATES

Chairpersons: Young Tak Kim, South Korea; Vijay Lakshmi Bhargava, India

1545-1715 hrs

DURBAR HALL

1-7.1 Management of early stage cervical cancer – Outcomes of surgery and radiotherapy
1-7.2 Surgical management of FIGO IB2 and IIB cervical cancer
1-7.3 Laparoscopic surgery in Gynaecologic Oncology
1-7.4 The place of chemotherapy in cervical cancer
1-7.5 Novel therapies for cervical cancer

SESSION 8: IARC SYMPOSIUM - PROMISING STRATEGIES FOR CERVICAL CANCER PROGRAMS IN LOW RESOURCE COUNTRIES

Chairpersons: Surendra Shastri, India; Martha Jacob; India

1545-1715 hrs

MUMTAZ HALL

1-8.1 VIA-based screening program in Bangladesh
1-8.2 The China experience on introducing population-based cervical cancer screening
1-8.3 Results from India
1-8.4 Results of cervical cancer prevention programs and SVA in Thailand.
O-8.1 Using best practices for advocacy to strengthen a cervical cancer prevention program in the Philippines
O-8.2 Initial experience with the HPV vaccine in Nepal

1900 ONWARDS: CONFERENCE BANQUET (RANDHAWA GARDEN)
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<th><strong>PLENARY SESSION 9</strong></th>
<th><strong>DURBAR HALL</strong></th>
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<tr>
<td><strong>STIs and Neoplastic Diseases in the Lower Genital Tract</strong></td>
<td>0800-0900 hrs</td>
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<tr>
<td><strong>Chairpersons:</strong> Jebun Nessa Rahman, Bangladesh; SS Trivedi, India</td>
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<tr>
<td>I-9.1</td>
<td>The role of HPV in VIN &amp; VAIN</td>
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<tr>
<td>I-9.2</td>
<td>HPV and HIV infections</td>
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<tr>
<td>I-9.3</td>
<td>Syndromic management of STI’s – The flip side</td>
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<tr>
<td>I-9.4</td>
<td>Treatment of Genital Warts - Efficacy &amp; limitations</td>
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<tr>
<th><strong>SESSION 10: PROFERRED PAPERS</strong></th>
<th><strong>MUMTAZ HALL</strong></th>
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<tr>
<td><strong>Cervical Screening and Colposcopy</strong></td>
<td>0800-0900 hrs</td>
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<tr>
<td><strong>Chairpersons:</strong> Shakti Bhan Khanna, India; Vijay Ahuja, India</td>
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<tr>
<td>O-10.1</td>
<td>Determinants of visual inspection of the cervix after acetic acid application (VIA) positivity in cervical cancer screening of women in a peri-urban area in Andhra Pradesh, India</td>
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<tr>
<td>O-10.2</td>
<td>VIA-VILI as routine gynecologic examination?</td>
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<tr>
<td>O-10.3</td>
<td>How to overcome the problem of unsatisfactory colposcopy?</td>
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<tr>
<td>O-10.4</td>
<td>Diagnostic accuracy of human papillomavirus testing in primary cervical screening: a pooled analysis of 18 population-based studies from China</td>
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<tr>
<td>O-10.5</td>
<td>Evaluation of the Cervista HPV Assay and Mass Spectroscopy for High-Risk HPV Compared To Hc-II? From the ShenCCAST II Trial</td>
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<td>O-10.6</td>
<td>Evaluation of the Cervista HPV assay and Liquid Based Cytology using the Thinprep Integrated Imager? From the ShenCCAST II Trial</td>
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<td><strong>Chairpersons:</strong> Vanita Suri, India; Ranajit Mandal, India</td>
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<tr>
<td>O-11.1</td>
<td>A CareHPV™ reflex test to triage HPV + women in economically constrained community screening programs</td>
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<td>O-11.2</td>
<td>Efficacy, immunogenicity and safety of HPV-16/18 AS04 adjuvanted vaccine In Japanese women: Final analysis at month 24</td>
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<td>O-11.3</td>
<td>Impact of a quadrivalent HPV 6/11/16/18 vaccine in women who have undergone definitive therapy</td>
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<td><strong>Chairpersons:</strong> Scott Wittet, PATH, USA; Mala Arora, India</td>
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<td>O-12.1</td>
<td>Assessment of the subject recruitment systems adopted in a beneficial cervical cancer screening trial (ShenCCAST II).</td>
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<td>O-12.2</td>
<td>It’s a logistical nightmare!*: Recommendations for optimizing HPV school-based vaccination from Australia.</td>
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<td>O-12.3</td>
<td>KAP studies on HPV Infection among Nursing Staff</td>
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### Session 13: Plenary
**New Issues on HPV Vaccination**

**Chairpersons:** Cecilia Llave, Philippines; Usha Saraiya, India  
**DURBAR HALL**  
**0930-1030 hrs**

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<td>I-13.1 Current evidence from prophylactic vaccines - Are we confused?</td>
<td>Eng Hseon Tay</td>
<td>Singapore</td>
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<td>I-13.2 Vaccination for older women: Evidence and practice</td>
<td>Jeffrey Tan</td>
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<td>I-13.3 Therapeutic Vaccines: Current status</td>
<td>Ian Frazer</td>
<td>Australia</td>
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**1030-1100 HRS: COFFEE BREAK/ POSTER SESSION III**

### Session 14: Proffered Papers
**Cervical Screening & Management of CIN**

**Chairpersons:** Smiti Nanda, India; Uma Singh, India  
**MUMTAZ HALL**  
**0930-1030 hrs**

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<td>O-14.1 Shenzhen Cervical Cancer Screening Study I (ShenCCAST I)</td>
<td>Ruifang Wu</td>
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<td>O-14.2 Evaluation Of The POI/NIH Cervico-Vaginal Self-Sampler For HPV - From the ShenCCAST II Trial</td>
<td>Jerome L Belinson</td>
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<td>O-14.3 Trend of management of high grade CIN in a colposcopy clinic of Bangladesh</td>
<td>Ashrafun Nessa</td>
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<td>O-14.4 Correlation of Human Papillomavirus DNA testing with residual disease in treated cases of Cervical Intraepithelial Neoplasia</td>
<td>Sunita Agarwal</td>
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<td>O-14.5 Evaluation of the conservative treatment effect of microinvasive cervical cancer by LLETZ</td>
<td>Huiru Tang</td>
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<td>O-14.6 Lessons from success and failure from cervical cancer screening in Japan</td>
<td>Ryo Konno</td>
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### Session 15: PATH Symposium
**Implementation of HPV Vaccination**

**Chairpersons:** GK Rath, India; Maqsood Siddiqi, India  
**DURBAR HALL**  
**1100-1200 hrs**

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<td>I-15.1 Lessons from vaccine introduction in the developed world (Scotland)</td>
<td>Heather Cubie</td>
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<td>I-15.2 Lessons from vaccine introduction in developing countries (Vietnam)</td>
<td>Aisha O Jumaan</td>
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<td>I-15.3 New tools for comprehensive cervical cancer prevention planning</td>
<td>Scott Wittet</td>
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### Session 16: Qiagen Sponsored Satellite Symposium – Primary Screening

**Chairpersons:** TY Chu, Taiwan; LK Dhaliwal, India  
**MUMTAZ HALL**  
**1100-1200 hrs**

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<td>I-16.1 Can HPV be the sole primary screening test?</td>
<td>Jack Cuzick</td>
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<td>I-16.2 HPV Screening - New data &amp; new algorithms.</td>
<td>Atilla Lorincz</td>
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<tr>
<td>I-16.3 The accuracy of colposcopy and its appropriate use in cervical cancer screening trials.</td>
<td>Jerome L Belinson</td>
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### MSD Sponsored Symposium: Reinforcing Benefits to Various Populations

**Chairpersons:** Ian Frazer, Australia; Sanjay Gupta, India  

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<td>Impact to Genital Warts: Australia Experience</td>
<td>Christopher K Fairley, Australia</td>
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<td>S-M.2</td>
<td>Efficacy in clinical trial population of FUTURE I-II</td>
<td>Suzanne M Garland, Australia</td>
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<td>S-M.3</td>
<td>Quadrivalent HPV vaccine: End-of-study efficacy against anogenital disease in men and women</td>
<td>Richard Manalastas, Philippines</td>
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**Monday, March 29, 2010**

**1300-1400 HRS: LUNCH**

### Session 17: Plenary - AOGIN Education Session

**Chairpersons:** You Lin Qiao, China; Raksha Arora, India  

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<td>Can cervical cancer be controlled in the developing world?</td>
<td>Lynette Denny, South Africa</td>
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<td>I-17.2</td>
<td>How to educate the public on human papillomavirus and cervical cancer prevention:</td>
<td>Hextan Ngan, Hong Kong</td>
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<td>I-17.3</td>
<td>CIN 1: When should it be treated?</td>
<td>Shalini Rajaram, India</td>
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### Session 18: Proffered papers – STIs

**Chairpersons:** Urmil Sharma, India; Nutan Agarwal, India  

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<td>Incidence of Herpes Simplex Virus Type 2 in young reproductive age women in Mysore, India</td>
<td>Purnima Madhivanan, India</td>
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<td>O-18.2</td>
<td>Vaginal douching facilitates infection of human papillomavirus and non-regression of its cervical intraepithelial lesion</td>
<td>TY Chu, Taiwan</td>
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<td>O-18.3</td>
<td>HPV detection from urine sample compared with cervical smear in women of reproductive age group with or without high risk factors</td>
<td>Jyoti Malik, India</td>
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<td>O-18.4</td>
<td>High Risk HPV DNA is a useful biological marker for diagnosis of early cervical cancer in HIV sero-positive women</td>
<td>Veena Acharya, India</td>
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<td>O-18.5</td>
<td>The behavior of CIN In HIV seropositive women</td>
<td>Seema Sharma, India</td>
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<td>O-18.6</td>
<td>Healthy women project: Organized population based screening</td>
<td>Lakhbir Dhaliwal, India</td>
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### Session 19 – Debates

**Chairpersons:** Kamal Buckshee, India; Hema Divakar, India  

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<td>D.1</td>
<td>HPV vaccination of older women is preferable to screening in developing countries</td>
<td>Partha Basu, India</td>
<td>Elizabeth Vallikad, India</td>
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<td>D.2</td>
<td>HPV test should be the sole primary screening test</td>
<td>Rama Joshi, India</td>
<td>Usha Rani Poli, India</td>
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### Session 20: Proffered Videos

**Chairpersons:** Rekha Kurian, India; Sabhyata Gupta, India  

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<td>Laparoscopic pelvic anatomy related to radical hysterectomy</td>
<td>Pradeep Garg, India</td>
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<td>V-20.2</td>
<td>Microcolposcopy in evaluation of cervical pathology</td>
<td>Meena Naik, India</td>
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<td>V-20.3</td>
<td>Bowen’s disease of vulva - Timing and technique of vulvectomy</td>
<td>Anju Rajesh Hajari, India</td>
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<td>V-20.4</td>
<td>“The Real Lady Killer” – a BBC documentary on cervical cancer prevention in Uganda,</td>
<td>Scott Wittet, USA</td>
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**Presentation of AOGIN Guidelines on Cervical Cancer Prevention**

**Chairpersons:** Suzanne Garland, Australia; Neerja Bhatla, India

**Presenter:** Hextan Ngan, Hong Kong

Panel Discussion and Q&A Session

1615-1645 hrs

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**AOGIN General Assembly & Closing Ceremony**

**Address by** Incoming President Professor Hextan Ngan

**Prize distribution**

Announcement of AOGIN 2012 venue and Close of Conference

1630-1715 hrs

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**See you in Hong Kong in 2012**
This publication contains the abstracts submitted for AOGIN 2010 Conference, held in New Delhi, India, from March 26-28, 2010.

The abstracts have been organized to reflect the scientific program and arranged session wise. The Poster Presentations are listed towards the end, the poster codes correspond to the poster board number allotted for the poster session.

The following codes have been used:

I – Invited talks
O- Oral Presentation
P- Poster
D- Debates
V- Video Presentation
G- GSK Symposium abstracts
M- MSD Symposium abstracts
W- Workshop

Disclaimer:
Publication of these abstracts does not imply that the information, data, result conclusion presented are endorsed by AOGIN or by the Organizing Committee or Scientific Committee of the AOGIN 2010 Conference.
KEYNOTE ADDRESS

BEYOND THE NOBEL PRIZE - REDUCING THE BURDEN OF CERVICAL CANCER

Keerti V Shah

Keerti Shah is Professor of Molecular Microbiology & Immunology at the Johns Hopkins Bloomberg School in Baltimore, USA. He received his medical degree as well as training in virology in Pune, India. He participated in the early IARC studies which helped establish the link between HPV infection and cervical cancer and in studies that defined the role of HPVs in subsets of vulvar and oropharyngeal cancers and in the etiology of juvenile-onset respiratory papillomas. Beginning in 2000, with financial support from NIH and the Dept of Biotechnology, Govt of India, Dr Patti Gravitt and Dr Shah collaborated with investigators in Medchal Mandal in Andhra Pradesh.

The Nobel Prize awarded to Dr. Zur Hausen in 2008 was a recognition of his contributions and leadership in the field where, in a short span of thirty years, the HPV etiology and pathogenesis of cervical cancer were understood and vaccines were developed to prevent HPV infections. These were spectacular achievements, but the goal of reducing the burden of cervical cancer remains unrealized.

Tens of millions of women in the industrialized nations, but hardly any in the developing nations, have received HPV vaccines. It would seem that the currently available vaccines, as well as the second generation vaccines, should be readily available in areas that need them most, considering that the knowledge that made it possible to develop these vaccines was acquired by unprecedented collaboration between investigators and with the help of tens of thousands of women who participated in studies, in all parts of the world.

We also need a simple and effective screening strategy that can be widely applied. An HPV assay on vaginal swabs self-collected at home would identify the approximately 10% of women who are HPV-positive and at high risk of disease; the other 90% do not have to visit the clinic at all. We don’t yet know how best to identify the small fraction (10-20%) of HPV-positive women who have pre-cancers or cancers and to provide facilities for treatment of these women. Community-based programs that combine vaccination, screening and treatment are required for us to write the second chapter of this story which will be as glorious as the first.

PRESIDENTIAL LECTURE

CHANGING TRENDS OF SURGERY FOR CERVICAL CANCER

Jong Sup Park

Division Gynecologic Oncology, Department of Obstetrics and Gynecology, Seoul St. Mary’s Hospital, The Catholic University of Korea, Seoul, Korea

Cervical cancer is one of the major gynecologic malignancies. Although its incidence has decreased by screening programs, yearly in the world, there are approximately 493,000 new cases of cervical cancer diagnosed and 274,000 deaths from this disease.

Radical hysterectomy, introduced by Ernst Wertheim and Friedrich Schauta in late 19th century, is now a standard therapeutic method for early stage cervical carcinoma (FIGO clinical staging IA1 with lymph-vascular space invasion to IIA). Disadvantages like severe complications, high morbidity and mortality have been gradually overcome through steady advances and modifications of surgical technology.

Currently, radical hysterectomy following neoadjuvant chemotherapy for size reduction is also selectively applied to locally advanced cases of cervical cancer with bulky disease (FIGO clinical staging IB2, IIA even to IIB) in premenopausal women who wish to preserve ovarian function. Minimal invasive modality, laparoscopic radical hysterectomy and pelvic or paraaortic lymphadenectomy was applied in early stage cervical cancers. Recently, robotic surgery was adopted for selected cases.

In the 1980s, Eugene Auberel and Daniel Dargent introduced abdominal and vaginal radical trachelectomy, respectively, which allowed young women with early stage cervical cancer to retain the potential for fertility. The concept of the radical trachelectomy procedure is to preserve the body of the uterus, which in turn allows preservation of childbearing potential.

The advent of pelvic autonomic nerve sparing surgery minimized complications of the urinary system by preserving sympathetic inferior hypogastric nerve and vesical (bladder) branch of parasympathetic pelvic splanchnic nerve. Introduction of sentinel node dissection, laparoscopic surgical staging and laparoscopic extraperitoneal lymphadenectomy may help avoid unnecessary procedures, decrease morbidity and improve quality of life. According to previous reports, novel minimal invasive approaches did not reveal any significant differences from the traditional radical hysterectomy in decrease of recurrence or improved survival rate in spite of advantages such as reduced blood loss and decreased hospitalization. Therefore, management of cervical cancer still remains a complex and difficult problem. More sophisticated, multi-center, prospective clinical trials are needed to elucidate the efficacy of each surgical approach, based upon which individualized treatment considering age, socioeconomic status, etc., can be realized ensuring maximum treatment efficacy and improved quality of life.
The development of invasive cervical cancer is preceded by well recognised cervical precancerous lesions collectively termed as cervical intraepithelial neoplasia (CIN). It is well established that cervical cancer and CIN are caused by persistent infection with oncogenic types of human papillomaviruses (HPV). HPV infection is very common and affects a vast majority of sexually active women in their lifetime. However, it is mostly a transient infection and the infection rates peak in young women after sexual debut; in more than 80% of the infected women, the infection is not detectable within 2 years. Oncogenic HPV infection prevalence rates among sexually active women vary between 3-30% in different populations and those populations with high risk of cervical cancer (incidence rates above 30/100,000 women) demonstrate HPV prevalence rates above 10%. Transient HPV infection leads to cellular changes in the cervical epithelium that are characterised as atypia or low-grade squamous intraepithelial lesions (LSIL) or CIN grade 1. As the HPV infection clears most of these low grade lesions revert back to normal. Less than 10% of low-grade lesions progress to higher grades. In the presence of persistent infection, a proportion of low-grade lesions may persist or progress to higher grades of CIN (CIN2 and 3) or HSIL. More than half of the high-grade lesions may persist or progress to invasive cancer in the absence of early detection and treatment, while the remaining may regress if the HPV infection eventually resolves. CIN3 lesions have the highest probability to progress to invasive cancer if left untreated and are considered to be true precursor lesions for invasive cancer. It may take 15-20 years to evolve from persistent HPV infection to invasive cancer and this long natural history offers several opportunities for screening to detect and treat precancerous lesions thereby preventing their progression to invasive cancer. It is important to treat women with high-grade lesions, whereas a wait-and-watch policy may be appropriate for those with low-grade lesions, provided follow-up can be ensured. Given the high probability of loss to follow-up, low-grade lesions among women above the age of 30 years may be treated in low-resource settings. The frequency of high-grade lesions is a reliable end-point for assessing interventions such as HPV vaccination.
Cancer of the uterine cervix is globally the second commonest cancer among women, being more common in comparatively developing countries. It is the commonest cancer among women in Eastern, Middle & Southern Africa; Central America; South-Central Asia (India, Bhutan & Nepal); and Melanasia. Globocan 2002 estimated that during the year 2002, 265,885 out of 493,243 incident cases (53.9%), were in Asia Oceania. India accounted for 26.8% of global incident cases. As per Cancer Incidence in 5 Continents, Volume IX (1998-2002), the age standardized incidence rates of cervical cancer varied between 2.1 and 47.3 per 100,000 women. During the years 2004-2005, age standardized incidence reported by Indian population based cancer registries varied from 5.1 to 25.4 per 100,000 women. There are wide variations in occurrence of cervical cancer within countries. Some areas have shown sharp decrease in incidence rates during recent times, without any organized screening programmes. Estimates and projections for future vary depending upon the criteria used. However, all the currently available projections are based on assumption that the incidence rates would remain same at current levels. Trends for some areas will be presented. The Indian data suggest an urgent need for initiation of community screening and educational programmes for control and prevention of cervical cancer.
HPV BURDEN AND GENOTYPE DISTRIBUTION IN ANOGENITAL CANCERS FROM ASIA-PACIFIC AND MIDDLE EAST REGION

Silvia de Sanjosé1, Laia Alemany1, Wim Quint2, Nuria Monfulleda1, Carles Miralles1, Joellen Klaustermeier1, Belen Lloveras3, Sara Tous1, Nubia Muñoz1, Francesc Xavier Bosch1

Unit of Infections and Cancer, Catalan Institute of Oncology, IDIBELL, Barcelona, Spain1, DDL Diagnostic Laboratory, Voorburg, The Netherlands2, Hospital de Mar, IMAS-IMIM, Barcelona, Spain3

Objective: To describe the HPV prevalence and genotype distribution in invasive cancers of the cervix, vulva, vagina, anus and penis from the Asia-Pacific and Middle East region.

Method: Paraffin embedded invasive cancer cases of the cervix, vulva, vagina, anus and penis were collected from historical archives. HPV detection was done through amplification of HPV DNA by SPF-10 broad-spectrum primers PCR subsequently followed by DEIA and genotyping by LiPA25 (version 1). Samples were tested at HPV laboratories at ICO (Barcelona, Spain) and at DDL (Voorburg, The Netherlands). Quality controls between the two labs occurred regularly. In this communication, results from cases recruited from Asia-Pacific and Middle East countries are presented (Australia, Bangladesh, China, India, Japan, South Korea, Kuwait, Lebanon, New Zealand, Philippines, Taiwan, Thailand and Turkey).

Results and Conclusion: 3,146 cases of invasive cervical cancer were recruited and HPV analysed. HPV detection and typing was successfully done on 2,787 cases (HPV positivity: 88.6%). Single HPV types were identified in 92.8% of HPV positive cases, multiple infections in 5.1% and HPVX in 2.1%. The five most common types detected as single types in the region were HPV16 (57.9%), HPV18 (11.1%), HPV45 (4.9%), HPV52 (3.4%) and HPV58 (3.3%). Furthermore, HPV DNA detection was performed in 349 vulvar, 53 vaginal, 57 anal and 58 penile cancers. HPV DNA was identified in 32.1%, 58.5%, 63.2% and 12.1% of the cases, respectively. Most of the cases had a single HPV type (range: 84.8%-100.0%) and HPV16 was the most frequent single type (range: 58.6%-83.3%).

Conflict of Interest: This study has been partially supported by GlaxoSmithKline Biologicals, Sanofi Pasteur MSD and Merck.
CROSS TALK OF NKT CELLS AND CD4+CD25+ REGULATORY T CELLS IN CERVICAL CANCER PATIENTS

Shubhada V Chiplunkar

Advanced Centre for Treatment Research and Education in Cancer, Tata Memorial Centre, Navi Mumbai, India

CD4+CD25+ regulatory T cells (Tregs) are increased in patients with several malignancies and correlate with disease stage and prognosis. Tregs play a major role in tumor escape from immune responses. The mechanisms used by Tregs to suppress anti-tumor immunity are not well understood. In the present study we investigated the role of CD1d restricted Natural Killer T cells (NKT) as antitumor effector cells in cervical cancer patients and further analyzed the crosstalk between NKT cells and Regulatory T cells (Tregs). NKT cells are a unique lineage of T cells characterized by CD1d restriction and biased TCR repertoire (V24/V11). We found low levels of circulating NKT cells in cervical cancer patients. NKT cells were enriched from peripheral blood after stimulation with glycolipid antigens PBS-14 & PBS-57 (modified -galactosylceramide), presented by autologous dendritic cells. NKT cells isolated from cervical cancer patients demonstrated low cytotoxicity against tumor cells compared to NKT isolated from healthy individuals. We further observed increased levels of circulating Tregs in cervical cancer patients compared to healthy individuals. High expression of CTLA4, GITR, CD45RO, CCR7 and CD62L were observed on immunomagnetically purified Tregs. Real time polymerase chain reaction demonstrated increased expression of Foxp3 mRNA in cervical tumor biopsies indicating presence of Tregs in cervical tumors. Addition of Tregs to PBS-14 pulsed dendritic cells during expansion phase of NKT cells resulted in marked decrease in outgrowth of NKT cells. To investigate the role of cytokines in maintenance of Tregs in tumor microenvironment, CD4+CD25 T cells were incubated in presence of cell-free supernatants obtained from cultured cervical tumor cells. Conversion of CD4+CD25 T cells to CD4+CD25+ phenotype was observed in presence of tumor supernatants containing TGF1. Increased expression of mRNA of TGF1 and SMAD3 was observed in cervical tumor biopsies. The results indicate that cervical tumor derived TGF1 plays an important role in maintenance of Tregs. Co-cultures of NKT and Tregs were set up using transwell assays to investigate if cell contact between Tregs and NK are needed to mediate suppression. Our studies demonstrate that factors released by Tregs suppress Granzyme-B levels in NKT cells. In summary, our studies demonstrate that Tregs inhibit NKT functions in cervical cancer and strategies aimed at inhibition or depletion of Tregs may be useful in achieving effective anti-tumor immunity with clinical impact.
HPV16 is the major viral isolate identified in cervical cancer (CaCx) cases worldwide and in India. Viral oncoproteins E6 and E7 bind, degrade and inactivate various host cell regulatory proteins, especially tumor suppressor (p53) and retinoblastoma (pRb) proteins. Alteration in cell cycle regulatory pathways causes increased cell proliferation and genomic instability. HPV16 E2 gene disruption, as a consequence of viral integration into the host genome, mediates the loss of negative feedback control of viral oncoprotein expression and is a critical event in cervical carcinogenesis. Recently, we and others identified the presence of intact E2 genes in a large number of CaCx cases, which prompted us to explore new paradigms of cervical carcinogenesis, i.e. alternative mechanisms of loss of E2 repression that could lead to sustained E6/E7 expression even with intact E2 gene. We identified genetic and epigenetic factors related to HPV16 genomes (European variants) harboring intact E2 genes, as well as high viral copy numbers as biological plausible mechanisms. 
Among viral genetic factors, we identified non-synonymous amino acid variations across the various proteins that could be deleterious to protein function. Such rare deleterious variations within genes implicated in productive infection (L2, L1, E2 and E5) over a common haplotype background of intact HPV16 isolates was observed only among cases and hence might be of causal relevance for CaCx development. In contrast to non-synonymous variations, which were significantly higher within L2, synonymous variations were overrepresented at L2, E2 and L1 genes among cases compared to controls. HPV use rare codons relative to their hosts, which allow the virus to escape immune surveillance. However, humanized codons within HPV genomes could lead to increased protein production. We identified that humanized codons were also significantly higher within E2, L2 and L1 genes of cases compared to controls. Thus synonymous variations leading to humanized codons within genes implicated in productive infection among intact HPV16 isolates might also be associated with disease risk. We further aimed at identifying the possibility of difference in methylation within HPV16 enhancer and promoter regions of the LCR, between (i) CaCx cases and cytologically normal controls harboring intact E2 and (ii) CaCx cases harboring intact and disrupted E2 genes. Analysis of CpGs within the viral promoter LCR revealed that E2BS-I (at nt 58) methylation was significantly higher among cases than controls with no difference in case of LCR-E6 methylation. Furthermore, E2BS-I methylation was almost exclusive, and CpGs of other E2BSs, were observed among cases having intact E2, compared to those with disrupted E2. Therefore, E2BS-I methylation is likely to be a key factor mediating cervical carcinogenesis possibly by overcoming E2 repressor activity. As a follow up, we aimed at identifying the possibility of difference in viral DNA copy number between HPV16 E2 disrupted and intact forms of CaCx cases and whether this correlates with viral oncogene expression and methylation of LCR within E2 binding site I (E2BS-I). The study revealed an association of high viral DNA load with CaCx concomitant with E7 and E2 expressions that increased linearly with viral load and E2BS-I methylation in presence of intact E2. The association of high HPV16 load with cases having intact E2 could possibly be attributable to functional E2, concomitant with E2BS-I methylation and loss of E2 repressor activity.

**Objective:**
To identify HPV16 E6, E7, L1 variants prevalent in normal controls, SILs and cervical carcinomas and their possible biological implications.

**Method:** Cervical scrapes/biopsies were collected from normals, SILs and cervical cancer subjects from North India. DNA was isolated and HPV presence was studied by PCR using consensus PGMY primers. Genotyping was done on HPV positive samples by PCR using HPV-16 type specific primer and by line blot. Variant analysis was done by sequencing of PCR amplified E6/E7/L1/LCR region of HPV-16 and classified into phylogenetic clusters.

**Results:** Majority of normals, SILs and tumors belonged to the European class with variant E350G being the most prevalent. Seven alterations in E6 region (3 nonsynonymous), 3 in E7 (1 nonsynonymous) and 21 in L1 (8 nonsynonymous) were seen in controls. 15 variants were seen in the E6 region, 7 in the E7 region and 51 in the L1 region of tumors. L83V was the most frequent alteration in E6 region, F57V in E7 and Ins 4485 and D465Del in L1 region. A number of samples showed co-mutations in E6, E7 and L1.

**Conclusion:** Similar sequence alterations were seen in normals, SILs and cervical carcinomas but to different extents. The observed alterations can interfere with the structure, function and antigenic properties of the protein. The distribution of these variants may be important for development of HPV diagnostic vaccines and for therapeutic purpose.
NEW MOLECULAR MARKERS IN PREDICTION OF HIGH GRADE DISEASE

Sandeep R Mathur

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Exfoliative cervical cytology and histology have been regarded as the gold standard for cervical cancer screening. Cytology is prone to errors in sampling, slide preparation and interpretation. Sampling for atypical glandular cells is difficult. False-positive and -negative rates range from 15–50% and 30% respectively. The sensitivity of a single Pap smear is only 60–80%. A major limitation of conventional Pap is the substantial proportion of inconclusive or mildly abnormal tests. There is inter- and intra-observer variation in CIN grading. It is also sometimes difficult to distinguish CIN from reactive processes. Thus there is a need for biomarkers that aid early detection, improve reproducibility of histopathological diagnoses, allow surveillance of persons at risk and post-therapy monitoring. Biomarkers in the context of cervical cancer precursor lesions can be classified into one of these categories:

**HPV DNA testing:** Incorporation of HPV testing in primary screening results in 50–70% more precancers diagnosed. HPV genotyping and high-risk HPV mRNA detection are useful biomarkers to predict lesions which are likely to progress. Viral capsid protein L1 differentiates productive infections from transforming infections. Surrogate biomarkers of deregulated HPV oncogene expression include p16 INK4a, a tumor suppressor gene and key regulator of the cell cycle, a sensitive and specific marker of squamous and glandular dysplastic cells of the cervix and a surrogate marker of high-risk HPV, which makes it a valuable adjunctive test in cervical cancer screening.

**Markers of chromosomal instability** include DNA aneuploidy, HPV integration, loss of heterozygosity (LOH) markers and methylation markers. Among markers of proliferation and host cell genome replication, Ki67 & PCNA immunoquantitation are important diagnostic adjunct for the grading of CIN. Myc, cyclins, telomerase, MAP kinase pathway markers and survivin have been evaluated. MCM2 is a protein involved in early stages of DNA replication through regulated assembly of the prereplication complex onto DNA during the G1 phase. MCM5 mRNA expression increases significantly with increasing severity of dysplasia. TOP2A is responsible for relaxing supercoiled DNA during replication. ProExC is an immunohistochemical marker consisting of a cocktail of MCM2 and TOP2A. HPV E6 oncoproteins interfere with the function of cellular tumor suppressor protein p53 through induction of increased proteasome-dependent p53 degradation. HPV E7 proteins interact with the ‘Rb associated pocket proteins’.

**Replication complex proteins:** DNA replication occurs only once in a single normal cell cycle, due to ‘licensing’ of DNA replication which requires assembly of a protein complex which includes the mini chromosome maintenance (MCM) proteins and the cell division cycle protein 6 (CDC6). These have been shown to be overexpressed in dysplastic cells.

**Markers of cellular stress and invasion:** Heat shock proteins, HSP40, HSP60 and HSP70 overexpression in cervical precursor, were associated with increasing lesion grade. Carbonic anhydrase 9 (CA9/MN antigen) has been identified as a marker for all grades of CIN. Laminin 5 is a late marker of the cervical transformation process indicating the first steps of invasion.

**Epigenetic markers, factors enhancing viral oncogene activity:** RASSF1 methylation; Frequent LOH and CGH losses detected at the 3p21 region; TSLC1 found inactivated by methylation in a subset of high grade dysplasias and cervical carcinomas.

**Chromosomal abnormalities:** The most consistently observed alteration is gain of chromosome 3q, which has been associated with the progression from severe dysplasia to invasive cancer. **Alterations of gene expression:** Proliferation associated gene C4.8 was found to be overexpressed in high grade cervical lesions. **Alteration of protein expression, serum based markers:** A number of protein biomarkers have been analyzed in serum to detect cervical cancer, among them the Squamous cell carcinoma antigen (SCC), IGF2 and VEGF-C and CYFRA 21.1. SCC belongs to the family of serine and cysteine protease inhibitors with increased expression in dysplastic lesions and cervical squamous cell carcinoma. PAI1 which is a downstream target for transforming growth factor 1 (TGF-1) may be a good prognostic marker for cervical cancer.

Many more biomarkers are under evaluation. Routine biomarker applications can change the way in which women with CIN are followed up and treated. Many of the new test methods are complex and can only be used in specialized laboratories and should only be used after they have been thoroughly validated.
SECOND GENERATION VACCINES - A SUITABLE ALTERNATIVE?

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Cervical cancer is the second most common gynaecological cancer worldwide but the leading cause of cancer-related deaths among women in developing countries. The disease is caused due to persistent infection of one or more high-risk types human papillomaviruses (HR-HPVs), most commonly by HPV types 16/18. In India, more than 98% of cervical cancer cases harbor HPV infection and HPV 16 is the type exclusively (80-90%) prevalent. Two successful VLP-based prophylactic HPV vaccines, a quadrivalent (HPV16/18/6/11) ‘Gardasil’ by Merck & Co. USA and a bivalent (HPV16/18) ‘Cervarix’ by GSK Biologicals, Belgium, have been developed and showed lot of promise. Despite successful clinical trials of these prophylactic HPV vaccines, there are several issues regarding affordability and accessibility in India. Therefore, development of second generation vaccine is warranted which will be more suitable to resource-limited countries and will address the limitations of already developed vaccines. So, several approaches are being employed such as plant-based edible, pentameric capsomere-based intranasal and DNA-based prophylactic vaccines. Also, several therapeutic vaccines either protein/peptide based or DNA based are in clinical trials but are yet to establish their efficacy. If cost is minimized, HPV related new technologies involved in screening tests and vaccines are expected to reduce incidence of cervical cancer and deaths it causes in women from developing countries.

NATURAL ANTIVIRALS AND IMMUNOMODULATORS

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Specific types of high risk human papillomaviruses (HR-HPVs), particularly HPV16 and HPV18 have been strongly associated with the development of epithelial cell carcinoma in cervical, oral and other anogenital cancers. Constitutive expression of two viral oncogenes, E6 and E7, which are responsible for tumorigenic transformation, is mainly dependent on specific host-cell transcription factors. Two such transcription factors, AP-1 and NF-kB, are essentially required for efficient HPV 16/18 transcription and therefore play a central role in tissue-specific transcription of HPVs. The aberrant expression and activation of these host cell transcription factors during infection of HPV and its persistence is associated with increased expression of viral oncogenes and thus provide a unique target of therapeutic significance in HPV related malignancies. Our recent data on epithelial cancer tissues and cell lines demonstrate downregulation of host cell transcription factors by herbal derivatives such as curcumin, berberine and leaf extract of Bryophyllum pinnata which resulted in decreased expression of viral oncogenes E6 and E7 at transcriptional level. These derivatives showed potent inhibitory activities against constitutively active NF-kB and AP-1. Curcumin was found to act at transcriptional level and down-regulated binding activity and expression of AP-1 in HPV18 positive cervical cancer cell, HeLa. Similarly, selective down-regulation of HPV16/E6 transcription in HPV18 positive oral cancer cells with parallel decrease in binding of NF-kB and AP-1 complex following curcumin treatment was observed. We further observed decrease in general expression pattern of NF-kB (p50 and p65) and AP-1 family of proteins (c-Jun, Jun B, Jun D c-Fos, Fos B, Fra-1 and Fra-2) after curcumin treatment. Leaf extracts of Bryophyllum pinnata as well as berberine were also found to possess remarkable anti-HPV and anti-proliferative activities. A 30-day intra-vaginal application of polyherbal cream ‘Praneem’ has been shown to eliminate HPV infection in Phase II clinical trials. Since herbal derivatives express little or no systemic cytotoxicity, these are the most suitable candidates for translation into much awaited anti-cancer and anti-HPV therapeutics. Recently, we have also developed a non-toxic low molecular weight curcumin-folic acid conjugate to specifically target only cancer cells which over-express high affinity folate receptors that facilitates cellular internalization of curcumin. Most importantly, such conjugation makes curcumin hydrophilic leading to its increased bioavailability and targeted delivery through systemic route.
RECENT ADVANCES IN CERVICAL CANCER PREVENTION IN LOW AND MEDIUM RESOURCE COUNTRIES

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Four-fifths of the global burden of cervical cancer is experienced in developing countries due to the lack of or inefficient screening programs. There are two strategies, namely screening and vaccination, for cervical cancer prevention. Currently available HPV vaccines target HPV16 and HPV18 and have been shown to be highly effective in preventing cervical precancerous lesions caused by the vaccine-included HPV types and high levels of antibodies during the follow-up period. While evidence supports introduction of HPV vaccines, there are several challenges and uncertainties that need to be resolved before HPV vaccination can be widely implemented through public health services in low-resource countries. Early detection by screening and effective treatment of high-grade cervical intraepithelial neoplasia (CIN 2 and 3) lesions is an established option of preventing cervical cancer. Difficulties in providing optimal cytology prompted evaluation of alternative screening methods such as HPV testing and visual inspection with acetic acid (VIA) and visual inspection with Lugol’s iodine (VILI). HPV testing has a higher sensitivity (pooled sensitivity 90%) but lower specificity (pooled specificity 88%) than cytology. VIA and VILI have moderate sensitivity (55-85%) and low specificity (40-85%), but real time results allow immediate treatment. In recent years, new paradigms such as reduced frequency of screening and single visit approach have been evaluated to maximise participation of women in screening and treatment. In a randomized trial in South Africa, cryotherapy for HPV test-positive women triaged by VIA resulted in 77% and 74% decline in the prevalence of CIN 2-3 at 6 and 12 months respectively, while VIA followed by cryotherapy resulted in a 37% and 46% lower prevalence compared with a control group. A 25% reduction in cervical cancer incidence and a 35% reduction in mortality following a single VIA screening have been shown in a randomized trial in South India. A 50% reduction in incidence of advanced cancers and cervical cancer mortality following a single round of HPV screening was reported from another randomized trial in India. A simple, user-friendly affordable, faster (results within 3 hours) and accurate HPV test (careHPVTM test) suitable for use in low-resource settings has now been evaluated in China and found to have similar accuracy as HCII, significantly higher sensitivity than VIA (90.2% vs.41.4%), but lower specificity (84.2% vs. 94.5%). It is expected to be commercially available in the near future. Findings of ongoing and completed research studies have catalyzed increasing awareness among policy makers and the general public that may hopefully lead to more widespread introduction of cervical cancer prevention services in developing countries.
I-3.2

START-UP PROGRAM RESULTS

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Nearly 85% of the 270,000 annual cervical cancer deaths occur in developing countries. Most are preventable if screening for pre-cancerous lesions and treatment is provided. Unfortunately most developing countries do not have the resources, infrastructure and trained personnel to replicate the success obtained by Pap smear in developed countries. Alternative options more suitable for low-resource areas have recently been explored.

The careHPV™ test was created for developing countries. It is highly sensitive, provides results in 2.5 hours, is more affordable than other molecular tests and its instruments make it suitable for any health-care facility. In 2009, PATH started demonstration projects using this test in Nicaragua and India and will start in Uganda in early 2010. Each woman enrolled has a self-collected vaginal sample and a provider-collected cervical sample for the test, as well as a Pap smear and VIA sample.

The objective of this project is to generate evidence comparing different screening strategies to help governments, international agencies and NGOs decide which approaches to use in cervical cancer prevention programs. We also intend to provide the manufacturer of the test with information needed to offer an affordable price at the final-user level, including public-sector investment risks, constraints, and potential barriers for commercialization.

Results from the first 1,000 women enrolled show that self-collected sampling was well accepted in Nicaragua where more than 85% of women agreed to take the sample. Other preliminary results on performance of the test will be presented at the meeting.

I-3.3

SELF-SAMPLING – EMPOWERING WOMEN TO SCREEN THEMSELVES

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The development of an affordable HPV test can change the paradigm of cervical cancer screening in low resource settings. But some of the logistic problems of cytology will still remain in primary health care settings, e.g., need for sterilization, electricity supply, instruments, etc. Self-sampling is a very attractive option that improves compliance and enables us to expand program coverage, facilitate outreach, streamline clinic processes, and remove barriers to care. It also reduces the number of trained medical personnel needed to implement the screening program.

Several devices exist for self-sampling but most of them fall under one of the following categories: Brush, tampon and lavage devices. Using a lavage device and instructions mailed to them, 99% women reported that it was easy to use and quick. Sensitivity of self-collection methods is slightly lower than that for samples collected by clinicians. However, there is fair agreement between self-collected vaginal & physician-collected cervical specimens for HR-HPV. We used the Digene® brush and found a 93.8% agreement between between physician-collected and self-samples (k = 76.31%, 95% confidence interval [CI]: 64.97–82.29%, p = 0.04)—complete concordance in 473/512 cases (57 positive, 416 negative), partial concordance in seven pairs and discordance in 32 pairs. Detection of CIN2+ was comparable.

Some of the barriers to self-sampling were uncertainty over performing the sampling correctly, fear of hurting themselves, concern about obtaining appropriate material and test accuracy. Overall, self sampling is a test with moderate accuracy, of specific importance to women with no access to a health care provider and those who are uncomfortable with physical examination. Self-sampling for HPV is a promising primary screening strategy for cervical cancer prevention.
INTERLEUKIN-10 -1082 G/A POLYMORPHISM IN HPV RELATED CERVICAL LESIONS

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Objective: To verify the frequency of interleukin (IL)-10 polymorphism at position -1082 and its association with Human Papillomavirus (HPV) infection.

Method: Nested case-control study that enrolled 84 cases and 211 controls. Cases were HPV-positive women with abnormal anatomo-pathological results, and controls included HPV-negative women with normal cytological exam. The amplification refractory mutation system (ARMS-PCR) technique was applied to identify the polymorphism of the IL10. Multiple logistic regression was used to verify the association between the study factors and the outcome (genital infection by HPV).

Results: The genotypic frequency observed among cases was 59% (50/84) GG, 29% (24/84) AG, and 12% (10/84) AA. In the control group, it was 29% (61/211), 49% (103/211), and 22% (47/211), respectively (p<0.0001). Regarding the case group, GG genotype was the most common either in HSIL (50%) or LSIL (63%) (p<0.0001). The genotype frequency among women positive for high risk HPV was 50%, and in those HPV negative was 28% (p=0.05). Variables independently associated with HPV infection were age (OR: 5.0; 95%CI: 2.33 - 10.75; p<0.001), and GG genotype (4.41; 1.87-10.42; p=0.01). A borderline significance was observed for HIV co-infection (10.64; 1.00; 111.11; p=0.04) and years of education (3.28; 1.0-11.18; p=0.08).

Conclusion: The results suggest that the genetic predisposition for production of high levels of interleukin-10 may be related with cancer development, showing the relevance of the immunologic response in the process of HPV infection and in the progression of cervical lesions caused by HPV.
O-4.4

A NEW GENERATION OF CERVICAL CANCER DETECTION? THE POWER AND PROMISE OF DNA METHYLATION BIOMARKER

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Objective: Testing for DNA methylation has potential in cancer screening. Novel genes with high accuracy and validated testing methods are needed.

Method: Differential methylation hybridization (DMH) and methylcytosine immunoprecipitation coupled with promoter tiling array (MeDIP) were used to uncover methylated genes in invasive cancer. An independent set of 185 patients was tested for validation, including normal uterine cervix (n = 53), CIN1 (n=37), CIN2 (n=22), CIN3 (n=24), CIS (n=22), and invasive cancer (n=27). Cut-off values of the percentage of methylation reference (PMR) for different diagnosis were determined to test the sensitivity and specificity. ROC curve was generated to test the accuracy.

Results: By DMH, we reported six genes (SOX1, PAX1, LMX1A, NKX6-1, WT1 and ONECUT1) more frequently methylated in SCC tissues than in their normal controls (P < 0.0001) by gel-based MSP. In the quantitative analysis, the PMRs of SOX1, PAX1, LMX1A, NKX6-1 are significantly higher in CIN3 and worse lesions (CIN3+) than those in normal cervix and CIN1-2 (p < 0.001). The sensitivities, specificities and accuracies, respectively, for detecting CIN3+ lesions are 0.88, 0.82 and 0.95 by SOX1; 0.78, 0.91, and 0.89 by PAX1; 0.77, 0.88 and 0.90 by LMX1A; and 0.93, 0.97 and 0.97 by NKX6-1.

Conclusion: The discovery and application of novel DNA methylation markers in cervical cancer screening is powerful and promising. A multi-center study using a standardized DNA methylation test is ongoing. Population-based studies are warranted to evaluate its impact in clinical practice.
**O-4.6**

**EVALUATION OF THE DIGENE HPV GENOTYPING PROBESET TEST (PS) RELATIVE TO TYPE-SPECIFIC qPCR**

Ha Thanh Thai, Dirk Loeffert, Irina Nazarenko, Dana Pfister, Sarah McLeod, Tanya Gay, Wen Chen

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**Objectives:** The digene HPV Genotyping PS Test, (PS) - a reflex test for the digene HC2 high-risk HPV DNA Test (HC2), was developed for the detection of HPV 16, 18 and 45. Performance of the PS test was assessed by determining its agreement to qPCR, an in-house established reference method.

**Method:** The PS test is based on Hybrid Capture technology. The assay uses similar reagents and follows a slightly modified protocol to the HC2 test. HC2 positive clinical specimens both negative and positive for HPV 16, 18, and/or 45 were utilized in the study. The PS test and qPCR testing for the presence and viral load of HPV 16, 18, and 45 was performed on the same specimens. Agreement between the two test methods was determined.

**Results & Conclusion:** The PS test has an analytical sensitivity for HPV 16, 18, and 45 plasmid of 5000 copies per assay with an S/N > 4.0 and 2500 SiHa cells with S/N > 10. PS total agreement to qPCR was evaluated with more than 100 cervical specimens using 5000 copies of HPV16 plasmid as the Positive Control 1. It was determined that an RLU/Positive Control 1 ratio > 1.3 correlated to a qPCR positive result. The total agreement between PS and qPCR for the detection of clinical specimens was greater than 95%.

Note: * This test is For Research Use Only. Not for use in diagnostic procedures. * This test is not commercially available in the United States.
I-5.1

HPV POSITIVE TEST: WHAT DO YOU DO?

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The HPV DNA positive woman after an ASCUS report is required to undergo a colposcopy. If colposcopy does not show cancer and repeat HPV DNA is negative, the patient is reverted back to routine screening. If however, repeat HPV DNA is positive, cytology is repeated at month 6 and month 12 and treated accordingly.

The ASC-H case undergoes colposcopy. If no lesion is detected, cases will have a review of cytology, colposcopy and histology. In those with no change in diagnosis, a Pap at month 6 and month 12 is done or HPV DNA testing at month 12.

The LSIL patient is HPV DNA positive in 83% of cases. A routine colposcopy is done with endocervical sampling. If no cancer is found, a Pap at month 6 and month 12 or HPV DNA testing at month 12 is performed. If negative, the patient reverts back to annual screening. If ASC or worse, or HPV DNA +, repeat colposcopy is performed.

HSIL cases who are HPV DNA positive and documented CIN2 or worse are treated by either LEEP or ablative cryotherapy/laser. Pap at month 6 and month 12 or HPV DNA at month 12 are performed. Annual colposcopy is required, endocervical sampling is usually performed as well.

Colposcopy of the vagina and magnifying lens inspection of the vulva with acetic acid application is likewise recommended for HPV DNA + patients. Tolidine blue test may be performed in some cases.

Both ACS and ACOG have endorsed the use of Pap test combined with HPV DNA screening in women 30 years and older. Women with negative results for both cervical cytology screening and high risk type DNA test should be screened no more frequently than every 3 years.

The use of reflex HPV testing following an ASCUS Pap test is a cost effective and more sensitive technique for identifying CIN2 or worse disease when compared with cervical cytology screening alone.

I-5.2

CIN MANAGEMENT OPTIONS AND POST-TREATMENT FOLLOW-UP

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Management involves diagnosis and treatment. The diagnosis of CIN is based on the three disciplines of cytology, colposcopy and histopathology. There is also increasing reliance on the significance of Human Papillomavirus (HPV) testing. The aim of management of CIN is to prevent subsequent development of cervical cancer, while reducing unnecessary treatment and removal of excessive normal tissue.

Q. 1. Who should be treated with which grades of CIN? CIN3 - invariably, CIN2 - usually, CIN1 – occasionally.

The rationale for treatment is assessed against the risk of progression of the abnormality. Untreated, 30-80% of women with CIN 3 will progress to invasive cancer in a mean time of 7-10 years.

<table>
<thead>
<tr>
<th>S.No.</th>
<th>CIN</th>
<th>Regression</th>
<th>Persistence</th>
<th>Progression</th>
<th>Invasion</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>CIN 1</td>
<td>56%</td>
<td>30%</td>
<td>13%</td>
<td>1%</td>
</tr>
<tr>
<td>2.</td>
<td>CIN 2</td>
<td>45%</td>
<td>35%</td>
<td>5%</td>
<td></td>
</tr>
<tr>
<td>3.</td>
<td>CIN 3</td>
<td>32%</td>
<td>56%</td>
<td>12%</td>
<td></td>
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</tbody>
</table>

Q. 2. How should patients be treated? In the 1950’s the treatment for CIN3, or carcinoma in situ as it was then called, was abdominal hysterectomy. In the 1960’s knife cone biopsy was employed, which offered a simultaneous method of excluding the presence of invasion and diagnosing the condition whilst maintaining a chance for fertility. However, a 12% combined primary and secondary haemorrhage rate associated with a 30% chance of future pregnancy-related morbidity encouraged clinicians to seek less radical treatments, particularly as the peak age of CIN3 was 29 years and in many western countries more than 50% of such women would be nulliparous. In 1981 the RCOG study group defined certain circumstances where locally destructive treatments might be employed rather than conisation: (1) The patient was seen and assessed by an expert colposcopist; (2) the entire transformation zone was visible; (3) neither referral cytology, colposcopic impression or directed histological biopsy suggested invasion; (4) the expert colposcopist carried out the destructive therapy; (5) the patient would attend for follow up cytology.

Of the destructive techniques, cryotherapy (Richart and Townsend) was effective against CIN1,2 and small volume CIN3, but inadequate for large volume CIN3 lesions. Radical diathermy (Channen and Rome), cold coagulation (Duncan) and laser evaporation therapy (Wright, Bellina,Sharp & Jordan) were effective for all grades of CIN. The ideal depth of destruction should be a minimum of 7mm. Success rates
Complications associated with treatment to the cervix for precancerous conditions include bleeding, infection, stenosis, problems with subsequent pregnancies, and psycho-sexual issues. While some of the complications may be technique dependant and avoidable, others are not and will occur in spite of even meticulous attention to operative technique.

The session will focus on the more significant long-term complications and their management.
Objectives: AS04-adjuvanted human papillomavirus (HPV)-16/18 vaccine (GlaxoSmithKline Biologicals) has demonstrated high prophylactic efficacy against oncogenic HPV-16/18 infection and associated precancerous lesions. We report baseline characteristics of women in the Asia-Pacific region enrolled in the Phase III PATRICIA trial.

Method: In this double-blind, international study (NCT00122681), women 15–25 years were randomised (1:1) to receive HPV-16/18 vaccine (N = 9,319) or hepatitis A vaccine (control; N = 9,325) at Months 0,1,6. Cervical samples were collected (for HPV typing), gynaecological and cytopathological examinations were performed, and a behavioural questionnaire administered. Baseline characteristics are presented for women in the total vaccinated cohort (women who received ≥ 1 dose) from the Asia-Pacific region (Australia, Philippines, Taiwan, Thailand).

Results and Conclusion: 6,352 women were enrolled: Australia, N = 548; the Philippines, N = 2,467; Taiwan, N = 1,485; Thailand, N = 1,852. Mean age at first vaccination was 21.9 years. 96.2% of Asia-Pacific subjects had ≥ 1 sexual partners the year before enrollment (Australia, 92.5%; the Philippines, 97.6%; Taiwan, 94.1%; Thailand, 96.7%). Positivity for chlamydia DNA was lowest in Australia (2.0%), followed by Taiwan (5.1%), Thailand (8.9%) and the Philippines (13.1%). Percentage of smokers (for ≥ 6 months) ranged from 6.0% (Thailand) to 34.8% (Australia). The majority of women (77.1%) were HPV-naive (DNA-negative and seronegative for HPV-16/18, and DNA-negative for 12 other oncogenic HPV types); 2.7% of women were DNA-positive for HPV-16, 1.5% for HPV-18 and 0.2% for both. For all parameters, baseline data were similar between HPV-16/18 vaccine and control groups. Observed variations in characteristics reflect the cultural diversity of the populations of participating countries in the region.

SUSTAINED IMMUNOGENICITY AND EFFICACY OF HPV-16/18-ADJUVANTED VACCINE UP TO 7.3 YEARS

Objective: Data from 6.4 years follow-up with the HPV-16/18 AS04-adjuvanted vaccine (GlaxoSmithKline Biologicals) have been previously described. We report efficacy, immunogenicity and safety up to 7.3 years, in a sub-cohort in Brazil.

Method: Healthy women (15-25 years, oncogenic HPV DNA-negative, HPV-16/18 seronegative, normal cytology at screening) were randomized to vaccine (N = 660) or placebo (N = 553) in an initial double-blind study (NCT00689741). A sub-cohort (N = 222 vaccine, N = 211 placebo) continued on an ongoing follow-up study (NCT00518336). Immunogenicity was assessed by ELISA and Pseudovirion-Based Neutralization Assay (PBNA). Cytopathological examinations were performed yearly.

Results & Conclusion: During the one-year follow-up in the sub-cohort, there were two new cases of HPV-16 incident infection in the placebo group vs no cases in the vaccine group. During the total 7.3 year follow-up of the sub-cohort, vaccine efficacy was 100% (95% CI 79.5%, 100%) against 6-month persistent infection, 100% (95% CI 55.7, 100) against 12-month persistent infection, 96.7% (79.9, 99.9) against ASCUS+, 94.2% (62.8, 99.9) against LSIL+ and 100% (<0, 100) against CIN2+ associated with HPV-16/18. Vaccine safety was similar to placebo. At 7.3 years, 96-100% of women were seropositive (ELISA/PBNA). Antibody levels plateaued 18-24 months after first dose and were several-fold above natural infection. Statistical modelling on these data confirm sustained longevity of HPV-16/18 antibodies for at least 20 years. The HPV-16/18 AS04-adjuvanted vaccine offers high and sustained immunogenicity and efficacy against HPV-16/18 infections and lesions up to 7.3 years. This is the longest follow-up of immunogenicity, efficacy and safety for a licensed HPV vaccine.

Conflict Of Interest: Funding through institution to perform vaccine studies for GSK and served on advisory board for GSK
OBJECTIVE: Women are at risk of oncogenic human papillomavirus (HPV) infection throughout their sexually active lives. The HPV-16/18 AS04-adjuvanted vaccine (Cervarix®, GlaxoSmithKline Biologicals) induces a robust immune response in women aged 15–55 years (103514/ NCT00196937). This long-term follow-up study assessed persistence of immune response and safety profile through 48 months after administration of first vaccine dose.

METHOD: In this open-label, age-stratified Phase III study in Germany and Poland (105882/NCT00196937), healthy women aged 15–55 years received 3 doses of HPV-16/18 AS04-adjuvanted vaccine at 0, 1 and 6 months. Anti-HPV-16/18 seropositivity rates and geometric mean antibody titers (GMTs) were assessed by ELISA in women aged 15–25 (n = 188), 26–45 (n = 186) and 46–55 years (n = 177) from time of first vaccination through 48 months.

RESULTS: At Month 48, all subjects were seropositive for anti-HPV-16 antibodies and 99.4% were seropositive for anti-HPV-18. Antibody kinetics were as previously reported: peak response at Month 7 then gradual decline towards a plateau in all age groups. As expected, an age-dependent decrease in GMTs was observed with increasing age. In all age groups, GMTs at Month 48 were at least 5-fold higher than natural infection levels, and the vaccine was generally well tolerated.

CONCLUSION: The HPV-16/18 AS04-adjuvanted vaccine induces high and sustained immune responses in women aged 15–55 years, with antibody levels remaining several fold higher than natural infection levels for at least 4 years after first vaccine dose.

CONFLICT OF INTEREST: Honoraria from GSK, Novartis & Wyeth (clinical vaccine trials, advisory board member & lecturing)
O-6.5

QUADRIVALENT HPV (TYPES 6/11/16/18) VACCINE: END-OF-STUDY EFFICACY AGAINST HPV6/11/16/18-RELATED PERSISTENT INFECTION AND DISEASE IN WOMEN AGED 24 TO 45

Ricardo Manalastas, for the FUTURE III Steering Committee

Philippine General Hospital, Infectious Disease Section, Philippines

Objectives: Quadrivalent HPV vaccine efficacy against vaccine type related cervical intraepithelial neoplasia (CIN) or external genital lesions (EGL [includes vulvar or vaginal intraepithelial neoplasia (VIN/VaIN) and condyloma]) in adult women was previously shown to be 92.4% (95% CI: 49.8-99.8). As this trial has now concluded, we evaluated the efficacy of quadrivalent HPV vaccine against CIN or EGL in women aged 24-45 through the end-of-study.

Methods: 3819 24-45 year old women received quadrivalent vaccine or placebo at day 1, and months 2 and 6. Ascertainment of HPV-related cervical and genital disease was accomplished via Pap testing, genital inspection and cervicovaginal sampling. Analyses were conducted in a per-protocol population (women who received 3 doses of vaccine/placebo within 1 year of enrollment, were naïve to the relevant HPV types at day 1, and remained free of infection through the completion of the vaccination regimen). Mean follow-up time per subject was 3.8 years, representing an additional 1.6 years of follow-up when compared to earlier analyses.

Results: The efficacy of quadrivalent HPV vaccine in the prevention of HPV6/11/16/18-related CIN or EGL was 95.7% (95% CI: 73.4-99.9) (23 placebo cases, 1 vaccine case). The one case among vaccinees was an HPV16-related CIN2 which was included in the original analysis. Efficacy against HPV6/11/16/18-related persistent infection was 89.6% (95% CI: 79.3-95.4) (85 placebo cases, 9 vaccine cases).

Conclusions: The qHPV vaccine is highly effective in preventing HPV6/11/16/18-related persistent infection, CIN and EGL in women aged 24 to 45 naïve to vaccine HPV types.

O-6.6

HPV GENOTYPING AND CONSEQUENCES FOR HPV VACCINATION IN 500 HEALTHY WOMEN ATTENDING A PRIVATE WOMEN’S CLINIC IN TOKYO

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Objectives: The HPV vaccine is finally licensed in Japan (October 2009) and will be available soon. HPV-DNA testing is not covered by insurance and few women see the need to pay for it. Consequently, little data is available on HPV genotypes in healthy Japanese women and the prevalence of HPV types included in the vaccination. This study investigated HPV genotypes and the prevalence of vaccine specific genotypes in 500 healthy women attending a private women’s clinic in Tokyo.

Methods: After written informed consent was obtained, 500 women aged 20 to 60 underwent HPV-DNA Testing using the Gene SQUARE HPV Genotyping Microarray (KURABO Industries Ltd.) between the period of August 1 and August 31, 2009.

Results: A total of 21.2% of women were HPV positive with no variation between age groups. Of those positive, HPV 58 (17%) was the most common type, followed by HPV 16 (16%), 52 (14.2%), 31 (10.4%) and 56 (10.4%). Only 4 women (3.8%) were HPV 18 positive and none were positive for HPV 6 or 11. For women in their 20s, vaccine type prevalence was 4.4% for HPV 16, 0.0% for HPV 18, 6, 11 and 3.3% for HPV 31.

Conclusions: While routine HPV vaccination is usually recommended for pre-adolescent girls, since vaccine type prevalence for women in their 20s was below 5%, screening rates in this group are around 10% and cervical cancer is sharply increasing, we believe it would be cost-effective for Japan to subsidize HPV vaccination beyond teenage girls.
THE CHALLENGES OF HPV IMMUNOLOGY

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The human papillomavirus (HPV) lifecycle takes place entirely within the target epithelium and includes several immune evasion strategies such that it can occur without alerting the host immune response.1 About half of all women who are exposed to oncogenic HPV infections do not make detectable antibodies to the viral capsids2,3 and in those who do make antibodies, the titres are low and not necessarily sufficient to prevent a subsequent infection.2

A key challenge for HPV vaccine development is to induce high levels of neutralizing antibodies, as these are believed to be a mediator of vaccine-induced protection.4 Adjuvants can have a significant impact on vaccine immunogenicity,5 including the magnitude of neutralizing antibody response achieved following vaccination.6 Cervarix® (HPV vaccine [types 16, 18]) contains proprietary Adjuvant System 04 (AS04) which combines aluminium hydroxide (Al(OH)3) and the immunostimulatory molecule 3-O-desacyl-4’-monophosphoryl lipid A (MPL) and the vaccine is generally well tolerated.2,7 Cervarix® formulated with AS04 has been shown to induce significantly higher anti-HPV 16/18 neutralizing antibody titres compared with the same antigens formulated with Al(OH)3 alone.8 The anti-HPV 16/18 neutralizing antibody titres induced by Cervarix® are several-fold greater than those following natural infection and these levels have been sustained for up to 7.3 years.9

A Phase IIIb trial comparing the immunogenicity of Cervarix® with Gardasil® (HPV vaccine [types 6, 11, 16, 18]; Sanofi Pasteur MSD) demonstrated that Cervarix® induced 2.3- to 4.8-fold higher and 6.8- to 9.1-fold higher HPV 16 and HPV 18 serum neutralizing antibody titres respectively,10 as well as higher frequencies of circulating HPV 16/18-specific memory B cells, compared with Gardasil® at Month 7.10 Higher positivity rates for anti-HPV 16/18 neutralizing levels of detectable antibodies in cervico-vaginal secretions were also seen with Cervarix® compared with Gardasil®.10 Although the immune correlates of vaccine-induced protection against cervical cancer are still unknown,4 neutralizing antibodies and immune memory are thought to play an important role in long-term protection against HPV infection and subsequent cervical cancer.1 This trial is ongoing; an update on recent data will be provided.

[Cervarix is a registered trademark of the GlaxoSmithKline group of companies; Gardasil is a registered trademark of Merck & Co Inc.]

References:
S-G.3

IMPACT OF VACCINATION ON COLPOSCOPY AND TREATMENT IN THE ASIA-OCEANIA REGION

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Based on epidemiological data, a human papillomavirus (HPV) vaccine achieving up to 100% protection against HPV types 16 and 18 is predicted to prevent approximately 70% of cervical cancer cases and significantly reduce the incidence of HPV-associated high-grade squamous intraepithelial lesions or cervical intraepithelial neoplasia (CIN) grades 2/3. The global prevalence of HPV16/18 is estimated to be 52.3% in CIN2/3 and 70.3% in invasive cervical cancer (ICC). HPV type 45 is one of the five most common HPV types in ICC globally, being associated with a further 3.7% of cases. A recent epidemiological study indicated that HPV16/18/45 types are the three most predominant in ICC in Asia and Oceania. The provision of cross-protective efficacy against non-vaccine HPV types, in particular HPV45, would thus be predicted to provide significant additional clinical benefits to women from the Asia and Oceania regions.

The PATRICIA trial, discussed during the previous presentation, is a Phase III global study which showed that vaccination with Cervarix® resulted in a 26.3% decrease in colposcopy referrals and a 68.8% decrease in cervical excision procedures. Approximately one third of the participants in the PATRICIA trial (34.1%, n = 6,352, Total Vaccinated Cohort) are from the Asia-Pacific region and in this presentation, experience of HPV vaccination in the Asia-Oceania region to date will be presented and the likely impact of HPV vaccination in the region will be discussed, based on the most recent findings on regional HPV epidemiology and from clinical trials. Cervarix is a registered trademark of the GlaxoSmithKline group of companies.

References

I-7.1

MANAGEMENT OF EARLY STAGE CERVICAL CANCER – OUTCOMES OF SURGERY AND RADIOTHERAPY

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Early stage cervical cancer may be asymptomatic and diagnosed as a result of an abnormal Pap smear or may be symptomatic. The modern approach to surgical management of any cancer is to target treatment to the prognostic variables. In early stage cervical cancer, treatment is determined by 1) histological features of the tumour e.g. squamous versus small cell or neuroendocrine tumours; 2) the depth and width of invasion; 3) lymph-vascular space invasion; 4) the risk of lymph node involvement; 5) fertility requirements and age of the patient; 6) surgical skills of the attending doctor. Options for management range from a cone biopsy where the cancer is fully excised with adequate margins and is less than 3 mm deep and 7 mm wide to trachelectomy or radical trachelectomy, simply hysterectomy or radical hysterectomy, depending on depth of invasion according to the FIGO staging. Pelvic lymph node dissection may be performed at laparotomy, via extraperitoneal route or laparoscopically. Most units consider pelvic lymph node dissection to be important in any stage from 1a2 and above. The role of adjuvant radiotherapy or chemoradiation in early stage disease is controversial and will be discussed in greater detail.
SURGICAL MANAGEMENT OF FIGO IB2 AND IIB CERVICAL CANCER

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In 1911 Ernst Wertheim introduced a new surgical management of cervical cancer: radical hysterectomy (RH). However, surgery in that period did not promise safety of the patient. In the early 20th century, radiation was also introduced as a new treatment modality and gradually became a standard treatment modality for invasive cervical cancer. However, in such period Hidekazu Okabayashi at Kyoto University in Japan had been trying to modify Wertheim’s RH with a belief that if the surgery is radical enough for the extent of the disease, RH still has a chance to become a standard treatment modality for cervical cancer. In 1921, he established an anatomy-oriented systematic RH much more radical than that of Wertheim. In 1951, Meigs re-evaluated RH and recommended its use in patients with early stage. Since then RH revived in USA and Meigs’ RH (classified by Piver et al in 1974 as Class III) became the standard RH in western countries. Meigs advocated restricting surgery to young healthy patients in early stage, ideal being stage IB. In contrast, in Japan where Okabayashi’s RH became standard treatment modality for cervical cancer, surgery was extended to stage I and II disease. Indeed in Japan (a report of Japan Society of Gynecologic Oncology 2005) the majority (90%) of stage IB patients, including stage IB2, are treated by Okabayashi’s RH and only 10% are treated by primary radiotherapy. Moreover, 62% of stage IIB are treated primarily by RH. The reason of this difference between western countries and Japan is the difference of division of the paracervical tissues: Wertheim’s RH (including Meigs’ RH) divides paracervical tissues including cardinal ligament, posterior leaf of vesicouterine ligament and paravaginal tissue (paracolpium) that is impossible to accomplish radical surgery in case of locally advanced stage IIB diseases, but Okabayashi’s RH can do this in stage IIB because it isolates and divides cardinal ligament, posterior leaf of the vesicouterine ligament and paracolpium respectively. Recently, locally advanced cervical cancers such as stage IB2 and IIB are recommended to be treated by chemo-radiation followed by hysterectomy. However, optimal management of patients with “bulky” stage IB2 cervical carcinomas is still controversial. The study was started for clarification of detailed anatomy of anterior and posterior leafs of vesicouterine ligament. In the anterior leaf of vesicouterine ligament, we could appreciate superior vesical vein that drains into the superficial uterine vein and cervicovesical vessels that run from the urinary bladder to the cervix crossing over the ureter. The separation of venous blood vessels in posterior leaf of vesico-uterine ligament revealed that all veins are coming from the urinary bladder and draining into the deep uterine vein. Beneath the posterior leaf of the vesicouterine ligament, we could identify the inferior hypogastric plexus (IHGP) that is a cross-shaped nerve junction formed by hypogastric nerve, pelvic splanchnic nerve, uterine branch and bladder branch from IHGP. By division of only the uterine branch from the IHGP, we can now preserve bladder and rectal functions safely (Nerve sparing RH).

In order to extend Okabayashi’s RH, in 1941 Ryuichi Mibayashi at Kyoto University showed total extirpation of cardinal ligament by resection of total blood supplies of both internal iliac artery and vein in the pelvic cavity and called this method super-radical hysterectomy. It is very useful in FIGO stage IIB or in case of lymph node metastasis adhered stiffly to the blood vessels in the cardinal ligaments. The usage of original Okabayashi’s RH and/or Mibayashi’s total extirpation of the cardinal ligament with internal iliac vessel system enable us to accomplish extended resection of the tissues in case of FIGO IIB or IB2 with lymph node metastasis. If invasion of the tumor is confined to one side, we can perform nerve sparing RH on the other side and thus preserve bladder function satisfactorily. Although the number of data are small, my own RH data followed by tailored postoperative therapy in the treatment of stage IB1, IB2, and IIB cervical cancer between 1999-2003 is as follows. The 5 year disease free survival rate was 93.6% (44/47) in stage IB1, 93.3% in stage IB2 (14/15), and 81.3% in stage IB (13/16). Okabayashi’s RH, Mibayashi’s total extirpation of the cardinal ligament with internal iliac vessel system with or without nerve sparing RH followed by tailored postoperative therapy looks like still one of the choices of treatment for patients with stage IB1, IB2 and IIB cervical cancer.
Cervical cancer in developing countries is characterized by young age at diagnosis (median 35-38 years), higher frequency of squamous histology (>90%) and presence of locally advanced stage (stage IIB to IVA) in >80% of patients with higher volume of disease. Five year survival rates vary from 50%-65% for stage IIB, 28%-35% for stage IIIB, and 5%-15% for stage IVA disease. Loco-regional recurrence is the main cause of failure. Initial studies explored role of chemotherapy for treatment of recurrent disease, Cisplatin being the most effective drug, other active agents include ifosphamide, bleomycin, paclitaxel, gemcitabine, docetaxel, methotrexate and 5-fluorouracil. Though combination chemotherapy produced higher response rates but overall survival was not significantly different compared to cisplatinum alone. Patients with extrapelvic recurrence had better outcome than those with pelvic disease. In some cases responses can be durable (J Obst Gyn Res 1998; 24:401-9).

Between 1990 and 2000, a number of randomized studies reported use of neoadjuvant chemotherapy prior to radiotherapy in patients with locally advanced disease (Gynecol Oncol 1994; 54:307-15). Most studies used cisplatin- based combinations. Following 2 to 3 cycles, complete (CR) and partial response rates varied from 40%-80% with CR in < 10% of patients. Progression-free and overall survival was not significantly different when compared to radiation alone (control arm) (Eur J Cancer 2003;39:2470-86, Cochrane Database Syst Rev. 2004;(2):CD001774). Patients who achieved CR to chemotherapy had a better outcome. However, in patients with early stage cervical cancer (IB, IIA), neoadjuvant chemotherapy prior to surgery was associated with improved outcome, about 10%-20% of patients achieved pathological CR following chemotherapy alone. In year 1999 and later, several randomized studies demonstrated therapeutic advantage of combining chemotherapy with radiation (concurrent chemoradiation, CCRT) over radiotherapy alone. In these studies, cisplatin was used alone or with 5 fluorouracil. A recent meta-analysis confirmed an absolute benefit of 6% in overall survival at 5-years with CCRT (hazard ratio (HR) = 0.81, P < 0.001). A larger survival benefit was seen for the two trials in which chemotherapy was administered after CCRT. Survival benefit was seen for both the group of trials that used platinum-based (HR = 0.83, P = 0.017) and non-platinum-based (HR = 0.77, P = 0.009) CCRT but no difference...
was seen in the size of the benefit by radiotherapy or chemotherapy dose or scheduling. CCRT also reduced local and distant recurrence and progression and improved disease-free survival. The benefit was higher for patients with early stage disease (7-10% for stage I-II vs. 3% for stage III). Acute hematological and gastro-intestinal toxicities were more in CCRT group (J Clin Oncol. 2008;26:5802-12, Cochrane Reviews 2010, (1):CD008285). Thus, with CCRT, five year overall survival rate of 66% and disease-free survival (DFS) of 58% was achieved in patients with locally advanced disease.

What next: Current survival figures with CCRT for stage IIB-IVA are far from satisfactory. Could alternative chemotherapeutic agents other than cisplatinum be more effective? Recently, a number of phase II trials have confirmed efficacy of taxanes (paclitaxel/docetaxel) and gemcitabine as single agent or in combination with cisplatin in locally advanced cervix cancer. Other possibility could be use of these drugs e.g. paclitaxel and carboplatin as dose dense therapy for 4-6 weeks prior to CCRT. Weekly dose dense therapy has recently been shown to be an effective strategy in breast (NEJM 2008; 358:1663-71) and ovarian cancer (Lancet 2009; 17:1331-8). Use of chemotherapy after CCRT could be another option to improve outcome in patients with positive lymph nodes, larger tumor volume and stage III-IVA disease. Adjuvant chemotherapy is currently being investigated for early stage (stages IA2, IB1 or IIA) cervical cancer with risk factors such as lymph node metastasis, lymphovascular space invasion, depth invasion of >10mm, microscopic parametrial invasion, non-squamous histology and positive surgical margins (Cochrane Database Syst Rev. 2009;(3):CD005342). Use of targeted therapy (e.g., bevacizumab - inhibitor of Vascular endothelial growth factor (VEGF) - a key promoter of tumor progression in cervical carcinoma, Gefitinib – inhibitor of EGFR which is moderately expressed in cervix cancer) is another area of active research.
**THE CHINA EXPERIENCE ON INTRODUCING POPULATION-BASED CERVICAL CANCER SCREENING**

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Cervical cancer is one of the major threats to Chinese women’s health and is over-represented in rural areas—due to lack of education, poverty and inability to pay for health care.

In 2005, two national demonstration centres for the early detection and treatment of cervical cancer were established respectively in Shenzhen, a prosperous neighbour of Hong Kong, and at poverty-stricken Xiangyuan County in the mid-western coal mining province of Shanxi. The two centers are committed to working out two different screening models, one catering to abundant urban areas and the other to underdeveloped regions burdened with high incidences, with simple, inexpensive, and yet safe and cost-effective technologies to screen for pre-cancerous lesions in the cervix, which would otherwise develop into invasive cancer if not detected early.

Since 2009, free cervical cancer screening has been available for rural women between 35 and 59 years under a government-sponsored program proposed by MOH and China Women’s Federation. During the next 3 years, 10 million rural women in less developed central and western regions will be able to access this free service. This new government-sponsored program is a step towards provision of universal cervical cancer screening nationwide, although with an estimated 500 million women in rural China the public health challenge is substantial. This is the first time China’s Government has proposed to gradually widen access to cancer prevention service so that women in rural China are included. If this program succeeds, it could provide a good experience on introducing population-based cervical screening for other developing countries.
RESULTS FROM INDIA
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Control of cervical cancer in India would have a major global impact as it accounts for one-fourth of the world burden of cervical cancer. Several research studies addressing feasible and cost-effective alternative screening options for possible wide-scale implementation in the future have been undertaken. Beyond research studies and demonstration projects there are no serious efforts to introduce population-based screening in the country.

Multi center cross-sectional studies in India addressing the accuracy of conventional cytology, human papillomavirus (HPV) testing by HC II method, visual inspection with acetic acid (VIA) and Lugol’s iodine (VILI) in the early detection of CIN2-3 lesions indicate that with quality assurance and good training of providers, cytology, HPV testing and visual tests had similar sensitivity to detect high-grade lesions, though HPV DNA testing was the most reproducible test.

The efficacy and cost-effectiveness of single lifetime screening with VIA, cytology or HPV testing in preventing invasive cervical cancer were evaluated in randomised controlled trials in Osmanabad and Dindigul districts. The RCT on VIA screening in Dindigul district showed a significant 25% reduction in cervical cancer incidence and 35% reduction in mortality, 7 years after the beginning of screening. Further a cluster-randomized, controlled, screening-trial for cervix cancer with four rounds of screening using VIA by trained primary health workers was initiated by Tata Memorial Hospital in May 1998. The interim results after three rounds of screening have already demonstrated significant downstaging for cervix cancer. In the Osmanabad randomised trial the detection rate of high-grade lesions was found to be similar in all intervention arms: 0.7% for VIA, 1.0% for cytology and 0.9% for HPV testing and conclusively showed that a single round of screening for HPV dramatically reduced the incidence of advanced cervical cancer and cervical-cancer mortality within 8 years far more than a single conventional cytology or VIA.

There is good evidence that VIA and VILI are suitable early detection tests in the context of developing countries settings; however, HPV testing may provide an objective method of investing limited resources for single life time screening in at risk women, provided simple, affordable, rapid and accurate HPV testing methods could be developed for use in low-resource settings.

Thus cost-effective strategies for cervical screening requiring fewer visits, leading to improved follow-up, testing and treatment are critical factors in cervical cancer control in India and would go a long way in establishing a sustainable programme, irrespective of the screening test used.

RESULTS OF CERVICAL CANCER PREVENTION PROGRAMS AND SVA IN THAILAND
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Thailand has implemented a cervical cancer prevention program using a single visit approach (SVA) by providing visual inspection with acetic acid and cryotherapy since 2000. It initially started with SAFE demonstration project – to explore safety, acceptability, feasibility and program effort of such screening, and, after finding it to be a very promising method, has increased accessibility, coverage and expansion of services from four to twenty districts within Roi Et province within a year. Now at least 29 out of total 76 provinces already provide SVA as one of the major screening modalities. Along with the expansion of services, the development of database and information system has been developed and has been then approved and integrated into a national database system by the National Cancer Institute. Up to January 2010, there were about 360,000 women tested with SVA provided by around 1000 nurses all over the country.
Session 8: Promising Strategies for Cervical Cancer Programs in Low Resource Countries

O-8.1

VISUAL INSPECTION WITH ACETIC ACID (VIA)- SCREENING TOOL FOR CERVICAL CANCER

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Objectives:
1. To find out the detection rate of cervical intraepithelial neoplasia by visual inspection with acetic acid and lugol’s iodine.
2. To evaluate the feasibility of screening program in the country.

Methods and Results:
NNCTR had introduced cervical cancer screening by VIA for the first time in Nepal in 2002. This is a community based study conducted in five districts of Nepal (Bhaktapur, Kavre, Lalitpur, Banepa and Kathmandu). This study was conducted from October 2002-June 2009. During this period 12268 cases were screened. All were married women of age 25-60 years. Colposcopic examination was done in all screened positive cases and guided biopsy was done in 267 cases. Among 590 screened positive cases CIN 89 (15%) cases (CIN I-64, CIN II-20, CIN III-5) and invasive cancer 7 (1.2%) was detected. Follow up was done at 1 month, 1 year and 5 years interval. Five years follow up was completed in 2007. Abnormalities were not detected in any follow up cases. Chronic cervicitis and other infection were treated with antibiotics. Invasive cancer cases were sent to Radiotherapy department.

Conclusion:
Visual inspection with acetic acid is considered as a simple test for detection of pre-cancers lesion. It can be performed by doctors, nurses, midwives and health workers.

O-8.2

USING BEST PRACTICES FOR ADVOCACY TO STRENGTHEN A CERVICAL CANCER PREVENTION PROGRAM IN THE PHILIPPINES

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Objective:
Jhpiego and the Cancer Institute partnered to start the Cervical Cancer Prevention Network Program (CECAP), an alliance for the prevention of cervical cancer in Filipino women through vaccine information and the use of Single Visit Approach (SVA) through Visual Inspection with Acetic Acid (VIA) linked to cryotherapy. Sharing best practices and successes sustained the effort to screen eligible women for cervical precancer lesions.

Method:
Baseline data on cervical cancer prevention capability at three pilot sites were collected and graded. Service providers and community health workers (CHW) underwent competency-based training and were followed up for transfer of learning. Service delivery indicators were regularly audited. Each project site presented their best practices and achievements during the first annual CECAP meeting.

Results:
The three initial pilot sites has grown to 6 more sites plus three regional training centers. Currently there are 89 SVA trained providers and 73 qualified CHW. After funding from Jhpiego ended, the program has generated local support for training and facilitated 25 advocacy events. Currently, 9,277 women were screened, 232 have been found VIA positive, 122 received cryotherapy and the rest were referred for advance care. The program continues to be challenged by lack of resources to scale up.

Conclusion:
The Best Practices forum has made contributions to improving the quality of services through positive replicable competition.
I-9.1

THE ROLE OF HPV IN VIN & VAIN
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Cancers of the vulva and vagina are rare tumors that jointly account for 6-9% of cancers of the genital tract. Although the majority are squamous cell keratinizing carcinomas (80-95%), two distinct histological subtypes are recognized. The morphologically warty or basaloid type, which is associated with HPV infection, is diagnosed at relatively younger ages, often concurrent with precursor lesions of vulvar intraepithelial neoplasia (VIN 2/3) and tends to follow the epidemiological pattern of a sexually transmitted origin (related to larger number of partners and a record of previous cervical lesions). In contrast, the keratinizing squamous cell vulvar cancers are diagnosed at older ages and often relate to chronic degenerative epithelial conditions such as lichen sclerosus. Cancers of the vagina is consistently rarer that vulvar cancer. The majority of cases are preceded by vaginal intraepithelial neoplasia (VAIN 2/3) and HPV, mostly HPV16, has been implicated in over 90% of cases.

Cancers of the anus are those arising in the anal canal, largely in a zone of transition epithelium similar to the one encountered in the cervix. In most populations, anal cancer is twice as common in females as in males and the incidence is particularly high amongst homosexual males. HPV DNA, notably HPV16, is found in 85-95% of cases. Other risk factors include co-infections with HIV, cigarette smoking, frequency of anal intercourse and the number of lifetime sexual partners. The quantitative estimates of the HPV implications of such lesions are still imprecise. Literature reviews signal that HPV DNA is found in some 40% of vulvar cancers and between 70-80% of cancers of the vagina and anus. Major limitations of these reports are the limited number of specimens in any single study, variability in the sampling methods and the laboratory techniques and the inconsistency in the treatment of the cases with multiple HPV types in a given clinical specimen. The geographical variability of such estimates suggests international consistency but remains largely unknown for extensive areas of the world. Some ongoing studies are advanced to generate more precise estimates.

I-9.2

HPV AND HIV INFECTIONS
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Human papillomavirus (HPV) infections play an important role in the pathogenesis of anogenital cancer and its precursors. HPV are the most prevalent sexually-transmitted agents worldwide. Most HPV infections are asymptomatic and are spontaneously cleared within a few months or years. The immune response to HPV is believed to play a critical role in the control of HPV infection. Hence, human immunodeficiency virus (HIV)-infected individuals are more prone to HPV infections and related diseases. The prevalence of cervical HPV infection is two to three times higher in HIV-infected women (about 70%) than in HIV-uninfected women (less than 20%). In HIV-positive women, persistent HPV infection and infection with multiple concurrent HPV types are frequent. Several studies have demonstrated that severe immunosuppression is the strongest independent risk factor for infection with high-risk HPV genotypes. HIV-infected women have a high incidence of abnormal Pap smears and premalignant lesions. The risk of abnormal cervical cytology is strongly associated with persistent HPV infection and the degree of immunosuppression.

The natural history of cervical disease in HIV-positive women is as yet poorly understood. The available data suggest that the widespread use of highly active antiretroviral treatment (HAART) has not resulted in a decrease in prevalence of genital HPV infection in HIV-positive women. Although some of the evidence remains controversial, several studies have now documented a modest positive impact of HAART on cervical disease. Treatment of cervical lesions in HIV-positive women fails more often than in HIV-negative women and the effect of HAART on outcomes of treatment remains poorly documented.

Case reports of unusual cervical cancers in AIDS patients have led to include cervical cancer as an AIDS-defining illness in the CDC classification in 1993. The increase in life expectancy under HAART may provide for increased opportunities for lesions to recur or to progress to invasive carcinoma. However, recent data have shown no change in the incidence of invasive cervical cancer since the introduction of HAART. HPV-related disease remains a significant issue even in the era of HAART. The prevention of HPV infection and screening of lesions are crucial. Studies of prophylactic vaccines in HIV-infected women should be pursued.
I-9.3
SYNDROMIC MANAGEMENT OF STI’S – THE FLIP SIDE
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WHO recognises that control of STIs can improve the health status of the population and prevent HIV transmission, and introduced the concept of syndromic management in settings where lab tests and experienced clinicians were not available. This approach entails treating the patient on a conglomeration of signs and symptoms. However, every strategy has an up side and a down side (one of the two being the flip side).

The up side (is this the real flip side?) of syndromic approach: (i) containment of HIV transmission; (ii) circumvents problems of resource paucity, such as at PHC and in some private settings; (iii) treats the patient at the first visit (full coverage) and mostly with single dose (supervised, hence complaint) regimens.

The down side (Or this is the true flip side?) of syndromic approach: (i) to apply syndromic management, the patient needs to be symptomatic but it is well recognized that 20-40% of the patients, especially women, are asymptomatic and will be missed. One solution is to treat partners and aggressively intervene in the commercial sex workers, many of whom are asymptomatic; (ii) overtreatment leads to drug resistance. A patient with non-recurrent, non vesicular genital ulcer disease is to be treated both for *T. pallidum* and *H. ducreyi* infection entailing use of benzathine penicillin and ceftriaxone and haven’t all of us encountered chancroid resistant to ceftriaxone or *N. gonorrhoeae* resistant to the same drug; (iii) does not treat less common/debatable pathogens (e.g., *Mycoplasma* and *Ureaplasma*) as shown by our study at AIIMS, so some patients remain symptomatic despite being treated syndromically; (iv) requires repeated large validation studies in different geographic locations, to test for sensitivity of the causative pathogens and to find out the pathogens; (v) no universal guidelines. Strategies need to be formulated regionally.

Briefly syndromic management in women (i) for genital ulcers is both valid and feasible, resulting in adequate treatment of large numbers of symptomatic women in a simple, cost-effective way. HSV2 is fast becoming the commonest cause of genital ulcer disease (GUD) in developing countries and since it is not always vesicular and recurrent (recent data from AIIMS) this may negatively affect the treatment outcome of GUD if antiviral therapy is not appropriately instituted; (ii) Flowcharts for lower abdominal pain are satisfactory; (iii) Flow charts for vaginal discharge (VD) have limitations, particularly in management of cervical (gonococcal and chlamydial) infections. In low-prevalence settings and in adolescent females, noninfective causes rather than an STI are the main cause of VD. Attempts to increase sensitivity and specificity of VD flowchart for diagnosis of cervical infection, by introducing appropriate, situation-specific risk assessments (based on demographics), have not been successful as they tend to classify too many adolescents as being at risk of cervical infection. Therefore, there is a need to identify the main STI risk factors (like sexual practices) for adolescents in the local population and tailor the risk assessment accordingly.

I-9.4
TREATMENT OF GENITAL WARTS - EFFICACY & LIMITATIONS
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This presentation will discuss the published studies to date on the treatment of genital warts. It will deal with the rationale for treating genital warts from a clinical and public health perspective and the natural history of HPV 6/11 infection without treatment. The remission rates and recurrence rates of different types of treatment will be discussed in addition to the side effects of different treatments. The treatments that will be discussed include trichloracetic acid, electrosurgical techniques, interferons, cryotherapy, podophyllin, podophyllotoxin, imiquimod and surgery. Public health issues such as the potential effects on transmissibility will also be discussed. The efficacy of other modalities including condom use for the regular partner and potential newer therapeutic vaccines will also be discussed. Finally the effect of HPV vaccines against HPV 6/11 on the projected community prevalence of genital warts will be discussed utilizing mathematical models.
O-10.1

DETERMINANTS OF VISUAL INSPECTION OF THE CERVIX AFTER ACETIC ACID APPLICATION (VIA) POSITIVITY IN CERVICAL CANCER SCREENING OF WOMEN IN A PERI-URBAN AREA IN ANDHRA PRADESH, INDIA

Kalpana Betha¹, Haripriya Vedantham¹, Rekha C¹, Meenakshi Jain¹, Vidyadharhi Kuppa¹, Gayatri Ramakrishna², Pavani Sowjanya², Vijayaraghavan K³, Keerti V Shah⁴, Patti E Gravitt⁴

¹Mediciti Institute of Medical Sciences, ⁰CDFD, ⁱSHARE INDIA®, Andhra Pradesh, India, ⁴John Hopkins Bloomberg School of Public Health®, USA

Objective: We conducted a population based study in peri-urban villages in Andhra Pradesh, India, comparing performance of Pap cytology, VIA and HPV testing by Hybrid Capture 2 (hc2) for detection of CIN2+ disease. The sensitivity of VIA (26.3%) was substantially lower than Pap and HPV (63.2% and 84.2% respectively). We, therefore, investigated the determinants of VIA positivity in our study population.

Method: We evaluated VIA positivity by demographics and reproductive history, results of the clinical examination and results from the other screening methods using chi-square tests and logistic regression.

Results: A total of 733(31.5%) women screened positive by one or more screening tests, 344 (14.8%) Pap+, 297 (12.7%) VIA+ and 240 (10.3%) HPV+. Nineteen cases were identified (8 CIN2, 7 CIN3 and 4 invasive cancers). Age over 60 years, positive Pap smear, visually apparent cervical examination and observer variation remained significantly correlated with VIA positivity. VIA positivity was more strongly associated with Pap positivity than hc2 (17.7% and 16.3% respectively). In women with cervical inflammation, VIA positivity was more common (15.5%) compared to Pap or HPV (9.8% and 8.3% respectively). VIA positivity ranged from a low of 4% to 31% for two gynecologists.

Conclusion: VIA screening is ineffective in reducing the incidence of advanced cervical cancer and associated mortality. Strategies employing VIA and performing cryotherapy for VIA positive women as the sole cervical cancer screening method in resource limited settings should be adopted with caution.

O-10.2

VIA-VILI AS ROUTINE GYNAECOLOGIC EXAMINATION?

Shalini Rajaram, Sumita Mehta, Bhawna Agarwal, Shilpa Kava, Ankit Gupta, Neerja Goel

UCMS & GTB Hospital, Delhi, India

Objective: To study VIA-VILI as a screening test for cervical cancer in out-patients attending Gynaecology clinics.

Method: Five hundred patients of reproductive age group who attended gynaecologic OPD of GTB hospital were included. After detailed history and before bimanual pelvic examination, patients underwent Pap test followed by VIA-VILI using standard procedure. Patients who were VIA-VILI negative and Pap negative were asked to follow-up after 3 years. Patients who were VIA-VILI positive were advised HPV DNA testing and underwent colposcopy and directed biopsy if required. Sensitivity and specificity of VIA/VILI were calculated with gold standard as cervical biopsy.

Results: Of total 500 patients, VIA-VILI testing was positive in 24.2% (n = 121). All VIA/VILI positive cases were advised HPV DNA testing but only six could afford it. Colposcopic directed biopsies were done in 38 patients of whom 7 showed CIN 2/3 and 1 patient had carcinoma-in-situ. Out of 379 patients (75.8%) who were VIA-VILI negative, 1 patient had HSIL on Pap test and underwent LEEP. Pap test missed four cases of CIN identified by VIA-VILI, giving 50% sensitivity and specificity of 90%. The sensitivity and specificity of VIA-VILI were 87.5% and 76.8% respectively. Bacterial vaginosis was diagnosed in 8.2% of patients on Pap test. An additional 2-3 minutes was needed for doing VIA-VILI during routine gynaecologic examination.

Conclusion: VIA-VILI as part of routine gynaecological examination is a simple, affordable, fast and effective method to detect cervical neoplasia.
**O-10.3**

**HOW TO OVERCOME THE PROBLEM OF UNSATISFACTORY COLPOSCOPY?**

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*Lok Nayak Hospital, Delhi, India*

**Objective:** To compare misoprostol with estradiol for improving complete visualization of the transformation zone in women with unsatisfactory colposcopy.

**Method:** Forty eight women in all age groups with unsatisfactory colposcopy were included. They were randomly allocated into two groups. In group I, 200μg of misoprostol was placed in the posterior vaginal fornix and colposcopy was repeated after 4-6 hours. In group II, 50μg of estradiol hemihydrate was administered vaginally for 7 days and repeat colposcopy was performed after 7 days. Efficacy of the 2 drugs in overcoming unsatisfactory colposcopy and their side effects were compared.

**Results:** Efficacy of misoprostol in overcoming unsatisfactory colposcopy was 70.8% as compared to 82.6% in case of estradiol. This difference was statistically insignificant. Side effects were overall more frequent in misoprostol group (41.6%) as compared to estradiol group (15%). In misoprostol group, 20.8% patients reported abdominal cramps, 12.5% had complaints of nausea and 12.5% had bleeding per vaginum respectively. In estradiol group, the only complaint was nausea, seen in 12.5% patients. Menopausal status and the site of unsatisfactory colposcopy did not significantly affect the response to the drug in either group.

**Conclusion:** Both estradiol and misoprostol were comparable in overcoming unsatisfactory colposcopy. However, side effects were significantly more in the misoprostol group as compared to estradiol. Thus overall, estradiol is a better medication as compared to misoprostol for improving unsatisfactory colposcopy.

**O-10.4**

**DIAGNOSTIC ACCURACY OF HUMAN PAPILLOMAVIRUS TESTING IN PRIMARY CERVICAL SCREENING: A POOLED ANALYSIS OF 18 POPULATION-BASED STUDIES FROM CHINA**

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**Objective:** To evaluate the performance of HPV DNA testing used as primary screening method for cervical cancer in Chinese population.

**Method:** We conducted a pooled analysis of the sensitivity and specificity of HPV DNA testing from 18 cross-sectional population-based cervical cancer screening studies in China. In total, 31807 women aged 17-59 from 6 urban areas and 8 rural areas were screened when they were enrolled in different studies during 1999 to 2008. Screening tests used in the studies at least included visual inspection with 5% acetic acid (VIA), liquid-based cytology (AutoCyte & ThinPrep), Hybrid Capture® 2 (hc2) High-Risk HPV DNA Testing. The criteria for gold standard application for all the studies included positive VIA or LBC > ASC-US or HPV positive. Cervical lesions were diagnosed by biopsies taken directed by colposcopy or randomly (4-quadrant) and endo cervical curettage if necessary. Histology and cytology assessments were based on consensus between national and international expert pathologists.

**Results & Conclusion:** The sensitive and specificity for physician-collected sample hc2 HPV test in detecting CIN2+ was 95.6% (95%CI: 94.2%-96.7%) and 84.7% (95%CI: 84.3%-85.1%), and for self-collected sample hc2 was 86.2% (95%CI: 83.1%-89.0%) and 80.8% (95%CI: 80.2%-81.5%). In conclusion, the objective and reproducible characteristics of HPV DNA testing indicate it is feasible to be implemented in the low resource setting if an affordable HPV DNA testing is available.
EVALUATION OF THE CERVISTA HPV ASSAY AND MASS SPECTROSCOPY FOR HIGH-RISK HPV COMPARED TO HC-II - FROM THE SHENCCAST II TRIAL

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Objective: The Shenzhen Cervical Cancer Screening Trial II (SHENCCAST II) is a planned 10,000 woman study examining self-sampling, multiple HPV technologies, and computer assisted cytology. We report an interim evaluation of the new Cervista assay for high-risk HPV and Mass Spectroscopy (MALDI-TOF) for HPV compared to HC-II.

Method: Women from 3 sites in rural Guangdong Province as well as “inner city” Shenzhen were eligible if non-pregnant, 25-59 yrs of age, no screening for < 3 years, no hysterectomy, and no pelvic radiation. Cytology, HC-II, the Cervista assay, and MALDI were all processed in that order from the same 20mL PreservCyt specimen, collected using the “broom” sampler. All women with ≥ ASCUS, positive Cervista test, and/or positive HC-II were asked to return for colposcopy and four-quadrant biopsy.

Results and Conclusion: 5,043 women had all results. 14.6% (736) were HC-II positive, 12.2% (617) Cervista positive, and 14% (705) MALDI-TOF positive. 3.0% (150) had ≥ CIN2, 1.9%(97) ≥ CIN3, .10%(5) with cancer. For > CIN2, the sensitivity, specificity PPV and NPV values for HC-II were 94.7%, 87.9%, 19.3% and 99.8% respectively, for Cervista 90.7%, 90.2%, 22% and 99.7% and MALDI-TOF 92.7%, 88.4%, 19.7% and 99.8%. For > CIN3 HC-II was 97%, 87%, 12.8% and 99.9%, Cervista 91.8%, 89.3%, 14.4% and 99.8% and MALDI-TOF 94.9%, 87.6%, 13.1% and 99.9%. Using McNemar’s test the probability of a positive test was different for the comparisons of Cervista to HC-II and Cervista to MALDI-TOF p < .01 for both but was not significantly different when comparing MALDI-TOF to HC-II.

EVALUATION OF THE CERVISTA HPV ASSAY AND LIQUID BASED CYTOLOGY USING THE THINPREP INTEGRATED IMAGER - FROM THE SHENCCAST II TRIAL

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Objective: The Shenzhen Cervical Cancer Screening Trial II (SHENCCAST II) is a planned 10,000 woman study examining self-sampling, multiple HPV technologies, and computer assisted cytology. We report here an interim evaluation of the new Cervista assay for high-risk HPV and ThinPrep cytology using the new integrated imager.

Method: Women from 3 sites in rural Guangdong Province as well as “inner city” Shenzhen were eligible if non-pregnant, 25-59 yrs of age, no screening for < 3 years, no hysterectomy, and no pelvic radiation. The ThinPrep cytology and the Cervista assay were processed from the same 20mL PreservCyt specimen, obtained using the “broom” sampler. All women with > ASCUS, positive Cervista test, and/or positive HC-II were asked to return for colposcopy and four-quadrant biopsy.

Results and Conclusion: Mean age of the women in the study was 38.8 years (25-59). 12.1% (628/5190) were positive for high-risk HPV, 6.3% (328/5190) had cytology read as ≥ ASCUS, 3.0%(153) had biopsies positive for ≥ CIN2, 1.9%(98) were positive for ≥ CIN3, and 0.10%(5) women had cancer. For Cervista the sensitivity, specificity PPV and NPV values were 90.2%, 90.3%, 22% and 99.7% for ≥ CIN2 and 91.8%, 89.4%, 14.3% and 99.8% for ≥ CIN3 respectively. Using a cutoff of ≥ ASCUS the sensitivity, specificity, positive and negative predictive values for ThinPrep using the integrated imager for the detection of ≥ CIN2 were 88.9%, 91.5%, 24.1%, 99.6% and for ≥ CIN3 94.9%, 90.8%, 16.5%, 99.9% respectively. McNemars test for marginal homogeneity p < .01 for the comparison of ≥ ASCUS cytology and Cervista.
**O-11.1**

**A careHPV™ REFLEX TEST TO TRIAGE HPV+ WOMEN IN ECONOMICALLY CONSTRAINED COMMUNITY SCREENING PROGRAMS**

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**Background:** In communities where immediate referral to colposcopy after a positive HPV screen test is not practical due to cost and/or infrastructure and screen-and-treat strategies are not acceptable, a follow-up test to triage patients based on risk would be beneficial and cost-effective. Patient management based on infection of some high-risk types (i.e., 16, 18) could be different from management of those who test positive for non-16, 18 HR types (immediate colposcopy vs. increased surveillance, respectively). The careHPV™ Triage Test (currently in development; for research use only) is designed to be performed similarly to the careHPV Screening Test. It detects one or more of the three most clinically important HR types - 16, 18, and 45 - in aggregate using a cocktail of RNA probes complementary to and specific for these types.

**Method:** More than 1500 women were examined as part of routine health care in Leogane, Haiti, over a several-month period. Two specimens were collected from the cervix by a professional health care provider. The first was used for testing by HC2 followed by locally accepted clinical management according to test outcome. The second was tested by careHPV Test to identify one or more of fourteen HR types. Positive specimens were reflexed to careHPV Triage Test.

**Results and Conclusion:** From the first 579 specimens screened, 79 (13.6%) were careHPV+. Of the 79 screen positives, 17 (21.5%) were 16/18/45+ by the careHPV triage test, meaning positive for one or more of the three types. Of the 17 triage positives, none (0/17) was false-positive using qPCR to adjudicate. This was the first research study to test the feasibility of the careHPV triage test to identify the most important HR types of HPV infection in a screening population. There was no evidence of false-positive results for the careHPV Triage Test.

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**O-11.2**

**EFFICACY, IMMUNOGENICITY AND SAFETY OF HPV-16/18 AS04 ADJUVANTED VACCINE IN JAPANESE WOMEN: FINAL ANALYSIS AT MONTH 24**

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**Objective:** Primary objective was to demonstrate efficacy of the HPV-16/18 AS04-adjuvanted vaccine against 6-month persistent infection associated with HPV-16/18 in women seronegative at Month 0 and DNA negative at Months 0, 6 for the corresponding HPV type. Secondary objectives included immunogenicity and safety.

**Method:** Phase II, double-blind, randomized, controlled study conducted in Japan. Healthy women 20-25 years received the HPV-16/18 vaccine (N = 519) or Hepatitis A vaccine as control (N = 521) via intramuscular injection at Months 0, 1, 6. Efficacy analyses were performed in the According-to-Protocol cohort for Efficacy (ATP-E, women who received three vaccine doses; vaccine, N = 501; control, N = 501) and in the Total Vaccinated Cohort of efficacy (TVC-E, women receiving 1 vaccine dose; vaccine, N = 514; control, N = 516).

**Results:** Vaccine efficacy against 6-month persistent infection with HPV-16/18 was 100% [95.5%; CI: 71.3, 100; p < 0.0001] in the ATP-E cohort and 100% [95.5%; CI: 79.4, 100; p < 0.0001] in TVC-E. All HPV vaccine recipients had seroconverted at Month 7 and remained seropositive at Month 24. Antibody responses to anti-HPV-16 and HPV-18 peaked one month after Dose 3 of HPV vaccine and were sustained through Month 24.

**Conclusion:** No clinical meaningful differences were identified between both groups in terms of SAEs, medically significant conditions and New Onset of Chronic/Autoimmune Disease(s). Overall, the HPV-16/18 AS04-adjuvanted vaccine showed excellent protection against 6-month persistent infection with HPV-16/18, a high immune response and clinically acceptable safety profile in 20-25 year old Japanese females.
**O-11.3**

**IMPACT OF A QUADRIVALENT HPV 6/11/16/18 VACCINE IN WOMEN WHO HAVE UNDERGONE DEFINITIVE THERAPY**

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**Objective:** Prophylactic HPV vaccination is highly effective in preventing pre-cancerous lesions and genital warts (GW). It is not known if women with a history of cervical, vulvar, or vaginal pre-cancers (CIN, VIN, VAIN) or GWs will benefit from vaccination. We report HPV6/11/16/18 vaccine efficacy for these endpoints, regardless of causal HPV type, in women after they underwent surgical therapy in the context of 2 randomized clinical trials.

**Results:** 17,622 women aged 16-26 were enrolled in 1 of 2 trials (FUTURE I and II). Vaccine or placebo was given at Day 1, Month 2 and 6. Pap testing occurred at Day 1 and every 6-12 months. Definitive therapy referral was as per standard of care. This intention-to-treat analysis identified women who underwent surgical therapy for CIN, VIN, VaIN or GWs. Case counting began after surgery. Within an average of 3.6 years, in the combined trials, 587 vaccine recipients and 763 placebo recipients underwent cervical definitive therapy (average follow-up post-therapy was 1.5-1.6 years). Vaccine efficacy for any CIN following surgery was 47% (95%CI: 17-66). In protocol 013, 222 vaccine recipients and 306 placebo recipients were treated for VIN1-3, VaIN1-3 or GWs (average follow-up post-therapy was 1.5-1.9 years). Vaccine efficacy for these endpoints post-therapy was 44% (95%CI: 14-64). Efficacy for endpoints associated with HPV6/11/16/18 was 74% for CIN (95%CI: <0, 97) and 79% for VIN1-3, VaIN1-3 or GWs (95% CI: 53-92)

**Conclusion:** Women who have been treated previously for CIN, VIN, VaIN or GW benefit from receiving the HPV6/11/16/18 vaccine.

**O-12.1**

**ASSESSMENT OF THE SUBJECT RECRUITMENT SYSTEMS ADOPTED IN A BENEFICIAL CERVICAL CANCER SCREENING TRIAL (SHENCCAST II)**

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**Objective:** To compare the rates of call-back of the subjects with any test positive for colposcopy and biopsy among 3 sites using three recruitment systems.

**Method:** Women who met the screening conditions were recruited from 3 sites in Guangdong province, each of the sites representing urban city, suburban city or rural area. Three recruitment systems defined as public advice (PA), government advice (GA), and health institute advice (HIA) are adopted in urban city, suburban city and rural area respectively and conducted separately by a private health institute, local government and 3 government-sponsored real health institutes. All women were informed that neither charge nor payment is needed for their participants. The rates of call-back of the subjects with any test positive for colposcopy and biopsy were compared among the 3 sites.

**Results:** Among the 5360 subjects, 1,439 (26.84%) were enrolled through PA in urban city, 1,816 (33.88%) enrolled through GA from suburban city, and 2,103 (39.23%) enrolled through HA in rural area. The call-back rates in urban city, suburban city and rural area were 77.3% (367/475), 91.8% (438/477), and 85.4% (607/711) respectively.

**Conclusion:** Our study demonstrates that government participation in the subject recruitment (advice and encouragement) plays a key role to the success of a beneficial cervical cancer screening project. Participation of the government in subject advice and encouragement is clearly the most determinative factor to the success of such projects, without which any beneficial cervical cancer screening would be inefficient and resource-wasted, even if it has got enough financial support.
KAP STUDIES ON HPV INFECTION AMONG NURSING STAFF

Usha Saraiya, Sona Pawar
Sir H. N. Hospital, Mumbai, India

Knowledge, attitude & practice regarding HPV infection was carried out amongst 200 Staff Nurses at Sir. H. N. Hospital. It was done with a questionnaire covering all aspects of the disease including the use of vaccine. The analysis revealed a very poor knowledge regarding etiology, diagnosis & clinical condition. No knowledge at all about diagnostics & vague information on vaccine gathered by TV commercials.

A powerpoint presentation with question & answer session was carried in 2 – 3 groups. The candidates showed a keen interest & were interested in further information.

The same questionnaire was repeated, candidates could answer with confidence.

Candidates felt confident of disseminating the knowledge to patients in the hospital. It is very important to undertake teaching and training of Nursing Staff to promote cancer detection in the general population.
CURRENT EVIDENCE FROM PROPHYLACTIC VACCINES – ARE WE CONFUSED?
Eng Hseon Tay
Thomson Women Cancer Centre, Thomson Medical Centre, Singapore

Following the widespread introduction of the two HPV vaccines since 2006, firstly Gardasil™ in 2006 and then Cervarix™ in 2007, new data regarding each of the vaccines have been presented year after year. As each of the two manufacturing companies work feverishly to deliver the new vaccines to world, their respective new data were announced at competing pace and pitch.

Extensive effort and resources were spent on preparing and educating key opinion-leaders and prescribers, to facilitate the latter in helping end-users decide on which of the two vaccines should be their vaccine of choice. In the process, many questions have been raised namely: ‘Which vaccine is more potent? ’; ‘Which is safer? ’; ‘Which protects against more and what HPVs? ’; ‘ What is cross-protection and how important is it? ’; ‘Which will stay effective longer? ’ and ‘Is one better than the other or would any one be? ’.

As a result, many are rather unclear about the similarities and differences between the two vaccines, prescribers and end-users alike, some to the point of confusion. This presentation endeavours to help prescribers clarify some of the ‘conflicting’ issues, or at least understand the basis of their existence, by appreciating the chronological introduction of those data in a consolidated and comparative manner, from a personal perspective.

VACCINATION FOR OLDER WOMEN – EVIDENCE AND PRACTICE
Jeffrey Tan
Royal Women’s Hospital, Australia

Persistent oncogenic HPV infection is a precursor to invasive cervical cancer. HPV16 and HPV18 account for 70% of cervical cancer, followed by HPV45 and HPV311. For HSIL abnormality of cervix (CIN2&3), approximately 50% are due to HPV16 and HPV18. Global prevalence of HPV infection is about 10%2. HPV infections continue to occur in women over 25 years of age. In women 15-25 years of age, ~80% of HPV infections are transient but is more likely to persist in older women 3. HPV has many immune evasion mechanisms 4. About 50% of women develop no measurable antibody response following HPV infection. In women who have detectable antibody levels following natural infection, levels of antibodies are low. Low antibody levels do not guarantee protection against re-infection or reactivation 5. Vaccination aims to prevent HPV infection by inducing high and sustained levels of neutralizing antibodies in all vaccinees. Active protection is mediated by neutralizing antibodies at the cervix. Two HPV vaccines have been licensed for use in women up to 45 years of age: Gardasil® (Merck & Co), a quadrivalent vaccine containing L1 virus-like particles (VLPs) of types –6, 11, 16 and 18, and Cervarix® (GlaxoSmithKline), a bivalent vaccine containing VLPs of types –16 and 18. In trials involving young women (16-26 years of age), both vaccines had shown high efficacy against their associated vaccine types. Additional cross-protection have been demonstrated against the next 3 most common types associated with cervical cancer, with both vaccines showing efficacy against Types 31, 33 and Cervarix® against Type 45 as well 6.

Gardasil® was first approved by US FDA in June 2006 for the prevention of cervical cancer, abnormal and precancerous cervical lesions, abnormal and precancerous vaginal and vulvar lesions and genital warts in females ages 9-26 years. It is also approved for 9-15 year old boys in some countries. In September 2008, US FDA added its use for prevention of some cancers of the vulva and vagina caused by Type 16 and 18 in girls and women ages 9-26. In August 2009, Gardasil® obtained approval in Australia and elsewhere for use in women up to aged 45.

Cervarix® was first approved in May 2007 in Australia for the prevention of cervical cancer and its precursor lesions due to HPV types 16 and 18 in women aged 10 to 45 years. This was on the basis of immunobridging studies which showed all women up to the age of 55 years seroconverted to both HPV types and, while mean antibody concentrations at Month 7 were lower than in the younger age group, they were still three to four times higher than those observed in 15–25 year-old women in the long-term follow-up study (up to 4.5 years after vaccination), where continued efficacy was demonstrated'. Data from clinical trials show that very few women are infected by all the
vaccine types at time of vaccination, as demonstrated by positive DNA or serology for all four types (HPV-6, 11, 16 and 18). HPV vaccine trials for ‘mature’ women are still ongoing but preliminary reports are encouraging, with high efficacy of 90.5% against the four HPV types in women aged 24-45 years with Gardasil®. There is evidence that women who have been previously infected to the same subtypes of HPV as the vaccine and subsequently cleared their infection (HPV-DNA negative and seropositive) are also protected after vaccination as shown in interim analyses of the Cervarix® trial, and long term follow-up is ongoing. High efficacy was also observed with Gardasil® in previously infected women for prevention of HPV types not previously acquired.

Vaccination should be recommended for all women over 25 years of age, especially those who are not yet sexually active. Screening is not mandatory prior to vaccination but women should be encouraged to continue with screening according to the local guidelines. There is an algorithm developed by the Asian Cervical Cancer Prevention Advisory Board (ACCPAB) for this age group. HPV vaccine acceptance among mid-adult women were more likely in those who had previous abnormal pap smears, and was understand that HPV causes cancer or feel at risk for HPV infection. In a 2009 survey, gynaecologists in Australia indicated that they were more likely to encourage HPV vaccination in women over 26 years if they rate themselves as having considerable or advanced knowledge of the HPV vaccines. We should therefore endeavour to continue educating both health professionals and the public on the benefits of the HPV vaccines.

References:
13. Tan J et al. (under submission – ASCCP HPV vaccine survey)

I-13.3

THERAPEUTIC VACCINES – CURRENT STATUS

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Clearance of genital HPV infection is significantly delayed in immunocompromised patients. However, over 98% of immunocompetent patients clear anogenital HPV infections spontaneously, suggesting that those who fail to clear HPV spontaneously may not be able to mount an appropriate immune response. Over 40 literature reports describe clinical trials of antigen specific immunotherapy for persisting HPV infection or its malignant consequences, and successes have at best been modest, with evidence that a combination of enhanced local innate and enhanced systemic antigen specific adaptive immunity gives the best outcome. Evidence from animal models confirms this hypothesis and suggests several mechanisms by which HPV evades not only induction of virus specific immunity but also vaccine-induced immune effector function.
O-14.2

EVALUATION OF THE POI/NIH CERVICO-VAGINAL SELF-SAMPLER FOR HPV- FROM THE SHENCCAST II TRIAL

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Objective: The Shenzhen Cervical Cancer Screening Trial II (SHENCCAST II) is a planned 10,000 woman study examining self-sampling, multiple HPV technologies, and computer assisted cytology. We report here an interval evaluation of a randomized trial of self-sampling (POI/NIH sampler and the Qiagen brush) within the SHENCCAST II study.

Method: 5043 women from 3 sites in rural Guangdong Province as well as inner city Shenzhen were eligible if non-pregnant, 25-59 years of age, no screening in >3 years, no hysterectomy or pelvic irradiation. The self-sampling was randomized between the POI/NIH sampler and the Qiagen brush and tested with the Cervista HPV assay and MALDI-TOF spectroscopy. Direct cervical samples were placed in PreservCyt liquid (PC) and used for Hybrid Capture (HC-II) and the Gen-Probe Aptima HPV assay (AHPV). Participants positive on any test were recalled for colposcopy and biopsy. All participants colposcoped had directed and random biopsies plus ECC (min.5 bx/patient).

Results and Conclusion: Mean age (SD) = 35.9 (7.6); Cytology > ASCUS 6.5 % (138/2095); > LSIL 1.1 % (24/2095); and > HSIL 0.38% (8/2095). Biopsy > CIN2 = 1.3% (27/2095) and; > CIN3 = 0.72% (15/2095). HC-II and AHPV were positive in 19.1% (401/2095) and 11.9% (251/2095) respectively. The sensitivity of Cytology > ASCUS, HC-II, and AHPV for > CIN2 was 66.7%, 89%, and 100% respectively; for > CIN3 it was 66.7%, 93.3% and 100%. The specificity of Cytology > ASCUS, HC-II, and AHPV for > CIN2 was 94.3%, 81.8%, 89.2%; and for > CIN3 was 94%, 81.4%, 88.7% respectively. The positive and negative predictive values of HC-II for the detection of > CIN2 are 6.0% and 99.8%; for Aptima PPV and NPV are 10.8% and 100%. Comparisons of area under the curve for HC-II and Aptima showed significant differences for the detection of > CIN2 areas .85 vs .95 chi²=8.91 p=.0028 and > CIN3, areas .87 vs .94 chi²=4.32 p=.0377.

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**O-14.3**

TREND OF MANAGEMENT OF HIGH GRADE CIN IN A COLPOSCOPY CLINIC OF BANGLADESH

Ashrafun Nessa¹, M A Hussain¹, Jebun Nessa Rahman², M H Rashid³

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**Objective:** To investigate the pattern of management of high grade CIN and to evaluate the acceptability of LEEP during the first visit at colposcopy clinic.

**Method:** A prospective study was done among VIA + ve women attending colposcopy clinic of Bangabandhu Sheikh Mujib Medical University (BSMMU). Patterns of management of high grade CIN were observed and compared between two periods - the first one was from January 2005 to June 2008 and the second one was from July 2008 to June 2009. Sensitivity and specificity of colposcopy findings was measured through histopathological findings considered as gold standard test.

**Results:** From January 2005 to June 2008, 15.3% of the colposcopy-proved high grade CIN received treatment through one or two visits and 61.1% women had failed to receive treatment. From July 2008, a colposcopy and treatment policy was introduced. During first colposcopy visit, 70.1% women with high grade CIN received LEEP. The sensitivity of colposcopy was 73% and 65% during first and second period respectively. Specificity of colposcopy in both periods was same (95%).

**Conclusion:** VIA followed by colposcopy is an effective way of screening of cervical cancer. Colposcopy and treat policy during the first visit at colposcopy clinic shows effective management of colposcopically diagnosed high grade CIN and decreases the rate of failure to receive treatment.

**O-14.4**

CORRELATION OF HUMAN PAPILLOMAVIRUS DNA TESTING WITH RESIDUAL DISEASE IN TREATED CASES OF CERVICAL INTRAEPITHELIAL NEOPLASIA

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All India Institute of Medical Sciences, Delhi, India

**Objective:** To correlate cervical HPV DNA status and titre, conventional Pap and colposcopy 6 months after treatment of cervical intraepithelial neoplasia (CIN) by Loop Electrosurgical Excision Procedure (LEEP).

**Method:** From August 2006 to November 2008, 64 patients referred to colposcopy because of abnormal Pap smear, HPV positive report or unhealthy cervix were enrolled. All patients underwent Pap, HPV test by Hybrid Capture 2 (HC2) assay and colposcopy with directed biopsy of any abnormal lesion. Thirty four HPV positive women with CIN on cytology/histology underwent LEEP and 28 (82.4%) were followed up at 6 months with all tests.

**Results:** Pre-treatment median HC2 titre 137.43 (range 0.2-1819.3 RLU), post-treatment median HC2 titre 0.26 (range 0.15 to 272.28 RLU). At cut-off 10 RLU, HC2 testing had sensitivity 89%, specificity 69% in diagnosing CIN 2/3. At HC2 titre > 100 RLU, the Odds Ratio (OR) of being diagnosed as CIN2+ was 4.5. Post-treatment HC2 + were 28.6%, Pap > ASCUS found in 11%, colposcopy unsatisfactory in 28.6%. Three (11%) patients had biopsy-proven residual disease: CIN1-2, CIN3-1. All 3 were HPV + (HC2 titre 6, 59, 273 RLU). Only 1 had abnormal Pap report of HSIL, she could be diagnosed by all method. None of the HPV cases had abnormal Pap smear, colposcopy or biopsy result.

**Conclusion:** High viral load on HPV test prior to LEEP is a predictor of CIN and residual disease. HPV test 6 months post-LEEP was the best test for residual/recurrent disease. A negative HPV test has a high negative predictive value for residual disease.
LESSONS FROM SUCCESS AND FAILURE FROM CERVICAL CANCER SCREENING IN JAPAN

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Objective: Although recent coverage of cervical cancer screening in Japan is the lowest among OECD countries (23.7%), the present incidence and mortality have decreased as well as in other developed countries. The aim of this presentation is to suggest the lessons from the effect of the screening to prevent cervical cancer.

Method: Historical survey of the organization and funding of cervical cancer screening in Japan was done. Also, the relationship between incidence, mortality and coverage of screening were investigated.

Results: The cervical cancer screening program was enacted as a national program in 1982 in Japan. The age-adjusted mortality rate of cervical carcinoma fell from 21.3% in 1980 to 5.3% in 1993, since we have a long history of cervical cancer screening. The screening program was successful in reducing the incidence and mortality. However, the Japanese national government stopped specific funding for cancer screening in 1998 for financial reasons, stating that local governments should provide funding for cancer screening. Recently, older women have continued participation but remarkably fewer younger women participate in screening programs. Because there is not enough health education in schools, young women do not have the right knowledge about cervical cancer and screening. Low coverage of screening caused a recent increase of cervical cancer in younger females.

Conclusion: Considering disease burden of cervical cancer, screening as secondary prevention has been effective. We should continue the effort to increase screening coverage in areas with or without sufficient resources even though we are in the era of HPV vaccination.
I-15.1

LESSONS FROM VACCINE INTRODUCTION IN THE DEVELOPED WORLD (SCOTLAND)

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Scottish HPV Reference Laboratory, Royal Infirmary, Edinburgh¹, Health Protection Scotland, Glasgow², United Kingdom

Objective: To develop a comprehensive cervical cancer prevention strategy based on HPV vaccination of schoolgirls, population based liquid based cytology cervical screening and HPV detection, backed up by appropriate evidence capture and research

Method: An HPV National Steering Group with wide stakeholder membership was set up in 2006 under the Chairmanship of a Health Board Chief Executive and included the Scottish Government Health Department. Significant sub-committees were established including Service delivery with vaccine procurement and pharmacy included Public & Professional Communications group; Data Management group and Epidemiology and Surveillance group. All met independently but reported through a core implementation group to the National Steering Group.

Results & Conclusion: Setting up comprehensive governance structures with Scottish Government buy-in in advance of commencing the HPV vaccine programme proved highly effective, with over 90% uptake of vaccine in schoolgirls (aged 12-13 plus catch-up to under-18s) in the first year of delivery. Scotland’s 3-yearly screening programme starts at age 20 and the first vaccinated women will be entering the screening programme in late 2010. Interaction with cervical screening and colposcopy/treatment services will ensure all relevant clinical information is captured and accessible throughout a woman’s life. The establishment of a Scottish HPV Reference Laboratory has achieved baseline prevalence data is available in the unvaccinated population. Finally the funding by Government of complementary research programmes ensures that robust evidence is accumulated to measure the success and impact of expensive vaccine and screening policies on women’s health.

I-15.2

LESSONS FROM VACCINE INTRODUCTION IN DEVELOPING COUNTRIES

Aisha O Jumaan¹, D. Scott LaMontagne¹, Nga Le², Emmanuel Mugisha³, Irma Ramos⁴, Carol Levin¹

PATH, Seattle, WA, USA¹, PATH, Hanoi, Vietnam², PATH, Kololo, Uganda³, PATH, Lima, Peru⁴

Objective: HPV vaccines containing types 16 and 18 (associated with 70% of cervical cancer cases) have the potential to reduce cervical cancer if used widely among sexually naive girls, especially in developing countries with greatest burden. However, challenges of implementing HPV vaccination in these countries include: lack of vaccine delivery mechanisms for young adolescent girls, cost and feasibility of vaccine delivery, and acceptance of vaccines targeting sexually transmitted infections. The PATH HPV Vaccines: Evidence for Impact project implemented HPV vaccination in selected areas of three low- to middle-resource countries to evaluate vaccination strategies for coverage, feasibility, acceptability, and implementation costs.

Method: Operational research studies included a modified WHO two-stage cluster survey for coverage; focus groups and key informant interviews for acceptability; vaccination observation, interviews, and focus group discussions for feasibility; and micro-costing using an ingredients approach and both primary and secondary expenditure data, including published salary data for estimating costs.

Results: Vaccine coverage ranged from 53% in Uganda to 94% in Vietnam. Acceptability was high due to government and Expanded Programs on Immunization support, trust in vaccines, and comprehensive sensitization and mobilization. Delivery was feasible due to collaborative planning between health centers and schools for implementation and strengthening of cold chain systems. Implementation costs varied by country and strategy used in each country.

Conclusion: HPV vaccination in diverse settings suggests that high HPV vaccine coverage can be achieved; delivery strategies are acceptable and feasible with implementation costs that are similar to other vaccination campaign strategies.
NEW TOOLS FOR COMPREHENSIVE CERVICAL CANCER PREVENTION PLANNING

Scott Wittet
PATH, Seattle, WA, USA

Objective: To describe resources available for planning effective, sustainable programs.

Method: New tools for prevention of cervical cancer include HPV vaccines, HPV DNA screening tests and simple, visual inspection methods for screening. The most rapid and extensive health benefits will result when national programs are able to offer vaccine to girls and affordable and effective screening and treatment to adult women. Unfortunately, until recently there have been few resources to guide design of comprehensive cervical cancer prevention programs. Guidance also is needed relating to evaluating cost-effectiveness, assessing affordability and planning for sustainable programs. Recognizing this gap, partners in the Cervical Cancer Action coalition decided that providing decision-making assistance related to comprehensive programs would become a top priority for 2009-2011. The strategy is two-pronged and includes 1) outreach to top level influentials (such as Parliamentarians, Ministers of Health and their advisors, and donor agencies, among others) and 2) technical assistance for mid-level program planners. The first strategy is being implemented through regional meetings, along with direct contact with key individuals in select countries. The second strategy involves in-depth work with multi-disciplinary teams, the focus being those responsible for immunization and those working on women’s health.

Results and Conclusion: New resources are available to help with planning comprehensive programs, including an interactive, web-based tool called the “Cervical Cancer Prevention Action Planner”. Demonstrations will stimulate discussion among participants about how the tools could benefit cancer prevention planning now and how they might be improved in future.

CAN HPV BE THE SOLE PRIMARY SCREENING TEST?

Jack Cuzick
Centre for Epidemiology, Mathematics and Statistics at Cancer Research, London

One of the most important medical discoveries in the last 50 years is the identification of the human papillomavirus (HPV) as the primary cause of cervix cancer. It is now known that virtually every case of cervix cancer is caused by HPV and this information has been used to develop vaccines against the two major types of HPV (types 16 and 18) which cause about 70% of cervix cancer worldwide, and also to develop improved screening tests based on identifying the virus directly in cervical cells, as opposed to the conventional approach of looking for the cytological abnormalities caused by the virus.

Here we focus on the role of high risk HPV (HR-HPV) testing in screening, where it has 3 main uses. The first is the management of lower grade smears where there is now overwhelming evidence that the detection of HR-HPV in this sample is an important indicator of the likelihood of high grade CIN being present. A second application is as a “test for cure” in women treated for high grade CIN. The third and most far-reaching use of HPV testing is as the primary screening test. The very high sensitivity of HPV testing in these studies indicates that it can serve as the sole primary screening test and that cytology is best used as a triage test in women who are HPV positive. We review evidence from a multitude of studies that HPV testing is more sensitive than cytology and can be safely performed at longer intervals. The recent evidence for greater protection against invasive cancer will also be reviewed and a new algorithm will be proposed for using HPV testing as the sole screening test in women aged > 30 years.
I-16.2

HPV SCREENING – NEW DATA & NEW ALGORITHMS

Attila T Lorincz

Department of Molecular Epidemiology, Wolfson Institute of Preventive Medicine, Barts and The London School of Medicine, Queen Mary University of London, England

Cervical cancer remains among the most important cancers of women in much of the world. We have extensive and widely published knowledge of its cause and of cost-effective prevention methods, information known for decades. Therefore one may wonder if some day the rampant presence of cervical cancer in our global populations will be generally regarded as among the growing list of more blatant failings of 21st century medicine? Long term infection of cervical metaplastic cells by carcinogenic human papillomavirus (HPV) is the sole necessary cause of cervical cancer. If the infection is prevented by prophylactic vaccination or discovered by screening and treated by simple epithelial ablation the carcinogenic process is blocked with remarkably high efficiency, as close to 100% as offered by any medical intervention known today. Perhaps it is the will to really succeed that is lacking or perhaps the algorithms are still evolving and too complicated? Regardless the old adage “as experts argue patients die” seems to have found a home with this disease.

In conjunction with HPV prophylactic vaccination, HPV DNA screening must become the new bulwark of defence against cervical neoplasia for the next 30 years. The reasons for this are quite simple, firstly the dissemination of the vaccine has turned out to be a slow and costly process that will take decades to approach reasonable population coverage and with remaining questions about real world levels of protection from malignancy. Secondly, HPV DNA testing is by far the most sensitive screening method, closely approaching a relative sensitivity of 100% and an absolute sensitivity of 90+% (compared to Papanicolaou cytology with an estimated absolute sensitivity of less than 50%). To be successful and cost-effective screening interventions must be organized and periodic, administered as infrequently as possible with superior tests. HPV DNA testing has emerged as the leading option in six independent developed-country randomized controlled trials (RCT) involving in aggregate more than 200,000 women. The RCTs demonstrated that HPV DNA testing is more effective than cytology in detecting women with high grade cervical intraepithelial neoplasia (HG-CIN) in a first round of screening, leaving significantly fewer HG-CIN to be detected in the second round. Thus, screening intervals could be lengthened by two to three years (to as long as 5 to 7 years) with little or no loss in programmatic sensitivity. A similar RCT conducted in India by Sankaranarayanan (NEJM 2009) showed HPV testing to be dramatically superior to cytology in reducing mortality from cervical cancer. It is fair to say that today the evidence for HPV screening is powerful and supports two preferred alternative algorithms: 1) HPV DNA screening with cytology triage and 2) HPV DNA screening with persistent-HPV genotyping triage. Details of these algorithms and supporting data will be discussed.

I-16.3

THE ACCURACY OF COLPOSCOPY AND ITS APPROPRIATE USE IN CERVICAL CANCER SCREENING TRIALS

Jerome L Belinson

Preventive Oncology International¹, USA

World-wide colposcopic directed biopsy has served as the gold standard for hundreds of cervical cancer screening trials including studies evaluating new technology. Based on our evaluation of more than 40,000 cervical quadrant matched colposcopic diagnoses and biopsies the inaccuracy of colposcopy was exposed. In addition, the major causes for colposcopy missing the true diagnosis and a solution has been determined and proposed.

The four major causes for lesions being missed in screening trials are: 1) Verification bias – patients being selected for colposcopy by screening techniques that miss the same lesions missed by colposcopy 2) One quadrant (small) lesions 3) Thin high-grade lesions that are not detectable because they do not appear as white lesions 4) The experience of the colposcopist.

The solution is the use of a small (2mm) virtually painless biopsy instrument, and changing the colposcopy protocol so the goal is first to identify the squamo-columnar junction and second to identify any potential abnormalities to be sure they are biopsied. The colposcopist evaluates the cervix by quadrants and biopsies any abnormal findings in each quadrant. If a quadrant is normal, biopsies are taken at 2, 4, 8, or 10 o’clock at the squamo-columnar junction depending on the quadrant. An endocervical curettage is then obtained on all patients.

Not only does this protocol improve the accuracy of colposcopy regardless of the skill of the colposcopist, but it will allow accurate evaluation of new technology. This is especially true for imaging technologies where implied clinical effectiveness may far overestimate the true accuracy of the technology. All of our HPV screening trials have used this verification protocol. Subjecting a variety of screening technologies to stringent verification leads to an accurate assessment of their effectiveness in screening algorithms for both primary as well as secondary screening.
IMPACT TO GENITAL WARTS: AUSTRALIA EXPERIENCE
Christopher K Fairley
Melbourne Sexual Health Centre and School of Population Health, University of Melbourne, Melbourne, Victoria, Australia

Background: Australia provided free quadrivalent human papillomavirus (HPV) vaccine to 12-18 year old girls in a school-based program from April 2007 and to women <27 years through general practices from July 2007. Coverage rates for three doses of the vaccine are about 70% in both groups.

Methods: The proportion of new clients with genital warts at Melbourne Sexual Health Centre (MSHC) from January 2004 to December 2009.

Results: 44,256 new clients attended MSHC between 2004-2009 and genital warts were diagnosed in 4,518 (10.2%; 95% confidence intervals (CI): 9.9-10.5). The proportion of warts in women <28 years fell from an average of 12.7% before 2008 to 4.4% in the last quarter of 2009.

The proportion of new clients with genital warts was significantly lower in 2008-9 than 2004-7 for women <28 years (RR=0.45 (95% CI, 0.39-0.52)), heterosexual men (RR=0.82 (95% CI, 0.75-0.90)) and men who have sex with men (MSM) (RR=0.80 (95% CI, 0.65-0.98)) but not women ≥28 (RR=1.1 (95% CI, 0.87-1.3)).

The falls in warts in women <28 and heterosexual men occurred despite significantly higher mean numbers of sexual partners per year in 2008-9 compared to 2004-7 (P<0.001 for both women <28, and heterosexual men). In contrast, the fall in warts in MSM was associated with a lower mean number of male partners in 2008-9 (11.5 partners per year) compared to 2004-7 (17.3 male partners per year, P<0.001).

Conclusions: Our data suggest that the initial rapid and marked reduction in the incidence of genital warts among women <28 years of age, originally seen in 2008, is continuing in 2009. The reduction in genital wart diagnoses observed in MSM may be due to a lower risk profile of MSM in 2008-9.

EFFICACY IN CLINICAL TRIAL POPULATION OF FUTURE I – II
Suzanne M Garland
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Objectives: At licensure (2006), GARDASIL was shown to prevent HPV16/18-related high-grade lesions (CIN2/3 and AIS) with up to two-year follow-up (protocols 013/015, women aged 16-26). Here we present end-of-study vaccine efficacy (VE) for up to four years.

Methods: Review of protocols 013/015 (FUTURE I and II)

Results: In the per-protocol-population of women aged 16-26, end-of-study VE for HPV16/18-related CIN2/3 or AIS was 98% (95%CI:94-100); VE for HPV6/11/16/18-related condyloma, VIN1-3, and VaIN1-3 was 99%, 100% and 100%, respectively. In PCR-negative subjects for HPV6/11/16/18/31/33/35/39/45/51/52/56/58/59 pre-vaccination, Gardasil significantly reduced CIN2-3/AIS associated with the 10 non-vaccine HPV types which cause ~20% of cervical cancers. In women aged 16-26 who had cleared a previous infection with one of the vaccine-HPV types at the time of vaccination, Gardasil recipients were protected against recurrence of disease from that type, unlike placebo recipients. In the extended follow-up of 16-23 year old women up to 9 years after vaccination with the HPV16 monovalent prototype-vaccine, per-protocol VE against HPV16 CIN was 100%.

Conclusions: Disease prevention remains the most important measure of long-term VE. Vaccination with GARDASIL is expected to reduce significantly the burden of cervical and other cancers, dysplasia and genital warts in women and men.
CAN CERVICAL CANCER BE CONTROLLED IN THE DEVELOPING WORLD?
Lynette Denny
University of Cape Town, South Africa

While cervical cancer is a relatively rare disease in countries that have implemented national screening programmes, the disease remains
the commonest cancer cause of death in countries with no screening programmes. The failure to initiate or sustain screening programmes
in developing countries is a reflection of the global inequity of the distribution of health care resources. Communicable diseases/maternal
and perinatal conditions and nutritional deficiencies are the predominant causes of death in developing countries, and this has diverted
attention away from cancers, even cancers related to infections, such as HPV and cervical cancer. In 2002, $3198 billion were spent on
health globally, but only 12% of this was spent in low and middle income countries, which account for 84% of the global population, 20%
of global domestic product and 90% of the global disease burden. It is in this context that we need to address the issue of cervical cancer
prevention. In the past 10 years innovative and alternative approaches to cervical cancer prevention have been extensively studied in both
cross-sectional and randomised controlled trials. Two screening methods most studied have been VIA and HPV DNA testing, particularly in
the context of on-site one visit ‘screen and treat’ strategies. The advent of two commercial HPV vaccines adds a whole other dimension to
the possibilities for cervical cancer control. The tools for a technological and more appropriate approach to cervical cancer prevention have
been studied and developed, what now needs to happen is for civil society and governments to create the political will for implementation.
I-17.2

HOW TO EDUCATE THE PUBLIC ON HPV AND CERVICAL CANCER PREVENTION

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The association between HPV and cervical cancer is well established. Our previous studies showed that public knowledge about HPV and cervical cancer was generally poor. Furthermore, public awareness of the sexual transmission of HPV was associated with a stigmatized attitude towards HPV infected individuals owing largely to the lay stereotypical belief linking a person who bears a sexually transmitted infection with promiscuity or sexual deviation. Correcting this misconception is necessary as women or adolescents who consider themselves “sexually proper” may see little need to take preventive measures against HPV or cervical cancer. In our recent study, we noted that apart from giving factual information, a public HPV message consisting of explicit anti-stereotypic contents targeting specific lay sexual beliefs reduced the stigma associated with high risk HPV. Furthermore, excluding low risk HPV in the context of cervical cancer control helped to avoid the potential stigmatizing effect of genital warts from tainting perceptions about high risk HPV infection. Utilizing multiple channels in public education is necessary to reach different populations. Newspaper, magazine, television and other mass media channels enable a one-way dissemination of information on HPV and cervical cancer to a wide spectrum of audiences. Public health talks allow for tailoring of the contents to meet the particular information needs of a target group as well as chances of interaction to aid understanding. For instance, we collaborated with local secondary schools to implement an educational program on cervical cancer prevention for their female students. A substantial knowledge gain and positive attitude towards HPV vaccination were found among the adolescent participants after attending the program. In public HPV and cervical cancer education, tailoring the contents and channels of delivery are crucial to impart knowledge to a variety of audiences without drawing backfire.

I-17.3

CIN 1: WHEN SHOULD IT BE TREATED?

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The management of CIN1 has changed over the last decade. Traditionally CIN was thought to be a disease continuum, with progression from CIN1 to CIN3 and hence women with CIN1 were treated to prevent progression to cervical cancer. However it is now known that women with normal immune function suppress HPV-induced low-grade CIN1 lesions, although with current screening tools it is not possible to predict the few who may progress. Thus, the future holds for triaging these lesions with molecular markers of progression such as p16INK4A. Additionally, studies have identified a lack of histologic reproducibility among even expert pathologists with more than 50% of specimens being down-graded to normal. Thus, CIN1 should be followed expectantly rather than treated, given the consequences of treatment and the high chances of regression over 2 to 4 years without treatment. In addition, CIN1 lesions may be associated with low-risk types of HPV infection. Findings from ALTS indicate that the risk for having a CIN2,3 lesion identified during 2-year follow-up in histologically confirmed CIN1 was 11%-13%.

The exception to the low risk potential of CIN1 is among women whose initial colposcopy was preceded by HSIL (high grade intraepithelial lesion) or atypical glandular cells (AGC) cytology. In women who had initial HSIL cytology or AGC cytology, CIN 2/3 or worse was identified in 83-97% of women undergoing ‘see and treat loop’ electrosurgical procedure(LEEP). Additionally, persistent CIN1 likely reflects not only persistent HPV infection but, more specifically, infection with an oncogenic subtype. Castle and colleagues found that among women who had LSIL and infection with HPV16, the 2-year risk for CIN3 or worse was 39% compared with 10% with any other oncogenic HPV type. Thus, although CIN1 typically represents transient infection (which should not be treated), persistent disease is more often associated with oncogenic HPV infection and subsequent high-grade neoplasia, implying a heterogeneous mix of CIN1 and the initial role for surveillance, with treatment reserved for those who have persistent neoplasia.
**O-18.1**

INCIDENCE OF HERPES SIMPLEX VIRUS TYPE 2 IN YOUNG REPRODUCTIVE AGE WOMEN IN MYSORE, INDIA

Purnima Madhivanan1, Yea-Hung Chen2, Karl Krupp3, Jeffrey D Klausner2, Anjali Arun3, Arthur L Reingold4

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**Objective:** Herpes simplex virus type 2 (HSV-2) is one of the most common sexually transmitted infections and the primary cause of genital ulcer disease worldwide. This study describes the incidence of HSV-2 infection among young reproductive age women in Mysore, India.

**Method:** Between October 2005 and April 2006, 898 women were enrolled into a prospective cohort study and followed quarterly for six months. Interviewer administered questionnaire to collect demographic and social risk factors, physical examination and collection of biological specimen to screen for reproductive tract infections was done at each visit. Serologic testing was conducted for the presence of HSV-2 antibodies using HerpeSelect herpes simplex virus type-2 enzyme-linked immunosorbent assay (ELISA). HSV-2 ELISA results were calculated with two different index cut-off values of 1.1 as suggested by the manufacturers, and 3.5 as suggested in the literature to increase performance of the test in low to medium prevalence settings.

**Results:** The HSV-2 acquisition incidence rate was 10.4 cases/100 woman-years using the manufacturer suggested index cut-off value of 1.1. Using a higher index cut-off value of 3.5, the incidence fell to 2.5/100 women-years. All detected infections were asymptomatic. By comparing the incidence estimates with a higher index cutoff value, we reduce the chance of misclassification of the outcome.

**Conclusion:** HSV-2 incidence is moderate in this community sample of young reproductive age women. More research is needed to establish an appropriate cutoff index value for the Focus HerpeSelect assay in Indian settings.

**O-18.2**

VAGINAL DOUCHING FACILITATES INFECTION OF HUMAN PAPILLOMAVIRUS AND NON-REGRESSION OF ITS CERVICAL INTRAEPITHELIAL LESION

Tang-Yuan Chu1, Chao Agnes Hsiung2, Chi-An Chen3, Hung-Hsueh Chou1, Chih-ming Ho4, Tsai-Yen Chien4, Hui-Ju Chang5, Cheng-Yang Chou3, Jui-Der Liou3, Chang-Yao Hsieh3

Buddhist Tzuchi General Hospital, Tzuchi University, Taiwan1, National Health Research Institutes, Taiwan2, National Taiwan University Medical College, Taiwan3, ChangGung Memorial Hospital, Taipei, Taiwan4, Cathay General Hospital, Taiwan5, Koo Foundation Sun Yat-Sen Cancer Center, Taiwan5, National Cheng-Kung University Medical College, Taiwan5

**Objective:** Practicing vaginal douching (VD) is common worldwide. The effect of VD on the natural history of human papillomavirus (HPV) infection and its primary lesion of the uterine cervix is unknown.

**Method:** In a nation-wide, multi-center cohort of Taiwan Clinical Oncology Group, prevalence of HPV and its correlates were studied in women referred for colposcopy with diagnoses of negative (n = 316), LSIL (n = 474), HSIL (n = 450) and invasive cancer (CA, n = 16). Natural histories of 295 LSIL were followed every three months up to 36 months. Cervico-vaginal secretions (CVS) collected before and after VD were tested for its effect on HPV6 pseudovirus infection in cells. To imitate the consequences of VD before and after sexual intercourse, CVS were washed from the cell culture before and after viral inoculation.

**Results:** Women who practice VD had 1.44 (95% CI, 1.01-2.04), 1.39 (0.98-1.96) and 3.14 (1.04-9.49) fold increased risk for prevalent HPV infection, persistent HPV infection and non-regression of LSIL, respectively; and longer persistence of LSIL (P = 0.02). Doucheing with hygiene products was even worse with odds ratio for HPV prevalence and LSIL non-regression of 2.23 (1.08-4.61) and 3.14 (1.04-9.49), respectively. CVS collected from either pre- or post-menopausal women protected 60% of infection, whereas CVS collected after VD protected only 26%. In the presence of CVS, washing of cells before viral inoculation enhanced viral infection, but washing after viral inoculation decreased infection.

**Conclusion:** The study provided clinical and in-vitro evidences supporting VD is risky to HPV infection and non-regression of LSIL, especially by using hygiene products, especially before intercourse.
**O-18.3**

**HIGH RISK HPV DNA IS A USEFUL BIOLOGICAL MARKER FOR DIAGNOSIS OF EARLY CERVICAL CANCER IN HIV SERO-POSITIVE WOMEN**

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**Objective:** In 1993, the CDC included invasive cervical cancer in the AIDS-defining syndrome. This study was conducted in the Birla Cancer Centre of S. M. S. Medical College in collaboration with STD HIV Department to determine the prevalence of high risk HPV DNA in HIV sero-positive women and female consorts of HIV positive males for early diagnosis of cervical cancer and to find out the sensitivity and specificity of cytology, colposcopy and HPV DNA Test for detecting early cervical lesions.

**Method:** 150 HIV seropositive and 50 HIV negative female whose consorts were HIV positive were enrolled in this study. All patients underwent detailed clinical history, sexual history and thorough clinical examination with complete hemogram, liver and renal function tests, cytology, colposcopy, HPV DNA Hybrid Capture test, CD4/CD8 count and viral load.

**Results:** Majority of the patients were in the age group of 26 to 44 years, 60% of their spouses were from a migrant population, 78% of the women belong to Shekhawati area of Rajasthan. 38% HIV sero-positive women were positive for high risk HPV DNA, while 8% HIV negative women who had HIV seropositive consorts were HPV DNA positive. On comparing the sensitivity and specificity of different methods for diagnosis of CIN, the sensitivity of HPV DNA detection was found to be 100% with 90.5% specificity, 100% negative predictive value, 66.7% positive predictive value, as compared to cytology and colposcopy which had sensitivity 60.9% and 95.7% and specificity 85.2% and 74.1% respectively.

**Conclusion:** HPV positivity is a common finding in HIV-Positive patients. HPV DNA detection is an important and very useful sensitive marker for early detection of cervical cancer in the HIV seropositive women.
Q-18.5

THE BEHAVIOR OF CIN IN HIV SEROPOSITIVE WOMEN
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Objective: To study the course of cervical lesions in HIV seropositive women and compare with seronegative women.
Method: This study was conducted at Birla Cancer Center with the STD and HIV Department of S.M.S. Medical College. A total of 1000 women were included in the study: Group A comprised 250 HIV seropositive women, Group B comprised 250 HIV seronegative women who had HIV positive consorts and Group C comprised 500 HIV seronegative women with HIV seronegative partners. All women underwent detailed clinical history, sexual history and thorough clinical examination with cytology, colposcopy, CD4/CD8 count and viral load. All women were followed up for 2 years to study their cervical lesions.
Result: In group A, cytology showed inflammation in 44.8% (112), ASCUS in 18% (45), LSIL in 10% (25) and HSIL in 6% (15) and normal in 21.2% (53). In group B, the lesions were inflammatory in 35.6% (89), ASCUS in 8% (20), LSIL in 5.2% (13), and HSIL in 2.8% (7) and normal cytology and colposcopy in 48.4% (121). In group C, 55% (275) were normal, 31% (155) were inflammatory, 9% (45) were ASCUS, 3% (15) were LSIL & 2% (10) were HSIL. On following the cases for a period of 2 years the progression rate was 30% in group A, 10% in group B while 1% in group C, which was significantly more in HIV seropositive women.
Conclusion: CIN is more aggressive in HIV seropositive women than in seronegative and these results point to the importance of cervical screening in HIV seropositive women at 6 month intervals. Complimentary HPV test and colposcopy are required for proper diagnosis and management.

Q-18.6

HEALTHY WOMEN PROJECT: ORGANIZED POPULATION BASED SCREENING
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Objective: To develop an organized population based screening of women aged 30-60 years for cancer of the cervix and breast.
Method: Pilot testing of Cervical Cancer Screening Programme Guidelines was done in three sectors of Chandigarh. Preparation of IEC material – Posters, pamphlets and screening cards providing complete information about cervical and breast cancer, available screening methods, self examination of breast. Training of personnel – ANM and Community Health nurses (CHN) were given 3 weeks training for VIA and clinical breast examination (CBE), their competency ensured and periodically checked. Field activity- ANM and CHN visited the houses, distributed health education pamphlets, explained the importance of screening apparently healthy women and gave an appointment for visiting the local dispensary where CHN and ANM performed CBE and VIA. CBE and VIA women were reassured and asked to return after 3 years. VIA or CBE positive women were referred to PGI for further management: Pap smear and colposcopy with biopsy as indicated; FNAC and/or mammography as indicated.
Results: 2665 houses were visited, 1984 women contacted and 833 women screened. Only 3.4% women refused screening VIA was positive in 169 (20.2%). All came for follow-up at PGI. Squamous metaplasia was found in 15, CIN2 in three and CIN3 in one. CBE was positive in 75 by screening, confirmed by surgeon in 52.
Conclusion: In the developing world, VIA is a useful simple alternative to cytology screening. Training health workers for VIA and CBE brings services closer to women’s homes and reduces clinic visits.
LAPAROSCOPIC PELVIC ANATOMY RELATED TO RADICAL HYSTERECTOMY
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Sound surgical technique is based on accurate anatomic knowledge of the female pelvis. The anatomy of the fundamental supporting structures of the pelvis and the genital, urinary, and gastrointestinal viscera are shown with the help of videos. Laparoscopy requires surgeons to revisit familiar anatomy from an unfamiliar perspective and pelvic anatomy can appear significantly different due to the effect of pneumoperitoneum, Trendelenburg position and traction from a uterine manipulator. In addition, with laparoscopy there are inherent limitations related to a fixed visual axis, loss of depth of field and magnification. The development of laparoscopes with different angles of view makes orientation more challenging.

Adequacy of the lymph node dissection is determined visually. The superior boundary of the lymph node dissection is the bifurcation of aorta; the inferior boundary the external iliac artery at the point it is crossed by the circumflex iliac vein; the lateral boundary the muscular sidewall of the pelvis; and the posterior boundary the obturator nerve. Dissection of the various spaces is demonstrated. Anatomic alterations secondary to disease, congenital variation, or intra operative complications may make even familiar surgical territory suddenly seem foreign.
**V-20.2**

**MICROCOLPOHYSTEROSCOPY IN EVALUATION OF CERVICAL PATHOLOGY**

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**Introduction:** Microcolpohysteroscopy (MCH) allows a gynaecologist to perform in vivo microscopic visual inspection of cervix and to combine colposcopic, cytologic and histological findings in the course of same examination. It helps in topographical scanning of suspicious areas of the cervix and localization of the center of lesions, which is useful for excisional biopsy procedures. It helps in endocervical evaluation and in cases where colposcopy is unsatisfactory. It helps identify the transformation zone, squamocolumnar junction and the upper extent of lesion thus guiding the depth of the cone and reducing the incidence of positive margins as well as an inappropriately large cone in young patients. It is a valuable adjunct to colposcopy and Pap smear for evaluation of the cervix in today’s era with increasing use of ‘see and treat’ approach and office based procedures.

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**V-20.3**

**BOWEN’S DISEASE OF VULVA - TIMING AND TECHNIQUE OF VULVECTOMY**

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**Objective:** To demonstrate operative technique, diagnostic and therapeutic role of vulvectomy in Bowen’s disease of vulva.

**Method:** A 45 year old lady was referred to us with chronic itching and burning of vulva. One year ago, biopsy showed Vulvar Intraepithelial Neoplasia (VIN) - III (Bowen’s disease) and was treated with cryotherapy. On examination there was a 3 X 2 cm sized ulcer near clitoris on left labia majora with depigmentation extending up to fourchette. Speculum and bimanual examination were normal. Groin nodes were not palpable. She was advised total vulvectomy.

Skin and mucosal incision were marked. Skin incision was deepened up to adductor fascia and deep fascia covering urogenital diaphragm. Vascular pedicle of clitoris was secured. At fourchette skin and mucosal incisions were joined to facilitate dissection. Mucosal incision was taken one cm above meatus anteriorly to fourchette posteriorly and deepened clockwise and anticlockwise stopping just short of urethral meatus. The two flaps were joined and the specimen removed en-bloc. Skin-mucosa, skin-skin approximation was done with simple and mattress stitches respectively. Due care was taken near the urethral meatus to avoid kinking. Histology showed VIN III, classical type with squamous cell carcinoma basaloid type (2mm invasion).

**Conclusion:** Bowen’s disease (Intraepithelial neoplasia) is treated conservatively (Imiquimod, 5FU, or cryotherapy). Surgery is advised for failures; and ranges from local excision to total vulvectomy. Our case highlights the limitation of incisional biopsy because invasion may be missed. Further, there is need for early vulvectomy in management of VIN especially in non-responding/ progressive ulcer.
**P-001**

**PREVALENCE AND CLINICAL RELEVANCE OF CYCLOOXYGENASE-1 AND -2 EXPRESSION IN STAGE IIB CERVICAL ADENOCARCINOMA**

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**Objective:** To determine the relationship between cyclooxygenase (COX) -1 and -2 and prognosis in patients diagnosed with FIGO stage IIB cervical adenocarcinoma who underwent concurrent chemoradiotherapy.

**Method:** Twenty-three patients diagnosed with stage IIB cervical adenocarcinoma and treated with concurrent chemoradiotherapy between 1990 and 1995 were included in this study. COX-1 and -2 expression and clinicopathologic features were evaluated. COX-1 and -2 expressions were determined by immunohistochemistry. The prevalence of COX-1 and -2 expressions were similar at 73.9%. Significant COX-1 and -2 expression was 47.8 and 60.9%, respectively. COX-2 expression was associated with poor response to treatment and cancer-related death (P=0.043 and 0.012, respectively). Poor survival was identified in patients who showed high COX-2 expression (P=0.016). There was no correlation between COX-1 expression and patient prognosis.

**Conclusion:** Only COX-2 was found to be a potent prognostic factor in patients treated with concurrent chemoradiotherapy for stage IIB cervical adenocarcinoma. However, further studies with more samples are needed to definitely demonstrate the relationship between COX expression and cervical adenocarcinoma.
P-002

FIELD METHYLATION SILENCING OF THE PROTO-CADHERIN 10 GENE IN CERVICAL CARCINOGENESIS, AS A POTENTIAL SPECIFIC DIAGNOSTIC TEST FROM CERVICAL SCRAPINGS

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Objective: PCDH10 is a member of the protocadherin cell adhesion molecules which are frequently down-regulated in cancers. This study aimed to characterize the methylation-silencing of the PCDH10 gene in the full spectrum of cervical carcinogenesis and to clarify if a field effect of methylation might be a target for a diagnostic test from cervical scrapings.

Method and Results: Methylation-silencing of PCDH10 was found in four of five cervical cancers and one of two precancerous cell lines, which could be reversed by demethylation treatment. PCDH10 methylation was detected in 85.7% (24/28) of invasive cancer tissues, 36.4% (4/11) of high grade squamous intraepithelial lesions (HSIL), 20% (1/5) of low grade SIL (LSIL), and none (0/17) of the normal cervix from non-cancer subjects. In addition, the methylation was also frequently found in histologically normal cervical tissues adjacent to cancer lesions (7/13, 53.8%) and, less frequently, vaginal and endometrial (1/8, 12.5%). Further investigation of cervical scrapings revealed a cancer-specific methylation of PCDH10 with methylation rate of 71% (22/31) in invasive cancer, 27.9% (12/43) in carcinoma in situ (CIS), and none in HSIL excluding CIS (n = 12), LSIL (n = 27) and normal controls (n = 66) (p < 10⁻¹⁶). Comparing to high risk HPV test, PCDH10 methylation test of cervical scrapings was more specific (92% vs 60%), but less sensitive (71% vs 96%) in detection of invasive cervical cancer.

Conclusion: This study demonstrated a field methylation of the PCDH10 gene specifically in the invasion stage of cervical carcinogenesis, which might be employed to a highly specific diagnostic test for cervical scrapings.

P-003

LOSS OF SOCS-1 GENE EXPRESSION AND ITS METHYLATION MEDIATED SILENCING IN THE DEVELOPMENT OF HPV MEDIATED CERVICAL CARCINOGENESIS

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Objective: Cervical cancer is a leading cancer in women worldwide. HR-HPV types play an important role in cervical carcinogenesis. SOCS-1 is a negative regulator of JAK/STAT signaling pathway due to its tumor suppressor activity. The present study was designed to analyze the expression pattern of SOCS-1, a negative regulator of JAK/STAT signaling in cervical cancer cases in comparison with normal controls and to find its correlation if any with HPV infection.

Method: The HPV infection and expression pattern of SOCS-1 was analyzed in different stages of cervical carcinoma biopsies. RT-PCR, Western blotting, immunohistochemistry and methylation-specific PCR (MSP) were used to assess the expression pattern and promoter methylation of SOCS-1 in a total of 130 fresh cervical tissue specimens comprising precancer (n = 12), cancer (n = 78) and normal controls (n = 30).

Results: Almost 58% of the tumor tissues expressed either undetectable or reduced SOCS-1 expression (>50% loss of expression) and was significantly associated with advanced clinical stage of the disease (p < 0.01). Aberrant promoter methylation of the SOCS-1 gene was found in 54 % of the cervical tumor tissues, which was also found to be significantly associated with the severity of the disease (p < 0.01). Cervical cancer cases infected with HPV demonstrated a significant correlation with loss of expression and promoter hypermethylation of SOCS-1 gene.

Conclusion: Present study demonstrates for the first time transcriptional inactivation of SOCS-1 gene, due to DNA hypermethylation and the synergism with HPV infection may play an important role in the process of deregulation of STAT signaling in cervical carcinoma.
AOGIN 2010

P-004

DETECTION OF HUMAN PAPILLOMAVIRUS TYPE 16 E7-SPECIFIC T CELLS BY ELISPOT ASSAY

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Objective: To evaluate the effect of a human papillomavirus type 16 (HPV16) E7 synthetic peptides on the antigen-specific T-cell response in carcinoma in situ (CIS) and cervical cancer patients.

Method: We characterized the HPV-16 E7 specific T-cell epitopes using E7 overlapping peptide pools with peripheral blood lymphocytes obtained from normal healthy donors and HPV-16+ from 5 CI patients and 3 invasive cervical carcinoma patients with informed consent. We then analyzed the difference in the HPV-16 E7-specific T-cell immune responses in patients during and after treatment of the lesion by ELISPOT assay. All of CIS patients underwent loop electrosurgical excision procedure (LEEP) and all of the cervical carcinoma patients had a type III radical hysterectomy.

Results and Conclusion: Analysis of peripheral blood lymphocytes obtained from patients with HPV-16+ CIS and cervical carcinoma showed that the HPV-16 + E7 peptide pool 2:3 (aa 16-55) specific CD4+ T-cell immune response was significantly higher than other peptide pool. The HPV-16 E7 peptide specific T-cell immune response correlates with regression of established HPV-16+ lesions and freedom from disease recurrence. Thus, this E7 epitope may be useful for the characterization of HPV-specific immune responses in patients infected with HPV-16 or immunized with HPV vaccines.

P-005

DIAGNOSTIC AND PROGNOSTIC VALIDITY OF HUMAN PAPILLOMAVIRUS E6/E7 MRNA TEST IN HR-HPV POSITIVE CERVICO-VAGINAL SAMPLES

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Objective: To verify whether the E6/E7 mRNA of HR-HPV can be an efficient diagnostic and/or prognostic marker for cervical high-grade preneoplastic lesions or cancer, in HC2 positive patients.

Method: We analysed 464 HC2 positive liquid based cervico-vaginal samples for cytological categorization and HPV mRNA assay (PreTect HPV-Proofer, Norchip). 231 patients also had a biopsy at baseline, and 75 HSIL- patients were followed-up within 2 years by cytology, colposcopy and possibly histology.

Results: Considering high-grade histological lesions as the end-point, we found that the highest sensitivity belonged to the mRNA test (69% vs 53%, p < 0.0001), whereas cytology showed the highest specificity and PPV (97% vs 74%, and 91% vs 58% respectively, both p < 0.0001). The NPVs were quite similar between the two tests. Interestingly, considering the 185 HSIL- patients, the mRNA positivity was significantly more often associated with CIN2+ than CIN2- (P (X2) < 0.0001). Moreover, among the 75 HSIL- followed-up patients, only 4 were diagnosed as CIN2+ within two years, two of which had presented a positive mRNA assay at baseline. On the other hand, only two out of the 65 baseline mRNA negative patients (3%) developed a CIN2+ lesion. Therefore, in HSIL/HC2+ patients, mRNA test showed high specificity and NPV for development of an high-grade lesion during the follow-up (89% and 97% respectively), even if the sensitivity and the PPV were only 50% and 20% respectively.

Conclusion: Our data suggest a diagnostic role of the mRNA test and a potential prognostic role in HSIL/HC2+ patients.
**P-006**

**USE OF HIGH RESOLUTION MELTING ANALYSIS (HRM) FOR DETECTION OF MULTIPLE HPV INFECTIONS**

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**Objective:** To develop a high throughput genotyping method for identifying HPV infections in a single reaction.

**Method and Results:** Among genotyping methods, high resolution melting analysis (HRM) is particularly inexpensive, simple, and rapid in that no expensive labeled primers and no post-PCR processes such as gel electrophoresis are required. The analysis requires PCR, double stranded specific dye, and melting instrumentation. Accurate genotyping depend on reproducible melting curves. In order to obtain reproducible melting curves, we optimized various PCR conditions such as GC content, length and sequence of amplicon as well as PCR conditions. Using the optimized PCR condition, we were able to successfully amplify the HPV DNA by broad-spectrum primers targeting the GP5+/6+ region and the subsequent detection of the products by HRM analysis. For all 15 high-risk, 3 putative high-risk and 9 low-risk HPV genotypes, a homogenous analytic sensitivity of $< 1,000$ plasmid copies.

**Conclusion:** This study showed that HRM analysis can be useful for the identification of HPV subtypes. The HRM method will be useful in low resource settings as it saves considerable time and resources compared to other methods.

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**P-007**

**PROGNOSTIC IMPLICATIONS OF HUMAN PAPILLOMAVIRUS DNA LOAD IN ADENOCARCINOMA OF THE UTERINE CERVIX**

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**Objective:** To determine the relationship between HPV DNA Hybrid Capture II (HCII) titer and clinicopathologic features of adenocarcinoma of the uterine cervix (ACC).

**Method:** Forty-four patients were diagnosed with ACC between January 2001 and March 2008 at Yonsei University Health system and got HCII test done. Their clinicopathologic features including clinical stage, pathologic diagnosis of lymph node metastasis after operation, lymphovascular space invasion, tumor mass size and invasion depth were reviewed.

**Results:** Thirty four patients did not have lymphovascular space invasion and their mean HCII titer was 282.98 RLU. Six patients with lymphovascular space invasion had a mean HCII titer of 34.75 RLU ($P = 0.017$). Twenty-six patients had no lymph node metastasis on pathologic findings after hysterectomy, and their HCII titer was 352.49 RLU, compared to 5 patients with lymph node metastasis in their pathology reports after operation, had a mean 2.12 RLU ($P = 0.006$). Three patients had less than 3 mm of cervical cancer invasion, and their mean HCII titer was 1136.31 RLU higher, compared to 40 patients who had invasion deeper than 3mm, and their mean HCII titer was 237.75 RLU ($P = 0.016$). Tumor mass size and stage were not significantly related to HCII titer.

**Conclusion:** In this study, higher Hybrid Capture titer was not associated with the high HCTT titer in ACC patients, but was associated with low stage, smaller lymphovascular space invasion and lymph node metastasis.
E-CADHERIN GENE ALTERATIONS AND PROTEIN EXPRESSION IN ENDOMETRIAL CARCINOMA AND HYPERPLASIA

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Objective: E-cadherin gene alterations including gene mutation, loss of heterozygosity (LOH), DNA hypermethylation and protein expression loss have been rarely studied in endometrial carcinoma of Korean women. The purpose of this study is to investigate E-cadherin gene alterations in 30 cases of endometrioid endometrial carcinomas and 20 cases of endometrial hyperplastic lesions and to correlate their results with various clinicopathological factors.

Method: E-cadherin gene mutation was detected by polymerase chain reaction-single stranded conformational polymorphism. E-cadherin promoter methylation status was studied by use of methylation specific PCR. The 16q22 E-cadherin LOH analysis was performed by using PCR for three polymorphic microsatellite markers (D16S419, D16S3106, D16S498). E-cadherin protein expression was studied by immunohistochemistry.

Results: Whereas mutation rate in endometrial cancer was 6.7%, DNA hypermethylation, LOH and protein expression loss were detected in 40%, 50% and 43.3% of the endometrial cancer. Hypermethylation rate was significantly higher in stage above Ic. LOH rates were significantly lower in carcinomas with grade 1 and stage below Ib. The incidence of protein expression loss also showed significantly higher with tumor grade 3, stage above Ic or lymph nodal metastasis. At least one kind of abnormality of E-cadherin gene alterations and protein expression loss was detected in 24 cases (80%). At least two kinds of abnormality were detected in 15 cases (30%). Correlation among four kinds of abnormality was not recognized.

Conclusion: These results suggest that various E-cadherin gene alterations including DNA methylation, LOH and protein expression loss may contribute to the endometrioid endometrial carcinogenesis in independent mechanism.

GENE METHYLATION TEST FROM CERVICAL SCRAPINGS EFFECTIVELY DETECTS CERVICAL CANCERS IN WOMEN WITH EQUIVOCAL PAP SMEAR RESULTS

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Background: We studied the efficacy of methylation test of PCDH10 (PCDH10-me), PAX1 (PAX-me) and WT1 (WT1-me) in detection of cervical cancer in a nation-wide cohort of women with equivocal Pap smear results.

Method: Cervical scrapings of women with equivocal Pap smear results (including 220 ASC-US, 50 ASC-H, 10 AGC and 5 AGC-FN) and valid histological diagnosis (including 143 Normal, 71 CIN1, 19 CIN2, 21 CIN3, 24 CIS and 7 Cancers) were tested for gene methylation by methylation-specific PCR and for HPV by Hybrid Capture and PCR-reverse line blot hybridization (PCR). All the cancers were stage 1; only one had grossly visible lesion.

Results: PCDH10-me was found in 3.5%, 4.2%, 15.8%, 42.9%, 58.3% and 100% of Normal, CIN1, CIN2, CIN3, CIS and Cancer, respectively; PAX1-me was found in 11.9%, 5.6%, 10.5%, 38.5%, 62.5% and 100%; and WT1 methylation was found in 9.1%, 9.8%, 15.8%, 47.6%, 66.7% and 85.7%, respectively. Hybrid Capture and PCR test were positive in 18.2%, 47.9%, 63.2%, 76.2%, 83.3%, 100%, and 28.0%, 56.3%, 84.2%, 85.7%, 79.2%, 85.7%, respectively. In detection of CIN3 or above diseases, PCDH10-me, PAX1-me, WT1-me and a combination of PCDH10-me and PCR conferred sensitivity/specificity/PPV/NPV of 58%/95%/73%/91%, 58%/90%/57%/91%, 62%/90%/58%/91%, and 52%/97%/79%/90%, respectively.

Conclusion: Methylation test of PCDH10 correctly detected all cancers and the majority of CIN3/CIS, while less than 8% of Normal/CIN1 were falsely detected. In combination with HPV test, the false positive rate was reduced to 4%. The results support gene methylation as the third generation screening test of cervical cancer.
RG3, Acetylated Analogue of Ginsenosid, Enhances Growth of Uterine Leiomyoma Cells

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Objective: Ginseng has been used world widely as a traditional medicine of Asian countries for treatment of various diseases including cancer. The purpose of this study was to determine the effect of Rg3, acetylated analogues of Ginsenoid, on the cell proliferation and cell cycle progression in human uterine leiomyoma cells.

Method: Primary cultured uterine leiomyoma cells were treated with Rg3. Cell viability analysis was analyzed by MTT assay and flow cytometry was performed to ascertain the effects Rg3. Expression of cell cycle related proteins and apoptosis related proteins were evaluated by Western blot analysis.

Results: Cell viability was significantly influenced by Rg3 treatment in a dose-dependent manner compared to control cells. Flow cytometry results showed that Rg3 did not affect cell cycle machinery. To reiterate this observation, DNA proliferation assay was carried out and cell proliferation in the treatment with Rg3 was detected. Up-regulation of clcin D with concomitant increase in cyclin A was observed. Rg3 treatment of uterine leiomyoma cells resulted in a concentration-dependent cell growth induced via the cyclin dependent mechanism.

Conclusion: These results suggest that Rg3 treatment in uterine leiomyoma cells leads to growth and that this growth is mediated at least in part by cyclin dependent mechanism.
Connect the text using the identifiers P-012 and P-013.
P-014

LOCALIZATION OF CELL CYCLE PROTEINS IN PREINVASIVE AND INVASIVE LESIONS OF UTERINE CERVIX BY IMMUNOHISTOCHEMISTRY

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Objective: Specific marker antibodies against various cell cycle specific proteins are used in diagnosing replicating virus in a host cell by a special staining procedure called Immunohistochemistry (IHC). IHC localization of p16, p21 and cyclinD1 could help in early diagnosis of disease.

Method: A cross sectional study of 35 patients attending outdoor and indoor clinics of Dept. of Obstetrics and Gynaecology and Peripheral Health Centres affiliated to JNMC, Aligarh. Cytology and histopathology was done in Department of Pathology JNMCH, Aligarh. Immunohistochemistry was done at Institute Of Cytology and Preventive Oncology (ICPO). Expression of p16, p21 and cyclin D1 in different grades of cervical lesions was studied.

Results: Squamous cell carcinoma (SCC) was found in 22 (60.8%) patients, high grade squamous intra-epithelial lesions (HSIL) in 2 (5.75%) patients, low grade squamous intra-epithelial lesions (LSIL) in 10 (28.5%) patients and normal in 1 (2.8%) patient. p16, p21 and cyclin D1 all showed a weaker signal in LSIL lesions and a strong signal in HSIL. The severity of dysplasia increases the expression of p16ink4a from sporadic to focal to strong and diffuse signals. In SCC lesions, p16, p21 showed very strong signal with intense expression in all the basaloid cells, while cyclin D1 showed a weaker signal.

Conclusion: There was a strong and positive correlation between degree of dysplasia and strength of p16 and p21 expression. The pattern of cyclin D1 expression is inconclusive as it neither shows good positivity in high grade lesions nor negativity in low grade lesions so it has limited value as a marker for malignant change.

P-015

INCIDENCE AND CYTOMORPHOLOGICAL PECULIARITIES OF LOWER GENITAL TRACT INFECTIONS IN VAULT (POST-HYSTERECTOMY) SMEARS VERSUS PAP SMEARS FROM NON-HYSTERECTOMY SUBJECTS: A RETROSPECTIVE STUDY

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Objective: To evaluate morphology and frequency of lower genital infections in post-hysterectomy vault smears of women.

Method: We analyzed vault smears from 500 women who had undergone hysterectomy, either for benign diseases (230) or for carcinoma cervix (270) and findings were compared with Pap smear diagnosis of non-hysterectomy subjects.

Results: A majority, 432/500 (87%), of the vault smears were negative for squamous abnormality in comparison to 381/500 (76%) Pap smears from non-hysterectomy subjects. It was observed that 48 (8.6%) vault smears showed lower genital tract infections, however frequency of infections was reported significantly higher 101 (20.2%) in non-hysterectomy subjects. Gardnerella vaginalis was the leading infection in vault smears 26 (5.2%) due to benign diseases and was prevalent in the fifth and sixth decades of life in women in comparison to 43 (8.2%) in Pap smears with higher prevalence in fourth decades of life. Trichomonas vaginalis and HPV infection were the second commonest infections in vault smears followed by Candida albicans.

Conclusion: Infections which mainly thrive at the squamo-columnar junction i.e. HPV, Chlamydia and HSV were absent or rare in vault smears. Incidence of infections in the vault smears where hysterectomy was done due to carcinoma cervix was low compared to where hysterectomy was done due to benign uterine diseases.
**P-016**

**EVALUATION OF CYTOLOGICAL CHANGES IN RTIS AND STIS IN FEMALE PATIENTS**

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**Objective:** To know the various cytological changes in RTIs and STIs patients and compare with control group.

**Method:** A total number of 383 women with RTIs and STIs were studied for cytological changes and compared with 300 normal women without RTI and STI, attending Gynae OPD due to other complaints in Mahatma Gandhi Medical College, Jaipur, who formed a control group. Diagnosis of RTIs and STIs was made by detailed clinical history and thorough clinical examination, pH of vagina, Gram staining, KOH mount, wet smear, whiff test, vaginal swab culture and serological tests. Pap smear was done in all patients to know the cytological changes and classified according to the Bethesda system.

**Results:** Maximum patients were in the age group 26 to 45 years, 89% patients were married. Cytological changes observed in various RTI and STI patients were normal (28%), inflammatory (58.2%), SIL (13.8%) and malignancy (2%) while normal patients without RTI and STI showed normal cytology (58.4%), inflammatory changes (39.7%), SIL (1.2%), and no malignancy.

**Conclusion:** RTIs and STIs are major health problems around the world and the prevalence of early SIL is more as compared to normal control group, so cytological screening is important for early diagnosis and prevention of cervical cancer especially in RTI’s and STI’s group.

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**P-017**

**POST-IRRADIATION CYTOLOGICAL EVALUATION IN PATIENTS WITH CARCINOMA CERVIX**

**Hemprabha Gupta, Urmila Singh, A N Srivastava**

CSMMU Lucknow, India

**Objective:** The present study was planned to evaluate cytological follow up of treated cases for detecting side effects and early recurrence.

**Method:** A total of 179 carcinoma cervix patients in different stages were treated with Surgery + EBRT, Surgery + EBRT + ICRT, EBRT alone or EBRT + ICRT. At follow-up, patients were additionally evaluated cytologically at 3, 6 and 9 months after completion of the treatment.

**Results:** Cytological evaluation of cervical smears at 3, 6 and 9 months after completion of the treatment demonstrated different grades and intensity of inflammatory changes, dysplasia, malignancy, recurrence and post-inflammation associated dysplasia. Follow-up at 9 months could also detect cytological recurrence in erstwhile completely treated cases.

**Conclusion:** Post-irradiation treatment evaluations in carcinoma cervix cases are accurate and important for the assessment for treatment response. Late interval follow-up gives clue to early recurrence. Post-irradiation dysplasia indicated progression with uncertainty, thus needing cautious approach and attention.
P-018

SERUM CYTOKINE LEVELS AND MICROMETRY OF PAP SMEARS IN WOMEN WITH LEUCORRHOEA AND WITH LOW-GRADE CERVICAL INTRAEPITHELIAL LESIONS (LSIL)

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Objective: Chronic inflammation is known to be a major culprit in carcinogenesis. Cervical cancer and precancer is associated with high risk HPV infection. The present study was undertaken to measure the early micrometric response in Papanicolaou smears, and serum IL-6, a proinflammatory cytokine, in women with leucorrhoea after therapy for nonviral infections in women with or without Low-grade Squamous Intraepithelial Lesions (LSIL).

Method: Manual micrometry was carried out in Pap smears for nuclear and cell diameters - Group A: Negative (N = 15); Group B: Inflammation (N = 14); Group, C: LSIL with inflammation (N = 13). Serum IL-6 was measured in Groups B and C after treatment of infections.

Results: Nuclear diameter and N/C ratio were significantly higher in Group C vs Group A and B (p < 0.05). After treatment for non-viral infections Serum IL-6 levels were > 50 pg/ml in 5 out of 13 cases of LSIL. Mean Serum IL-6 levels were significantly higher in LSIL Group C vs. negative cases (p < 0.05), and correlated positively with N/C ratio within the LSIL group (r 0.659, p<0.02).

Conclusion: Raised IL-6 levels despite treatment of non-viral infections may indicate an early neoplastic process. Further studies on biomarkers are indicated for the identification of cases who need urgent or long term follow up.

P-019

MODIFIED ULTRA FAST PAPANICOLAOU STAINING: IS IT SUPERIOR TO CONVENTIONAL PAP STAINING?

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Objective: Early and definitive detection of cervical neoplasia is still a major challenge. The present study was aimed to evaluate the advantage of modified ultra fast Pap staining (MUPS) over the conventional Pap technique.

Method: Two cervical smears were collected from each of 100 women who were registered at Gynae OPO of Queen Mary Hospital of the C.S.M. Medical University, one for MUPS and the other for Pap staining. MUPS consisted of air drying of the slide, rehydration in the cytology lab followed by staining with modified staining technique and evaluation by cytologist. Colposcopy and cervical biopsy were performed whenever indicated.

Results and Conclusion: The comparative study with the two staining techniques revealed following advantages of MUPS over Pap technique – a) good quality of staining, b) clear background of the smears, c) less time taken and d) the overall comparative diagnostic accuracy in the detection of cervical intraepithelial neoplasia. The MUPS technique appears to be reliable, quicker and effective staining method for detection of cervical cancer may replace the conventional Pap staining in years to come after ascertaining its utility by performing similar studies in large number of cases.
**P-020**

THE NEW SCREENING METHODS FOR CARCINOMA CERVIX

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**Introduction:** Carcinoma cervix is the most common gynecological cancer and continues to be a major public health problem. VIA and VILI can reduce the incidence of cervical cancer by 25% and mortality rate by 35%.

**Objective:** (I) To estimate the sensitivity and specificity of VIA and VILI for screening preinvasive and invasive cancer cervix lesions. (II) To compare these with the conventional Pap smear.

**Method:** A total of 4039 patients in the 30 to 65 year age group (85% in 30-49 years group) were recruited in the study at the Madras Medical College from March 2005 till March 2007. All women tested positive on VIA, VILI or with abnormal cytology - a total of 939 women had punch biopsy taken from the abnormal areas of the cervix. The gold standard for calculating the accuracy of the tests was histological diagnosis after biopsy.

**Results:** 8% of all patients tested VIA positive and 10.5% VILI positive. Out of these, 57 had biopsy proved high-grade precursor lesions (HSIL) and 6 had invasive cancers. The sensitivity of cytology, VIA and VILI was 57.4%, 59.7% and 75.4%, respectively. The specificity was 98.6%, 88.4%, and 84.3%, respectively. The parallel combination of VILI, VIA and conventional Pap smear resulted in sensitivity of 92.0% and specificity of 80%.

**Conclusion:** VIA and VILI are very useful, quick, effective, cheap and easy methods to assess the cervix in detecting lesions in preinvasive as well as invasive stage. The results are in concordance with the findings of other authors.

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**P-021**

SCREENING BY LIQUID CYTOLOGY AND HPV DNA TO AVOID COLPOSCOPY

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**Introduction:** Cervical cancer is still the most common cancer in Indian women (WHO/ICO report 2009) though it is the only cancer which is highly preventable due to its long latent period of precancerous cervical intraepithelial lesions, highly effective screening programmes and the development of the vaccine. Screening by liquid cytology with the addition of HPV DNA testing can avoid many an unnecessary colposcopy and biopsy especially in young females sparing them of undue apprehension and anxiety.

**Case Reports:** Liquid cytology smears of three patients with recurrent vaginal discharge and cervicitis being managed conservatively to avoid colposcopy:

*Case 1:* 28 yr P1 + 0 with cervicitis showed a normal smear on liquid cytology with negative HPV DNA test.

*Case 2:* 38 yr P2 + 2 with PID and inflammatory smear on liquid cytology but negative HPV DNA test.

*Case 3:* 27 yr P0 + 0 with cervical erosion showed LSIL on liquid cytology but a negative HPV DNA test.

**Conclusion:** Sampling and interpretation errors due to lack of recognition of abnormal cells by the laboratory is associated with 30% of new cases of cervical cancer each year (ACOG guidelines AAFP Nov.15 2003). Liquid cytology and HPV DNA though expensive turns out to be cost effective and reliable in avoiding colposcopy because it reduces the number of false negative hence repeat samples, provides more uniform and easier to read samples with nuclear details, eliminates blood, mucous and cells interfering with the reading, it also offers more than one test in the same sample.
**P-022**

**HPV TESTING: HOW USEFUL IS IT IN THE PRESENT SCENARIO?**

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**Background:** In India, cervical cancer is the most common cancer in women. The role of HPV as a causative agent of cervical cancer is well established. Together HPV 16,18,31,33,45 are responsible for 80% of squamous cell carcinomas and 93.2% of adenocarcinomas of cervix.

**Objective:** To know about the usefulness of HPV testing in present scenario.

**Method:** Eighty patients were included in the study. HPV testing was done in all these patients by Digene Hybrid Capture test. The results were correlated with one or more of the other tests i.e. Pap smear, colposcopy and histopathological examination.

**Results:** HPV-DNA test was negative in 58 patients, positive in 19 patients and 3 patients had a borderline result. Out of 19 patients with positive HPV-DNA test result, 14 had invasive cervical cancer, 1 had cervico-vaginal warts, 1 had CIN-I and 3 had chronic cervicitis. Negative HPV test was found in 50 patients with cervicitis and 8 patients of CIN1.

**Conclusion:** All patients with invasive cervical cancer had a positive HPV test, thereby reinforcing the role of HPV testing as a primary screening test. Primary prevention by vaccination of the target population can help reduce the burden of disease.

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**P-023**

**PREDICTION OF ABNORMAL HISTOPATHOLOGY USING PAP SMEAR AND HPV DNA TEST IN WOMEN WITH UNHEALTHY CERVIX**

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**Objective:** Prediction of abnormal histopathology using HPV DNA test and Pap smear in women with unhealthy cervix.

**Method:** This prospective study conducted from January 2006 to December 2008 enrolled 200 women of age group 25 to 60 years with unhealthy cervix. DNA Hybrid Capture II technique was used to detect high risk HPV. Pap smears were reported using the Bethesda system. All women underwent colposcopy and cervical biopsy and histopathological correlation was analysed.

**Results:** Out of 200 women, 32 (16.0%) were positive for high risk HPV. On cytology, 133 (56.5%) women had normal Pap smear while 67 (33.5%) women had abnormal smear (ASCUS or worse). Out of 67 (33.5%) women with abnormal smears, ASCUS was reported in 24 (12.0%), LSIL in 20 (10.0%), HSIL in 20 (10.0%) and AGUS in 3 (1.5%) women. Eighty six (43.0%) women had abnormal colposcopic findings (Reid’s Index 0-8). Cervical biopsy was abnormal if reported as CIN1 or worse. Histopathology was normal or chronic cervicitis in 172 (86.5%) biopsies, abnormal in 28 biopsies of which 9 (4.5%) had CIN1, 13 (7.5%) had CIN2, 3 (1.5%) had carcinoma in situ and 3 (1.5%) had carcinoma cervix. HPV DNA had highest specificity 92.5% followed by Pap smear 73.3% in predicting abnormal histopathology. Combining the tests significantly improved the specificity to 98.9%.

**Conclusion:** The combined use of cytology and HPV can detect precancerous lesions of cervix which can reduce the prevalence of carcinoma of cervix.
TRIAGE OF CERVICAL CYTOLOGY WITH BORDERLINE NUCLEAR AND LOW GRADE ABNORMALITY: HPV DNA Versus mRNA TESTING

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Background: Cytology with Borderline nuclear abnormality (BNA) and mild dyskaryosis can harbor undetected high grade CIN in 5-20% cases. HPV DNA testing is now accepted as an effective tool to triage these cases. However, it has very low specificity rate and hence a low positive predictive value. We wanted to find out whether mRNA E6 can be used as an alternative or adjunct tool to detect high grade CIN in this population.

Method: Prospective cohort study from January 2008 to August 2008. Inclusion criteria: Women with liquid based cytology results suggesting borderline nuclear abnormality or mild dyskaryosis. All women had colposcopy and two cervical scrape specimens were collected prior to examination. HPV DNA was detected by Hybrid Capture method and mRNA E6 was detected by real time PCR. Colposcopy directed punch biopsies were taken if there were any abnormality suspected. All suspected high grade CIN (detected either by colposcopy or punch biopsy) had excisional biopsy.

Results: Two hundred women were recruited and the results are as follows.

<table>
<thead>
<tr>
<th></th>
<th>HPV DNA</th>
<th>95% CI</th>
<th>mRNA E6</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity</td>
<td>100%</td>
<td>75 - 100</td>
<td>93.7%</td>
<td>67.7 - 99.6</td>
</tr>
<tr>
<td>Specificity</td>
<td>42%</td>
<td>35.7 - 50.4</td>
<td>81.5%</td>
<td>74.9 - 86.7</td>
</tr>
<tr>
<td>PPV</td>
<td>13%</td>
<td>7.9 - 20.8</td>
<td>30.6%</td>
<td>18.6 - 45.5</td>
</tr>
<tr>
<td>NPV</td>
<td>100%</td>
<td>94.2 - 100</td>
<td>99.3%</td>
<td>95.8 - 99.9</td>
</tr>
</tbody>
</table>

Conclusion: This prospective study showed that mRNA E6 has high predictive value to detect high grade CIN. It can be an effective alternative tool which will reduce unnecessary referral to colposcopy for BNA and mild dyskaryosis cytology.
P-026

Epidemiological and Cost-Effectiveness Analysis of the Bivalent Compared with the Quadrivalent HPV Vaccine in Taiwan

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Objective: To compare the epidemiological and economic impact of additional cross-protection against oncogenic HPV types beyond 16/18 of the bivalent vaccine (bi-v) vs. protection against non-oncogenic HPV types 6/11 of the quadrivalent vaccine (quadri-v), in Taiwan.

Method: A lifetime Markov model calibrated to the Taiwanese setting was developed to reflect the natural history of low (engendering genital warts - GWs) and high-risk HPV (engendering cervical cancer - CC) infections, including screening and vaccination (100% coverage) effects, for a cohort of 153,000 12-year-old girls. Transition probabilities, costs and utility were estimated from published data and expert opinion. Vaccine efficacy was obtained from recent phase-III clinical trials, for comparable pre-sexual cohorts. Price-parity and life-long protection was assumed for both vaccines. Number of CIN lesions, CC, CC deaths and GW, QALY and costs were estimated. Costs and outcomes (discounted at 3% and 1.5% respectively) were compared from a societal perspective without indirect costs.

Results: The model estimated that the additional cross-protection of bi-v vs. quadri-v leads to an additional 11,592 CIN1, 1,773 CIN2+, 186 CC and 69 CC deaths prevented, while quadri-v prevents 3,981 GWs, undiscounted; and in additional discounted 766 QALY and NT$11.6Mio less for the bi-v vs. the quadri-v. Therefore, bi-v dominates the quadri-v (i.e. results in more QALYs and less cost).

Conclusion: Both vaccines have a different epidemiological impact with an increased number of CC related lesions prevented for bi-v. Under the Taiwanese model, the economic impact of HPV mass vaccination shows dominance for the bi-v vs. the quadri-v vaccine.

P-027

Health and Economic Impact of HPV Vaccination in Malaysia: Differences Between the Bivalent and Quadrivalent Vaccines

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Objective: Two human papillomavirus (HPV) cervical cancer (CC) vaccines are currently available: a bivalent HPV-16/18 vaccine and a quadrivalent HPV-6/11/16/18 vaccine. The quadrivalent has an additional effect against genital warts, while the other offers broader protection against oncogenic non-vaccine types (cross-protection). The annual impact of both vaccines on HPV-related morbidity (i.e. ASCUS, CIN1, CIN2/3 lesions, CC and genital warts) and costs in Malaysia were evaluated.

Method: A static prevalence-based model was developed in Excel®. The efficacy figures for both vaccines were based on the latest results from each vaccine’s clinical trials. Costing was performed from a societal perspective. Epidemiological and cost data were obtained from a Malaysian burden of disease study and published sources. Results are reported over one year after reaching steady state (when most women are vaccinated).

Results: HPV vaccination with the bivalent vaccine leads to a reduction in CC cases of 4,095 and to savings in HPV-related costs of RM 44 million, annually. In comparison with the quadrivalent vaccine, the bivalent vaccine results in an additional reduction of 28 ASCUS; 4 CIN1; 100 CIN2/3 and 394 CC cases while the quadrivalent vaccine results in 1,668 genital warts cases prevented per year. The additional costs avoided with the bivalent were estimated at RM 2.5 million per year compared with the quadrivalent vaccine.

Conclusion: Vaccination with the bivalent vaccine is expected to have a substantial impact on CC and HPV-related morbidity in Malaysia and lead to larger cost offsets than the quadrivalent vaccine.
P-028

ECONOMIC BURDEN OF PRECANCEROUS LESIONS AND CERVICAL CANCER IN MALAYSIA

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Objective: To quantify the economic burden (outpatient and inpatient) of precancerous lesions (ASCUS, CIN1, CIN2/3) and cervical cancer (CC) in Malaysia, both from a provider and a societal perspective.

Method: The annual inpatient medical resources used related to CC were assessed with a retrospective review of 444 patient’s medical records (2007-2008) from four Malaysia hospitals across the country. Out of those 444 patients, 120 (27%), 166 (37%), 97 (22%), and 61 (14%) had stage I, II, III, and IV CC respectively. The annual outpatient resources used (visits, medications, procedures) related to CC and precancerous lesions and the days of leave associated with inpatients and outpatient visits were assessed by an expert panel. Unit costs applied were extracted from official tariffs. Indirect costs (productivity losses) included in the societal perspective, were calculated by multiplying the number of leave days by the average GDP/capita/day. The total burden was assessed by multiplying each lesion’s and CC annual prevalence by the estimated annual average costs per patient per case.

Results: It was estimated that the annual total costs of treating precancerous lesions and CC are RM 39,153,669 and RM 51,532,091 from a provider’s and societal perspective respectively. About 76% of those costs incur within the healthcare sector. Among the direct costs, 77% (RM 30 millions) relates to inpatients care for CC.

Conclusion: The cost burden of precancerous lesions and CC is high in Malaysia, and is driven by inpatient CC related costs.

P-029

IMMUNOGENICITY AND SOCIO-DEMOGRAPHIC PROFILE OF WOMEN RECEIVING HUMAN PAPILLOMAVIRUS-16/18 AS04-ADJUVANTED VACCINE: A SINGLE CENTRE EXPERIENCE

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Objective: To evaluate the socio-demographic profile and immunogenicity of the HPV vaccine in Indian women aged 18-35 years.

Method: This double-blind, randomized controlled trial comprised of 132 healthy women, randomized 1:1 to receive three doses of HPV-16/18 AS04-adjuvanted L1-VLP vaccine (n=66) or aluminium hydroxide (n=66) according to a 0, 1 and 6 month schedule. Detailed socio-demographic data was recorded for each subject. Anti-HPV-16/18 antibody titres were quantified using ELISA before vaccination and one month post Dose 3. Anti-HPV-16/18 seroconversion rates and Geometric Mean Titres (GMTs) were calculated (± 2 SD).

Results: The median age was 28 yrs and mean parity was 1.9. There were 23 unmarried women. Seroconversion rate in vaccine group was 100% for both HPV-16 and -18 in seronegative women. Baseline seropositivity was observed in 4% women for both HPV-16 and HPV-18, 16.7% women for HPV-18 and 5.6% women for HPV-16 respectively. Anti-HPV-16 GMT was 7284.74 EL.U/ml (95% C.I. 6000.5-8843.8) and anti-HPV-18 GMT was 2557.49 EL.U/ml (95% C.I 2039.2-3207.5) in baseline seronegative women. Baseline seropositive women also exhibited significant increase in titre. Anti-HPV-16 GMT was 6038.07 EL.U/ml (95% C.I 3693.4-9871.1) and anti-HPV-18 GMT was 3914.41 EL.U/ml (95% C.I 2448.3-6258.4) in this group. There was no significant effect of age or marital status on immunogenicity results.

Conclusion: HPV vaccine is safe and highly immunogenic, even in baseline seropositive women. Further studies are required to determine its efficacy in mid-adult Indian women and frame appropriate guidelines.
**P-030**

**IMPACT OF A QUADRIVALENT HPV6/11/16/18 VACCINE ON THE INCIDENCE OF CIN, EGL, ABNORMAL PAP TESTS AND CERVICAL PROCEDURES**

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**Objective:** Prophylactic administration of a quadrivalent HPV6/11/16/18 vaccine is up to 100% effective in preventing HPV16/18-related CIN2/3 and AIS. We report the impact on the incidence of any CIN2/3 or worse, external genital lesions (genital warts, VIN1-3, or VaIN1-3), abnormal Pap tests and procedures, regardless of causal HPV type.

**Results:** A total of 17,822 women were enrolled in two Phase 3, randomized, placebo-controlled trials (FUTURE I and II). We estimated the number of cases prevented annually per 100,000 vaccinated women, in terms of risk difference based on subtracting the rate in the vaccine arm from the rate in the placebo arm in: 1) an unexposed population that approximates sexually naïve females; 2) a mixed population of HPV-exposed and unexposed women; and 3) the population of women already exposed to HPV. After an average follow-up of 3.6 years, significant reductions in the number of CIN lesions ( ~700-1000 cases prevented), abnormal Pap tests ( ~1300-1500 cases prevented), colposcopy ( ~1300 cases prevented), cervical biopsy ( ~1000-1300 cases prevented), and definitive therapy ( ~600 cases prevented) were observed in all three populations.

**Conclusion:** Our data suggest that whether we offer HPV vaccination to a population of women who are HPV naïve, a mixed population of naïve and exposed, or a population of previously exposed women, we could expect to have similar public health impacts in terms of disease reduction in the years immediately following vaccination.

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**P-031**

**DEVELOPMENT OF PROPHYLACTIC VACCINE BASED ON HPV L2**

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**Background:** The diversity of diseases caused by Human papillomavirus (HPV), its worldwide prevalence, the occurrence of multiple HPV infections and the existence of geographical variations in type distribution - all demand the need of a pan-oncogenic HPV vaccine. Considering the alarmingly high rates of cervical cancer incidences in developing countries, it is desirable to have second-generation vaccine that can be affordable. The minor capsid protein, L2, has a unique capability to induce protection against several oncogenic HPV types.

**Objective:** The objective is to develop a broad-spectrum vaccine based on fusion protein constituting tandem repeats of immunogenic portions of N-terminal L2.

**Method:** Fusion proteins comprising of a string of L2 immunogenic segments were expressed in *E.coli*. The recombinant fusion proteins were purified using methods that are suitable for scale-up. Formulated preparations were assessed for their immune responses in mice and rabbits. IgG response in animals was analyzed by ELISA and HPV16 neutralization assay. Protection against infection was assessed by challenging immunized mice with viral pseudotypes.

**Results:** L2 fusion proteins induced neutralizing antibodies against several HPV types in both rabbits and mice. Additionally, mice challenged with pseudovirus were protected from HPV infection. Our observations on the minor capsid protein based second generation HPV vaccine will be presented.

**Conclusion:** L2 fusion proteins are ideal candidates for developing low cost HPV vaccine.
CERVICAL CANCER PREVENTION WITH THE HUMAN PAPILLOMAVIRUS-16/18 AS04-ADJUVANTED VACCINE: IMMUNOGENICITY AND SAFETY IN 18-35 YEAR-OLD MALAYSIAN WOMEN

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Objective: Cervical cancer is the second most commonly reported malignancy in Malaysian women. The immunogenicity and safety of the Human Papillomavirus (HPV)-16/18 AS04-adjuvanted cervical cancer vaccine were evaluated in 18-35 year old Malaysian women.

Method: Healthy women were enrolled in this phase Illb (105926/NCT00345878), double-blind, placebo-controlled trial conducted at 2 Malaysian centres; randomized (1:1) to receive three doses of the HPV-16/18 AS04-adjuvanted vaccine (n = 135) or aluminium hydroxide (n = 136) according to a 0,1,6 month schedule. Anti HPV-16/18 antibody titres were measured by ELISA before vaccination and one month post-Dose 3. Safety was evaluated throughout the study.

Results: One month post-Dose 3, the seroconversion rate was 100% for HPV-16 and HPV-18 in initially seronegative women (ATP immunogenicity cohort), with corresponding geometric mean titres of 110.75 EL.U/mL (95% CI: 97.27;3;126.83.4) and 427.3 EL.U/mL (95% CI:377.1;8;484.1.9), respectively. All initially seropositive women (HPV group) remained seropositive for HPV-16 (n=14) and -18 (n=16) at Month 7. Compliance to the 3-dose vaccination course was high (~96%) in both groups. The most commonly reported solicited symptoms in both groups were injection site pain (local) and myalgia, fatigue, arthralgia and headache (general), with myalgia and arthralgia reported more frequently in HPV group. Eight SAEs (five in HPV group; three in ALU group) were reported and all considered as non vaccine-related by the investigator. All women recovered. One withdrawal due to AEs (throat and vagina burning sensation) was reported; considered unrelated to vaccination by the investigator.

Conclusion: Overall, the HPV-16/18 AS04-adjuvanted vaccine was highly immunogenic and generally well tolerated in Malaysian women.

RETROSPECTIVE EVALUATION OF CARCINOMA CERVIX (ONE YEAR) IN GMC PATIALA

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Objective: The incidence of carcinoma cervix in India is high as screening programs are not as good as in the West. Punjab is a state with 20,000,000 people with seven medical colleges. The aim was to evaluate cases of carcinoma cervix received and managed in GMC Patiala.

Method: The present retrospective study evaluated the case files of 68 patients from 1st June 2008 to 30th June 2009.

Results: The age distribution was: < 40 years - 28%; 41-50 years - 35%; 51-60 years - 19%; 61-70 years - 14.7%; > 70 years - 2.9%. The majority (39.7%) patients belonged to Patiala, Sangrur (17.6%) and Barnala (10.3%). The majority were diagnosed in Stage IIb (32.3%) or Stage IIb (39%). Only 7.4% were diagnosed in Stage I; 10.3% had TAH with BSO done and came with report of carcinoma cervix. On histopathology, 94% had squamous cell carcinoma while 3% had adenocarcinoma and 1% transitional cell carcinoma. Out of 68 patients, 41.2% had moderate anemia and 45% received blood transfusion. Blood urea levels were more than 40mg/dL in 2.9% cases. Only 1 patient was found out to be HIV positive. All patients received radiotherapy, 45% received concurrent chemoradiation. Combined EBRT and ICRT was given in 76%. About 64% had mild radiotherapy reactions. Twelve percent of them were lost to follow up.

Conclusion: Cases are presenting in advanced stages due to lack of knowledge and practically no screening. General surgeons are doing hysterectomy without screening or pelvic examination and not guiding patients properly for future treatment.
P-035
THE STUDY OF 103 NEW CASES OF CERVICAL CANCER IN BEIJING
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Objective: To explore the character of new cases of cervical cancer.
Method: Study new cases of cervical cancer in our hospital from 2004 to 2008.
Result: There were 103 new cases of cervical cancer during this time. Eighty six (83.5%) cases were squamous cell carcinoma and 17 (16.5%) cases were adenocarcinoma. The average age of all cases was 45.4 years, of squamous cell carcinoma group was 45.0 years and of adenocarcinoma group was 47.1 years. Some cases had no cytology test or HPV DNA test and were diagnosed by directed biopsy. Sixty seven cases had cytology test in squamous cell carcinoma group. They were 7 cases of ASC-US, 6 ASC-H, 2 LSIL, 38 HSIL, 9 SCC, 3 AGC and 1 NILM. One case was an unsatisfactory sample. Fourteen cases had cytology test in adenocarcinoma group; they were 3 cases of ASC-US, 1 ASC-H, 5 HSIL, 4 AGC and 1 NILM. Sixty-two cases had HPV DNA test in squamous cell carcinoma group. Fifty eight (93.5%) cases were positive and 4 (6.5%) were negative. Sixteen cases had HPV DNA test in adenocarcinoma group. Ten (62.5%) cases were positive and 6 (37.5%) were negative. Sixty-five had no cervical cancer screening before and 14 had normal result in the last one year.
Conclusion: Cervical cancer screening was a useful tool. We need more tools to detect adenocarcinoma.
PREVALENCE OF HIGH RISK HUMAN PAPILLOMAVIRUS IN PRECANCEROUS AND CANCEROUS CERVICAL LESIONS AT GCRI

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Objective and Method: Cervical infection with High risk HPV (HR-HPV) types is a precursor event in the genesis of Cervical Cancer. 181 tumor biopsies were collected in transport medium from clinically diagnosed untreated cervical cancer patients and 23 biopsies from precancerous lesions of patients, who attended the Gynaec-oncology OPD and colposcopic clinic of GCRI respectively, which were kept frozen at -20°C until later date. After the extraction of DNA by proteinase K column method, amplification was performed by preparing master mix and using desired primers for the amplification of 16, 18, 31, 33, 35, 18, 45, 59, 52, 56, 58, 66. Finally the amplified products were detected by gel electrophoresis and gel documentation.

Result: In cervical cancer, HPV DNA was detected in 131 (72.4%) cases, of which 90 (68.2%) were infected with a single type. The most common HPV types in descending order of frequency were HPV 16, 45, 18, 31, 33, 52, 39, 59. Of which, 59.9% HPV16, 2.3% HPV18 and 1.5% HPV45 were found singly. 27.4% HPV16, 15.2% HPV18 and 12.9% HPV45 were found in mixed infection. In precancerous lesions (CIN) biopsies, HPV DNA was detected in 11 (47.8%), of which 10 (90.9%) patients were infected with single HR HPV (16) and 1 (9.1%) patient was infected with multiple HR HPV (33, 45 and 59).

Conclusion: HPV16 was the most predominant HR-HPV, total 87.24% in cervical cancer (single and multiple) and 90.91% (single) in CIN. Other types like 45, 31, 33,58,35,39 and 52 were also identified.
P-038

DETECTION OF HIGH RISK HPV IN PRECANCEROUS AND CANCEROUS LESIONS OF CERVIX

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Background: Cervical cancer, the most common malignancy among females in developing countries, is associated with high mortality. Preinvasive and invasive cancer of cervix are known to have an infectious etiology i.e., human papilloma viruses (high risk types).

Objective: To detect the presence of high risk HPV (types 16 and 18) by in situ hybridization and to correlate their role in pathogenesis of Ca cervix.

Method: Sixty cases comprising of preinvasive cervical lesions / malignancy of cervix and 10 cases with normal cervical biopsies were taken for the study. In situ hybridization was performed in all the cases to detect presence of HPV.

Results: The age varied from 28-70 years, mean age was lower in preinvasive lesions. The commonest symptoms in preinvasive lesions were vaginal discharge and post coital bleeding while in cancer it was bleeding per vaginum. HPV DNA was detected in 53.3% of cervical malignancies. HPV16 was more common in squamous cell carcinoma and SIL of cervix. However in adenocarcinoma only HPV18 was found. The mean age of HPV positive cases was significantly higher. HPV18 was correlated with a higher stage and grade of the tumor.

Conclusion: In situ hybridization is a clinically applicable technique which can detect HPV in formalin fixed cervical biopsies. The presence of HPV16 and 18 in preinvasive and invasive cervical cancers, reaffirm their role in carcinogenesis. Moreover, HPV18 was associated with higher stage and grade of cancer suggesting a more aggressive behaviour and poor prognosis.

P-039

LONG ENVIRONMENTAL SURVIVAL OF HUMAN PAPILLOMAVIRUS SUGGESTS CAPABILITY OF INDIRECT TRANSMISSION

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Objective: Human papillomavirus (HPV) is one of the most common sources of sexually transmitted infection. Possibility of indirect transmission via fomites has been raised but without biological evidence. We explored the durability of the HPV infectivity in different scenario of environmental contamination.

Method: HPV16 pseudoviruses carrying GFP gene were generated by using 293TT transfection model. After environmental exposures, viruses were inoculated to HeLa cells and GFP expression was measured by flowcytometry. To simulate different contamination sources and targets, viruses were mixed with PBS (contamination of wet surface directly by HPV lesions), cervico-vaginal secretion (CVS) (contamination by vaginal discharge) and medium with serum (contamination by menstrual discharge). We also tested the durability of native HPV16 obtained from cervical scrapings of infected women by conformation specific antibody.

Results: HPV maintained a high infection ratio (30%) in PBS and a relative lower ratio (18%) in CVS for as long as seven days. In serum-containing medium, the infection ratio raised from 35% to 55% in the first 24 h (probably by in-vitro maturation), maintained for three days and rapidly decreased thereafter. These infection activities were abolished after desiccation. A majority of protein signals of HPV16 in CVS if infected women decayed by 24h, but a small proportion of them remained for up to five days.

Conclusion: The study provided a biological basis of indirect transmission of HPV by wet environment contaminated with HPV lesion. Transmission by virus-containing vaginal secretion is less likely but cannot be neglected. This transmission can be abolished by desiccation.
HUMAN PAPILLOMAVIRUS GENOTYPE DISTRIBUTION IN CERVICAL CANCER AMONG VENEZUELAN WOMEN

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Objective: The aim of the present study was to determine the HPV genotype distribution in cervical carcinoma among Venezuelan women.

Method: A total of 150 cervical cancer cases were selected from the files of the Oncologic Padre Machado Hospital, Caracas. DNA, from paraffin blocks, was obtained to conduct HPV genotyping, using InnoLIPA HPV Genotyping Extra (Innogenetic N.V., Belgium), at the Molecular Genetic Laboratory, Oncology and Hematology Institute.

Results: The mean age of the female population was 46.4 years, (range 21-76 years). Fifty-four percent (81/150) of the carcinoma cases were in the age range of 31-50 years. Cervical carcinoma was observed in 8% (12/150) of the patients in the 21-30 age range. HPV DNA was detected in 98.7% of the cases. Genotype 16 was detected alone in 57.3% of cases; genotype 18 was detected as a monotype in 14.2% of the cases, and genotype 52 was the third most common type (12.2 %). Overall, genotypes 16, 18, 52, 33, and 45 were among the most common types detected. Frequent co-infection was as follows: HPV-31, 33, 44 (2.7 %), as well as HPV-16, 52 with 2.7% (4/150).

Conclusion: HPV16 is the most frequent genotype in cervical cancer among Venezuelan women. The currently available HPV prophylactic vaccines targeting types 16 and 18 have the potential to reduce the burden of cervical cancer in Latin-America’s population.

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TREND IN DISTRIBUTION OF HUMAN PAPILLOMAVIRUS TYPE 58 VARIANTS IN PROGRESSION OF CERVICAL DYSPLASIA IN KOREAN WOMEN

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Objective: We aimed to analyze the sequence variations of HPV 58, the third most common genotype in Korean women.

Method: This analysis was part of a prospective study for a hospital-based cervical cancer screening program conducted between January 2002 and July 2006. Data were collected on 1,750 Korean women aged 15-75 years with informed consent from each patient. Samples from cervical cytology were collected during clinical examination. HPV genotyping was performed using the HPV DNA oligonucleotide chip. The open reading frames (ORFs) including E2, E6, E7 and L1 of HPV 58 were amplified based on specific primers designed using the HPV prototype (GenBank Accession No. D90400). The sequences of the three regions of interest were obtained by PCR-based cycle sequencing using BigDye Terminator v. 3.1. Sequence reactions were performed on the 3130 Genetic Analyzer and the sequences of the above gene regions were aligned by the computer software SeqScape v.2.5. Distribution of HPV58 variations with respect to disease severity were examined by the exact Haenszel’s linear trend test (P trend) and Fisher’s exact test (P).

Results and Conclusion: Among 1,750 Korean women, 53 women were positive for HPV58 single infection, of whom 26 were without disease, 20 were with cervical intraepithelial neoplasia (CIN) 1, and 7 with CIN 2 or 3. Altogether, 36 different nucleotide sequence variations were identified with the L1, 20 within E2, 5 within E6, and 10 within E7. Further studies on variants of oncogenic HPVs are necessary, particularly for the purpose of developing more predictive detection methods.
PREVALENCE OF HUMAN PAPILLOMA VIRUS IN CERVICAL LESIONS IN A VENEZUELAN POPULATION

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Objective: The aim of this study was to establish the presence of HPV infection in cervical lesions in a Venezuelan population, by Hybrid Capture Assay II (HCA II), and its association with cytological diagnosis.

Method: The study included 1483 cervical samples analyzed from different gynecological services, Caracas, Venezuela. The age range of the women was between 20 and 58 years, and the mean age was 28.8 years. HPV infection was determined using HCA II.

Results: The cytological diagnosis of the smears showed LSIL in 1120/1483 samples (75.5%), HSIL in 354/1483 (23.9%) and ASC-US, in 9/1483 (0.6%). The positivity of HPV DNA detected by HCA II was 54.6% (811/1483). Of the positive cases, 138/811 (17%) presented HPV DNA of low oncogenic risk and 673/811 (82.9%) had high-risk HPV. There were significant differences in the low and high oncogenic HPV type frequency of the evaluated samples (p > 0.0001). Low risk HPV types were detected in 127 cases of LSIL, 9 of HSIL and 2 of ASC-US. High-risk HPV was detected in most of the cases: 361 LSIL, 308 HSIL and 4 ASC-US.

Conclusion: Our study showed a high prevalence of cervical infection by human papillomavirus of high risk genotype. The variability in oncogenic HPV type distribution will significantly impact vaccine efficacy in Latin America. More studies determining HPV type’s distribution and risk factors need to be conducted in Venezuela.


PRESENCE OF HUMAN PAPILLOMAVIRUS INFECTION DETERMINED BY HYBRID CAPTURE ASSAY IN CERVICAL LESIONS IN A VENEZUELAN POPULATION

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Conclusion: Our study showed a high prevalence of cervical infection by human papillomavirus of high risk genotype. The variability in oncogenic HPV type distribution will significantly impact vaccine efficacy in Latin America. More studies determining HPV type’s distribution and risk factors need to be conducted in Venezuela.


PREVALENCE OF HUMAN PAPILLOMA VIRUS IN CERVICAL LESIONS

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Introduction: Cancer cervix is the most common cancer in Indian females. The risk of cervical cancer is strongly influenced by risk factors for acquisition of human papilloma virus, which is preventable.

Objectives: To identify the prevalence of HPV infection in cases with abnormal vaginal discharge, chronic PID and cancer cervix, and to correlate cytological findings with HPV positivity.

Method: The study was conducted from January 2006 to September 2008 in the Department of Obstetrics & Gynecology and the Department of Pathology, JNMCH Aligarh. All high risk cases were subjected to Pap smear and HPV DNA testing, which were sent to ICPO, Noida.

Results: A total of 347 cases were included in the study. Out of these 154 (44.4%) were positive for HPV DNA. The maximum number of positive cases were in the age group 41-50 years (51, 33.1%), parity 4 (37, 24.0%), Hindu (100, 64.9%) and age at marriage 15-17 years (99, 64.3%). The most common cytological finding in HPV positive cases was squamous cell carcinoma (83, 53.9%), followed by inflammatory smear (30, 19.5%), HSIL (16, 10.4%), LSIL (13, 8.4%), and ASCUS (3, 1.9%). Six (3.9%) positive cases had normal cytology while the specimens were inadequate for comment in 3 (1.9%) cases.

Conclusion: Screening high risk cases by Pap smear and HPV DNA detection can help in early detection and triaging disease.
EPIDEMIOLOGY OF HPV INFECTION IN THE UTERINE CERVIX: A POPULATION SURVEY FROM EASTERN INDIA

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Introduction: Oncogenic Human Papillomavirus (HPV) infection is the necessary cause of cervical cancer. Worldwide more than 90% of CA-Cervix are associated with HPV infection, among them HPV16/18 subtypes are most frequent. In India, few studies that looked into the cervical HPV prevalence in apparently normal women population found that 10-12% of women were infected with HPV. But the study populations are either discrete or sample size is small to give an overall HPV prevalence scenario. HPV genotype prevalence also differs among populations and geographical regions.

Method: Cervical scrapes of apparently normal women (N=2308) were screened for HPV presence by Nested PCR using L1 consensus primers. Prevalence of HPV types were determined by type specific PCR followed by hybridization with type specific probes. HPV load was measured in HPV positive samples (N=35) by quantitative Real Time PCR. CA-Cervix samples (N=10) were used as Positive control.

Results and Conclusion: Prevalence of overall HPV was 9.4% (205/2180) of the samples. Among the HPV positive samples HPV16 and HPV18 prevalence was 6.8% (14/205) and 17.5% (36/205) respectively, along with 3% (6/205) co-infection with HPV16/18. Correlation between HPV infection and different Clinicopathological parameters, like: age group, age at marriage, parity, crude tobacco chewing habit were studied. 14% (28/205) of the HPV positive samples were found to have abnormal cervical cytology. In infected cervical samples from normal population the HPV load varied either between 15-30 copies/diploid cell or, less than the value range. The HPV load in samples with cervical neoplasia varied from 44-230 copies/diploid cell.

ROLE OF VIA AND VILI IN CERVICAL CANCER SCREENING IN TERTIARY CARE CENTRE

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Objectives: To evaluate the performance of visual screening methods and its comparison with cytology in cervical cancer screening in a tertiary care centre.

Method: 400 non-pregnant reproductive age women were subjected to VIA, VILI and Pap in a prospective study done in tertiary-care centre in Delhi (2005-2007). For VIA, high-threshold criterion used only well demarcated, opaque white areas near the squamo-columnar junction as positive while low-threshold criterion considered faint or ill-defined acetowhite and well defined areas away from SCJ also as positive. Detection of definite yellow iodine non-uptake areas in transformation zone close to or touching the SCJ were considered as positive VILI test. Reference-standard used was colposcopy and colposcopy-directed biopsy when required.

Results and Conclusion: Of 400 Pap smears done 11.75% were normal, 77.5% inflammatory, 5.5% had ASCUS, 0.25% ASC-H, 0.5% AGUS, 2% LSIL, 1.5% HSIL and invasive cancer 0.5%. With LSIL and worse smears as significant, sensitivity and specificity of Pap were 50% and 97.7% respectively. VIA positivity was 29.3% with low-threshold criteria and 9.3% with high-threshold criteria. While sensitivity and specificity of low-threshold criteria were 100% and 72.7% respectively the same with high-threshold criteria were 85.7% and 95% respectively. VILI had positivity rate of 12.75%, sensitivity 85.7% and specificity 89.9%. Thus the characteristics of visual tests encourages their routine use as screening tests in all sexually-active patients presenting to any of the health-care facilities. Accordingly, they can be further investigated, referred or treated at the same visit whichever is cost effective in that setting.
P-046

VISUAL INSPECTION WITH ACETIC ACID (VIA) – SCREENING TOOL FOR CERVICAL CANCER

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Background and Objectives: Cervical cancer is a public health problem and its incidence is very high in developing countries due to lack of screening programs. Cervical cancer is the most common cancer in Nepal. Till date there is no national cancer screening programme, hence it is difficult to quote accurate incidence of cervical cancer. NNCTR (Nepal Network Cancer Treatment and Research) introduced cervical cancer screening by VIA for the first time. The purpose of this screening programme was to find out the precursor lesion and treat them to reduce incidence of cervical cancer.

Method: This study was conducted from Oct. 2002 to June 2009 in different districts of Nepal (Bhaktapur, Kavre, Lalitpur and Kathmandu). During the period 12268 cases were screened among which 4.8% (590) were screened positive. All screen positive cases were referred for colposcopy and guided biopsy was done in 267 cases.

Results: Among 590 screen positive cases, CIN was found in 89 (15%) cases [CIN I-64, CIN II-20, CIN III-5, invasive cancer 7 (1.2%), chronic cervicitis and other infection 177 (30%)]. All CIN cases were treated with cryotherapy and LEEP (Loop Electrosurgical Excision Procedure). Follow up was done at 1 month, 1 year and 5 year interval, which was completed in 2007. Abnormalities were not detected in any follow up cases. Chronic cervicitis and other infection were treated with antibiotics. Invasive cancer cases were sent to Radiotherapy department.

Conclusion: The incidence of cervical cancer can be reduced by using the simple screening method of visual inspection with acetic acid and treating the precursor lesion.

P-047

DOES THE SENSITIVITY OF VISUAL INSPECTION WITH ACETIC ACID (VIA) TEST ALTER WITH THE COLOUR OF LIGHT USED?

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Objectives: The various studies on the efficacy of VIA do not comment on colour of light used. This prospective pilot study was carried out to know which type of light is better in detecting a VIA positive case.

Method: This study was carried out in the gynaecology OPD of Lok Nayak hospital. VIA was performed on all 50 patients using first the yellow light with examination lamp and then a portable white light. Those who were found VIA positive had colposcopy and directed biopsy if needed.

Results: The test was positive in 7 patients, all of them were detected as positive with portable white light. The yellow examination light detected only 2 patients. The colposcopic diagnosis in patients who were VIA positive were found to be normal in 3, ectropion in 3 and CIN in 3.

Conclusion: White light is better and improves the sensitivity of VIA test and should be the standard light used for examination.
Objective: To evaluate test characteristics of VIA and VILI in detecting CIN

Method: The study was conducted in rural as well as urban areas of Jaipur from February 2001 to December 2004 in two phases: Phase I lasted for 24 months and 6000 women were screened; Phase II lasted for 20 months and 5000 women were screened. Women of age group 25-49 years, were screened by Pap smear, VIA, VILI, colposcopy, biopsy if needed and treatment by cryotherapy and LEEP in Phase I. In Phase II no Pap smear was taken, other tests were same, cryotherapy was done at Camp sites and for LEEP women were asked to come to hospital.

Result: In Phase I, 6000 subjects were examined at 108 camp sites and in Phase II, 5000 women were examined at 90 camp sites. In Phase I, 1500/6000 (25%) women were positive and treatment was done in 13% [Cryotherapy 12%, LEEP 0.4%, Conization 0.01%, Surgery 0.01%, CT + RL 0.1%] in Phase II, 811/5000 (16%) women were positive and treatment was done in 5% [Cryotherapy 3.8%, LEEP 1.2%, Conization 0.02 %, Surgery 0.01%]

Conclusion: VIA is more sensitive (94%) and specific test (86%) in low resource setting for detecting CIN than VILI where sensitivity is 82.3%, specificity 84%. By giving treatment at camp sites all subjects can be benefitted in the presymptomatic stage and it is cost effective also.

Grants: This study was funded by the Bill and Melinda Gates Foundation
**P-050**

HIGH RISK HPV DNA TESTING AS A SECONDARY TRIAGE TO VIA IN SCREENING FOR CERVICAL CANCER IN RESOURCE POOR SETTINGS

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**Objective:** To evaluate the role of testing for high risk human papilloma virus (HPV) DNA as a secondary triage to visual inspection of cervix with acetic acid in screening for cervical cancer and its comparison with cytology.

**Method:** 800 symptomatic patients from the gynecology outpatient department were screened using Pap smear, VIA and Colposcopy. Those found positive on any or all of the screening tests were subjected to cervical biopsy. In later half of the study, HPV DNA testing was done in 162 patients using polymerase chain reaction (PCR). This included all screen positive patients.

**Results and Conclusion:** The sensitivity of HR DNA testing was 86%. VIA had a sensitivity of 93.9% to detect any grade of dysplasia. The sensitivity of the combination test (VIA + HPV) was 80.6%. The specificity of the combination test (VIA + HPV) was 68.3% which was significantly higher than that of VIA alone (37.7%) and also higher than that for HPV DNA detection when used alone (56%). Pap smear had the highest specificity but lowest sensitivity.

As organized screening is difficult to implement in low resource countries, a feasible alternative could be to use HPV DNA testing as a secondary triage procedure to VIA. This would not only reduce costs but also make coverage of a larger population possible.

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**P-051**

POPULATION BASED SCREENING AND EARLY DETECTION OF CERVICAL, BREAST AND ORAL CANCERS IN KANCHIPURAM DISTRICT, TAMIL NADU

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**Objective:** The aim of this ongoing programme is to provide population based screening and early detection of cervical, breast and oral cancers with appropriate referral and treatment services in the study area.

**Method:** Female health workers visit the villages in Tambaram and Chengelpet taluks, provide health education and awareness and invite eligible women to attend field clinics for screening and early detection. Visual screening for cervix (VIA) and oral cancers and clinical breast examination are offered by medical officers. A standard protocol is adhered to and screened positive subjects are referred to Cancer Institute (CI) for further management free of cost.

**Results:** Between August 2008 and July 2009, 4337 eligible women were invited, 3,122 were registered and 2,388 (55%) underwent visual inspection with acetic acid (VIA) for cervical cancer screening. 440 were VIA positive (18.4%). Among the 716 total referred cases (VIA positive, major erosion, bleeding on touch etc.), 379 (52.9%) underwent further evaluation, at CI. 16 cases of high grade dysplasias and 4 cases of invasive cancers were detected at the rate of 6.7 and 1.67 per 1000 screened women respectively.

**Conclusion:** The detection rate of high grade dysplasias correlates with earlier studies, though the VIA positivity rate is slightly higher. This on-going comprehensive cancer control program will serve as the basis for organization of specific intervention studies on cancer prevention in future.
PROPOSAL OF MODEL SCREENING FOR ORAL CANCER PREVENTION INTEGRATING HYBRID CAPTURE-2 AND ORAL COLPOSCOPY IN WOMEN WITH ORAL LESIONS AND HPV INFECTION IN THE LOWER GENITAL TRACT

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Objective: There is evidence about association between HPV and oral/pharyngeal cancer. The aim of this work is to describe the correlation between HPV infection in mouth/oropharynx and Squamous Intraepithelial Lesion (SIL) from low genital tract and identification of viral genotypes in both regions.

Method: This was an observational and comparative study. We selected 126 patients and their partners with and without SIL/HPV infection and screening with Hybrid Capture-2 for high risk HPV and colposcopy from oral cavity in areas with erythroplasia, erythroleukoplakia and leukoplakia and areas with acetoreactive mucosa, for the opportune detection and treatment of lesions for prevention within integral management in patients with SIL.

EXPERIENCES OF AN ORGANISED CERVIX CANCER SCREENING PROGRAMME IN RURAL INDIA

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Introduction: The National Cancer Control Programmes have lacked the required thrust for organized screening strategies in the prevention and control of cervical cancer in India. The Tata Memorial Hospital, Mumbai, has initiated a rural organized cervix cancer screening programme under a Model District Cancer Control Programme in two rural districts of Western India, since August 2003.

Method: Systematic enumeration of the eligible women in the age group of 30-65 years was undertaken by House to House surveys followed by Cancer Awareness and Screening camps at village levels with Diagnosis and Treatment of screen detected cases through appropriate referral mechanism.

Results: Out of 146,435 total eligible women in the age group of 30 to 65 years listed by household surveys, 52,575 (35.9%) women participated in an organised community based cervix cancer screening programme. 1897 (3.6%) women were found positive on primary screening by Visual Inspection with Acetic Acid (VIA). Compliance to diagnostic confirmation was 90.6%. The programme detected 149 cervical pre-cancers and 64 cases of cervical cancer. The cervical cancer detection rate, at first prevalence screen per 1000 women screened was 1.2 and the mean age at diagnosis was 51.3 years.

Conclusion: Awareness about preventable cancers, availability of early detection services and accessibility to treatment services is crucial for the success of cancer control in the region. Thus cervical cancer screening by simple cost effective technologies at the grass root level by primary health care workers is feasible and can be integrated in the general health care infrastructure services.
**P-054**

**COMPARATIVE STUDY BETWEEN PAP SMEAR AND VISUAL INSPECTION WITH ACETIC ACID AS A METHOD OF CERVICAL CANCER SCREENING**

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**Objectives:** To compare visual inspection with 5% acetic acid (VIA) and Pap smear for cervical cancer screening; to determine the proportion of women screened positive with each method and to determine the prevalence of cervical intraepithelial neoplasia (CIN) and carcinoma cervix in the study population.

**Method:** Three hundred women presenting to the outpatient gynecologic clinic and cervical cancer screening programme from 1st January 2007 to 30th September 2007 were included. All were examined by both conventional cytology and VIA. Distinct acetowhite areas touching the transformation zone were categorized as VIA positive cases. ASCUS or worse lesions by cytology were considered as positive smears. Women who tested positive on any test underwent colposcopy and directed biopsy. Histology was taken as the reference standard.

**Results:** On VIA, 23/300 (7.7%) women and on Pap, 14/300 (4.7%) women were screen positive. Eleven were positive on both VIA and Pap; 12 on VIA only; and 3 on Pap only. Twenty six cervical biopsies were taken and histologic diagnosis of CIN/cancer made in 18/26 (6%). Pap smears detected 10/18 biopsy-proven cases, missing 5 low grade and 3 high grade lesions. VIA could identify 17/18 cases; missing one low-grade lesion. Sensitivity of VIA and Pap was 94.4% and 55.5% respectively, which was statistically significant. Specificity of VIA and Pap was 97.9% and 98.8% respectively. Number of false positives was higher in VIA. The PPV of VIA was 73.9% vs 71.4% for Pap. Accuracy of VIA was 94.4% vs 55.6% for cytology.

**Conclusion:** VIA was more sensitive and accurate but less specific than cytology, resulting in high false-positive and hence unnecessary referral for colposcopy/biopsy. It is a simple, rapid and cost effective method, therefore its use can be recommended as a primary screening method.

**P-055**

**EVALUATION OF VISUAL INSPECTION WITH ACETIC ACID AND LUGOL’S IODINE AS CERVICAL CANCER SCREENING TOOLS IN A RURAL AREA OF CHINA**

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**Objectives:** To evaluate the visual inspection with acetic acid and Lugol’s iodine as cervical cancer screening tools.

**Method:** In the six rural areas of north China, visual inspection with acetic acid and Lugol’s iodine was applied in reproductive women to screen cervical cancer. Once the result was positive, a colposcopy followed. If the colposcopy was abnormal, biopsy was carried. According to the pathological result, appropriate treatment followed.

**Results:** In six areas, 12204 women were recruited. The positive rate of VIA/VILI was 11.5%, 17.9%, 21.8%, 6.18%, 3.30%, 6.11%, respectively. For colposcopy cases, the rate of biopsy is 70%, 83.3%, 8.3%, 48%, 100%, 74.4%, respectively. By colposcopy, the diagnosis rate of cervical intraepithelial neoplasia is 18.0%, 54.3%, 31.6%, 10.0%, 34.3%, 35.5%, respectively. For high grade lesion, the diagnosis rate of colposcopy is 6.83%, 15.6%, 18.42%, 1.67%, 16.42%, 21.51%, respectively. For high grade lesion, the diagnosis rate of VIA/VILI is 4.8%; 13.1%; 1.5%; 0.8%; 16.4%; 16.0%, respectively.

**Conclusion:** In different areas, the technology of VIA/VILI and colposcopy is different. We should pay more attention to the clinical training and quality control; it is the most important thing in cervical cancer screening program.
P-057

MAKING COLPOSCOPIC ASSESSMENT OF CERVIX EASY AND ACCURATE BY SIMPLIFIED REID COLPOSCOPY INDEX METHOD

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Objectives: Colposcopy is a method accepted worldwide for the detection of early cervical neoplasia. In conventional colposcopy lack of standard diagnostic protocol causes interpretation difficulties, also time required for documentation is more than time required in making colposcopy diagnosis. The objective of this study was to minimize disagreements and make colposcopy assessment quick, easy, accurate and useful for follow up.

Method: This cross sectional study was undertaken at Gynecology department of NSCB medical college Jabalpur, from September 1, 2003 to August 31, 2007. Data were analyzed using Epi Info (2003) statistical software. The study protocol was approved by the institutional ethics committee.

Observation: A total of 596 women were included in the study, however 61 women were excluded due to incomplete data. The mean age of the study population was 35.4 ± 9.1 years. In conventional colposcopy mean time required was 19 ± 2.4 minutes, whereas by simplified RCI method it was 3.6 ± 1.2 minutes. The diagnostic sensitivity of cytology as compared to histopathology was 48.1% and specificity was 88.3%. The difference in cytology and histopathology results was statistically significant (p < 0.001). The overall sensitivity of colposcopy was 100%, but specificity was 30.9%, however in high grade lesion it was 48.6%.

Conclusion: Due to inadequate expertise, interpretation difficulties and time consuming outdoor procedure, colposcopy is not a popular method for cervical cancer detection among practicing gynecologists of developing country like India. In present study new equation style for documentation simplifies learning as well as makes documentation easy and time saving for overburdened gynecology outpatient departments of tertiary care hospitals.
**P-058**

**COLPOSCOPY IN SYMPTOMATIC POST-MENOPAUSAL WOMEN: CORRELATION WITH HISTOPATHOLOGY**

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**Objectives:** Cancer of the cervix is the commonest cancer in Indian women, in the age group of 50 to 64 years have the highest annual age-adjusted incidence rates (AAR) ranging from 93.7 to 106 per 100,000 women. Anatomical and histopathological changes occurring in the cervix after menopause can lead to false positive and negative results of Pap smear and colposcopy. This study was therefore done to evaluate exclusively post-menopausal women by cytology, colposcopy and histopathology.

**Method and Results:** Fifty symptomatic post-menopausal women underwent at least 2 of the 3 parameters. On HPE, 39 women were diagnosed to have no pathology and 11 were diagnosed with pathological lesions (2 with CIN-III, 7 with Squamous cell Ca, 2 with AdenoCa). On colposcopy, 12 patients were diagnosed with HSIL and suspected Ca, of which 11 correlated correctly on HPE. On Pap screening 14 patients were diagnosed as HSIL and Squamous cell carcinoma, thereby having 3 false-positive results. Colposcopy with Pap smear had a sensitivity of 100% and diagnostic accuracy of 94%. However, in 58% of patients there were problems in colposcopic interpretation due to atrophy and inflammation associated with menopause which was significantly resolved after local estrogen therapy which also helped in avoiding unnecessary biopsies.

**P-059**

**A STUDY OF CERVICAL LESIONS BY USING DIGITAL COLPOSCOPE IN PRIVATE SET-UP**

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**Objectives:** The need for cervical cancer screening in our country is obvious as it is the commonest cause of cancer deaths in women. The present study was done to find out the nature of cervical pathology in married non-pregnant women, by Digital Colposcopy, and their correlation with biopsy findings.

**Method:** Women aged 21 years and above, with white discharge, burning sensation in their birth passage, post-coital bleeding, unhealthy cervix, postmenopausal bleeding, and abnormal Pap-smears were studied. Some asymptomatic women also were enrolled. Appropriate pre-procedural counseling was done. The study period was August 2008 to December 2009.

**Results:** Out of a total 171 cases, 23 were between 21-30 years, 76 between 31-40 years, 49 cases between 41-50 years, and 23 cases were over 50 years old. There were 30 positive cases by colposcopy of these 27 were LSIL and 3 cases had HSIL. Histopathology was done in 6/27 LSIL cases, of whom 4 cases showed mild dysplasia and 2 cases chronic cervicitis. Of the 3 HSIL cases, one showed infiltrating squamous cell carcinoma, one showed chronic cervicitis and one did not consent to biopsy exam. Only one patient underwent HPV testing – tested positive for high risk HPV and was asked to come for follow up after 1 year.

**Conclusion:** It appeared from the present study that more motivation is required for women agreeing to undergo biopsy. There should also be easy availability of HPV testing.
P-060

COLPOSCOPY AND CYTOLOGY STUDY FOR CERVICAL PRECANCER LESION

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Objectives: To compare colposcopy study with cytology for cervical precancerous lesion.

Method: Study conducted at Sai Nursing Home, Chikhli, Dist Buldana, (MS), a rural area. One hundred and sixty six patients having dense acetowhite area, unsatisfactory colposcopy or DUB were selected for Pap smear. Cytology study was done under the CCPP program at Nargis Dutt Cancer Hospital, Barshi.

Result: Out of 166, 40 patients were abnormal, of which 17 were HSIL, 3 were AGC, 17 were ASCUS or LSIL, 1 was cervical carcinoma in situ and 2 had invasive cervical cancer.

Conclusion: Colposcopy is useful for diagnosis of cervical precancer and cancer lesions.

P-061

CANCER CERVIX SCREENING IN A HIGH RISK POPULATION AT DELHI URBAN SLUM

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Background: High incidence and mortality due to cancer cervix is a public health problem in India. Lack of awareness, shyness, fear and inability to understand or identify the warning signals related to cancer cervix are the impediments to reducing the disease burden.

Methods: A pilot project was initiated as a community outreach program from our hospital. We conducted the study at an urban slum of North Delhi, survey of the study area conducted and 565 questionnaires filled by trained health workers. All the eligible women (287) were invited for examination and Pap smear testing at Community Health Center. A total of 170 women underwent Pap smear test.

Results: Over 83% of women of this community were married prior to 18 years of age, 49% had more than three children, 45% had three or more pregnancies. Age at first child birth was less than 18 years in 67% of the women. More than 90% had symptoms of per vaginal discharge for more than three months. On Pap smear examination, 60 were reported inflammatory, 2 squamous metaplasia, 1 clue cell, 9 CIN (CIN1 & CIN2), 1 adenocarcinoma, 1 squamous cell carcinoma.

Conclusions: The high incidence of positive cases in the small sample size is a cause for concern. A focused and concerted cancer awareness drive targeting women of high risk group (Urban slum population) is required.
P-063

DISTRIBUTION PATTERN OF HPV GENOTYPES AMONG INDIVIDUALS REFERRED FROM INDIA, BANGLADESH AND U.A.E

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Background: Human Papilloma Viruses (HPVs) are DNA viruses that infect cutaneous or mucosal epithelia. Classification is based on their propensity to cause invasive cervical cancer. Thus, HPV genotyping is important for following up of patients with persistent HPV infection and for evaluation of prevention strategy for the individual patients to be immunized with type specific vaccines. Empirical knowledge of locally prevailing HPV genotypes may aid in devising preventive, therapeutic and prognostic protocols in resource limited countries.

Objective: To evaluate the distribution pattern of different HPV genotypes in individuals referred from India, Bangladesh and U.A.E.

Method: Between, January 2007-November 2009, 404 cervical specimens (swabs, smears, biopsies) from India, Bangladesh and U.A.E. were referred for HPV genotyping to a clinical reference lab in India. The 33 specimens which tested positive for HPV infection were genotyped by sequencing the hypervariable L1 region of the HPV genome.

Result: Median age 32 years (16-75). Specimens from India (n=340), HPV positive were 25 (7.35%) · genotyped as HPV-16 (60%), HPV-18 (8%), HPV-66 (4%), HPV-6 (12%).

Specimens from Bangladesh (n = 34), 4 were HPV positive (11.76%) 2 each of HPV- 6 and HPV -11. Specimens from U.A.E (n=30), 4 were positive for HPV (13.3%) only one HPV-16 and rest were HPV-6.

Conclusion: HPV16 was noted as the predominant HPV genotype in India. In addition, high risk genotypes were more preponderant in patients above 30 years of age while low risk types were more prevalent in below 30 years of age.

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P-062

THE NOT SO SUSPICIOUS CERVIX

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Objective: To present a collection of unsuspected cases of cancer cervix

Method: Ten cases of grossly normal or benign appearing cervix which later turned out to be invasive cancer would be presented and their diagnostic and management pitfalls discussed.

Results and Conclusion: All the cases in the study ultimately turned out to be invasive cervical malignancies. All the cases were incidental detections in the age group of 21 to 48 years with diagnostic pitfalls in most. The natural history of carcinoma cervix appears to be undergoing a change and the management should take this into account.
**P-064**

PREVALENCE OF HUMAN PAPILLOMAVIRUS IN CYTOLOGICALLY NORMAL WOMEN IN NEW DELHI

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**Objectives:** Human papillomavirus (HPV) infection is a major cause of invasive cervical cancer and its precursor lesions. The aim of this study was to estimate both the age and the prevalence of cervical human papillomavirus DNA using Hybrid Capture II test (Qiagen, Gaithersburg, MD) in women with normal cervical cytology.

**Method:** A total of 6255 samples were received from various hospitals in New Delhi for HPV DNA testing (Hybrid Capture II test (Qiagen, Gaithersburg, MD) during 2003-2009. These samples were obtained according to the ThinPrep method in PreservCyt solution. Of these 4644 were cytologically normal.

**Results and Conclusion:** In the study group, HR-HPV DNA was detected in 434 women with normal cytology, therefore in New Delhi, India the prevalence estimate among women with normal cytology was 9.34%. The highest age-specific HPV prevalence was seen in women in the 35-44 year group, and prevalence decreased in the 45-54 year group. An increase was observed in the older age-group, more than 54 years. The fact that HPV prevalence increases after menopause should be considered in the evaluation of the age at which women should stop having regular screening exams.

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**P-065**

HPV PREVALENCE AND CYTOLOGY AMONG YOUNG WOMEN IN NORTH INDIA

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**Objectives:** Evaluation of HPV prevalence and cytological abnormalities in young women and correlation with time since coitarche.

**Method:** Married, non-pregnant women aged 16-24 years, residents of an urban slum, underwent conventional Pap and HPV DNA testing by Hybrid Capture 2 (HC2) Probe B. HPV genotyping was done on all positive samples by Reverse Line Blot Assay (Roche").

**Results:** 1300/1873 eligible women were enrolled. Median age 22 years, 110(8.4%) women were HC2 positive. On genotyping, 104 were positive, with single infections in 64 and multiple infections in 40 women. The five most common types were HPV16, 52, 51, 39, 59 and 18. HPV16/18 accounted for 41 cases.

Group 1 – Married for <3 years (n=356, 27.4%); Group 2 – Married for >3 years (n=944, 72.6%). In Group 1, 42(11.8%) were HPV positive, 31 were positive on line blot assay. HPV16/18 were seen in 35.5%, other high risk types in 41%, low risk HPV in 23.5%, multiple infections in 29.4%. In Group 2, 68/944 (7.2%) were HPV positive, 47 were line blot positive. HPV16/18 were seen in 44.3%, other high risk types in 30%, low risk HPV in 25.7%, multiple infections in 32.8%.

On cytology, inflammatory smears were found in 869 (66.9%) women. Pap abnormalities were seen in 29 women (ASCUS – 7, LSIL – 20, HSIL – 2), 19/29(65.5%) abnormal Pap smears were HPV positive. There was no significant difference in the prevalence of cytological abnormalities with respect to time since coitarche (2.2% vs 1.9%) but HSIL cases were married >3 years.

**Conclusion:** Inflammation is a common finding even in the younger age group. High grade lesions were seen >3 years after coitarche. HPV16/18 account for a substantial proportion but a wide spectrum of HPV genotypes is seen in this young population.

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INCREASED RISK OF PRE-MALIGNANT LESIONS AND HPV INFECTION AMONG WOMEN LIVING IN VILLAGES WITH HIGH GROUND-WATER ARSENIC LEVEL IN WEST BENGAL

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Background: Several districts in West Bengal are facing severe arsenic contamination of groundwater leading to over 23 million people under threat of arsenic related diseases. Arsenic, a known human carcinogen with epidemiological evidence shows dose-response of ingested arsenic with increased risk of lung, liver, bladder, kidney and skin cancers in exposed population, but with no report on incidence of cervical cancer or pre-cancer.

Objective & Method: To understand the carcinogenic role of extended arsenic exposure in cervical cancer, asymptomatic women (30-64 years old) were screened from high arsenic (100-300 μg/l) and arsenic-free (below 25 μg/l) villages using VIA and VILI followed by colposcopy. A punch biopsy of suspected lesions was taken for histological evaluation. High risk HPV test using Hybrid Capture II assay (HC-II) was done only on specimens from screen positive cases.

Results: Out of 1040 asymptomatic women screened, 95 screened positive, 22 (2.4%) had histologically confirmed CIN, 3 (0.29%) had invasive carcinoma cervix. From arsenic-free villages, 62/735 women screened positive, with 12 (1.6%) CIN and 1 (0.13%) invasive cancer. Of the 95 women with positive screening results in high Arsenic area, 12 showed high risk HPV infection (12.6%) compared to 4 (6.5%) from arsenic-free area. Among the lesions from high arsenic area, CIN 2/3I were 21.7%, whereas low arsenic area showed no high grade CIN.

Conclusion: Preliminary results from the study suggest an increased risk of pre-malignant lesions, high risk HPV and cervical cancer among women chronically exposed to arsenic through ground-water contamination.
EVALUATION OF GROUP B STREPTOCOCCI COLONIZATION RATE IN PREGNANT WOMEN AND PREGNANCY OUTCOME (NEWBORN)

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Objectives: Group B Streptococcus (GBS) is one of the most important bacteria in the majority of maternal and neonatal infections. In addition this microorganism causes severe infections such as chorioamnionitis, endometritis, bacteremia, septicemia and neonatal meningitis in mothers and neonate. GBS screening is one of the recommended strategies that has been mentioned by the CDC during pregnancy. Taking the importance of the issue into consideration, we decided to study the percentage of colonization of the microorganism in mother and neonate and its probable outcomes in order to show responsible factors and frequency of the colonization, its outcomes and moreover to recommend practical approaches towards prevention of this infection.

Method: Two hundred pregnant women who were admitted at the Ghaem Hospital were involved in the study, the information of mother and neonate were mentioned in the questionnaire and cultures were taken from vaginal secretions of mother during delivery and secretions of umbilical cord in the post partum period.

Results and Conclusion: The colonization in the pregnant women and neonates studied was reported 6% and 5% respectively. All mothers of neonates who carried GBS were in the group of GBS carriers and all of them had premature rupture of membrane (PROM) 18 hours before delivery. There is a meaningful relationship between maternal and neonatal GBS colonization and moreover 80% of neonates among GBS carrier mothers were colonized by GBS. Colonization rate in mother and neonate were 11%.
**P-070**

**HPV PREVALENCE AND GENOTYPE CONCORDANCE AMONG 125 ITALIAN SEXUAL COUPLES**

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**Objectives:** To investigate the prevalence and the genotype distribution of HPV in genital cytological specimens of a series of Italian men and their sexual partners, and to assess the viral genotype concordance between the infected partners.

**Method:** Penile and cervicovaginal brushings of 125 sexual couples were screened for HPV infection by polymerase chain reaction (Linear Array, Roche) which recognizes 37 high, low and intermediate risk HPV types. The enrolled men had no visible penile lesions, while their female partners were affected, or had been previously affected, by Cervical Intraepithelial Neoplasia (CIN), or were HPV infected.

**Results:** We found HPV positivity in 55% (69/125) of the females and 38% (48/125) of the male samples. The genotype HPV16 was the most frequent in both populations (13% of women and 10% of the men) followed by genotype 53 (8% in both populations). Regarding the HPV status, we found HPV concordance in 92 out of the 125 couples (concordance rate 73.6%, K = 0.46, CI 0.3-0.63, p < 0.0001). In particular, both partners were HPV negative in 50 couples, whereas 42 couples showed HPV positivity. Notably, 38 out of the 42 HPV positive couples (90%) harboured at least one identical genotype.

**Conclusion:** These data support the hypothesis that male HPV infection is more frequent in sexual partners of HPV positive or CIN affected women, indicating that men could represent an important means of HPV transmission between sex partners.

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**P-071**

**PREVALENCE OF CHLAMYDIA TRACHOMATIS, HUMAN PAPILLOMA VIRUS AND TRICHOMONAS VAGINALIS IN CERVICAL INTRAEPITHELIAL NEOPLASIA**

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**Objectives:** To study the prevalence of sexually transmitted infections in cases of established cervical intraepithelial lesions and utilize that knowledge in downstaging of cancer cervix.

**Method:** A total of 75 women were evaluated. Fifty women with CIN were in a study group and 25 women were in a control group. For the present study the women were selected by screening the women attending OPD on the basis of symptoms of excessive vaginal discharge, post coital bleeding, post menopausal bleeding and visual inspection of cervix. All the women were subjected to examination of *Trichomonas vaginalis*, Pap smear, HPV examination, colposcopy and colposcopy-guided biopsy for confirmation of CIN. For *Chlamydia* infection 5ml blood was taken for serological study by ELISA technique to measure IgG antibodies against known Chlamydia antigen.

**Results:** Association of HPV with CIN was found to be maximum 74%. 46% of the study group women were positive for IgG antibodies against *Chlamydia* while 20% of controls were positive. Only 16% of the study group women were positive for *Trichomonas* in comparison to 12% in controls.

**Conclusion:** Results show that commonly found STD infections have significant relationship with CIN hence timely diagnosis and treatment of these infections may lower the incidence of cancer cervix.
CLINICAL EFFICACY OF PLACENTREX INJECTION IN PELVIC INFLAMMATORY DISEASE

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Objective: To evaluate efficacy of placental extract in combination with single-agent antimicrobial therapy in pelvic inflammatory disease (PID).

Method: Randomized clinical trial; 100 cases aged 20-45 years presenting with PID, were randomized into Group 1 (n = 50) who received doxycycline 100mg twice daily with intramuscular Placentrex® injection (placental extract, Albert David Ltd.) 2mg/daily for 14 days and Group 2 (n = 50) who received only doxycycline. Exclusion criterion was previous antibiotic therapy within 1 month. Patients were followed up at 2, 4 and 12 weeks to assess immediate relief, persistence of relief and recurrence respectively.

Results: Mean age was 31 years in both groups. Forty four patients in group 1 and 32 in group 2 completed the study. Mild gastritis occurred in 2 cases each. No patient discontinued treatment due to side-effects, there was no allergic reaction or pain at injection site in group 1. Overall, group 1 had better and sustained effect on relieving dyspareunia, fornix tenderness and uterine mobility (p < 0.05). Complete remission with treatment occurred in 21 (45.6%) vs. 13 (28.8%) cases at 2 weeks, in 30 (68.2%) vs. 6 (18.7%) at 12 weeks respectively. Eleven (23.9%) cases of group 1 and 18 (40%) cases of group 2 had no response at 2 weeks. At 10 weeks, further improvement occurred in 9 (22.6%) cases in group 1 vs. recurrence in 3 cases in group 2.

Conclusion: Combination of Placentrex® with antimicrobial therapy is better option for PID than only antimicrobials as it gives more sustained effect and lesser recurrences.

WEIGHTAGE OF DIFFERENT DIAGNOSTIC MODALITIES FOR DIAGNOSIS OF GENITAL TUBERCULOSIS

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Objective: To evaluate the weightage of different diagnostic modalities for the diagnosis of genital tuberculosis.

Method: A retrospective study on 80 women who were started on antitubercular therapy on the basis of various diagnostics at All India Institute of Medical Sciences, New Delhi.

Results: The mean age of the women was 28.2 years. Past history of tuberculosis was present in 28 (35%) women. A total of 5 (6.25%) women had positive TB granuloma while only one woman had positive AFB culture. PCR was found positive in 60 (75%) women. While ultrasound or CT scan and hysterosalpingogram (HSG) showed positive findings in 5 (6.25%) cases each. Positive laparoscopy findings of genital TB were observed in 42 (52.5%) cases while positive findings on hysteroscopy were observed in 43 (53.75%) women, with many cases having more than one finding.

Conclusion: Genital TB is an enigmatic disease which requires a high index of suspicion and a combination of diagnostic modalities for its diagnosis.

Key words: Female genital tuberculosis, laparoscopy, hysteroscopy, Acid fast bacilli, infertility, Polymerase chain reaction.
**P-074**

**ROLE OF GENITAL HYGIENE AS A RISK FACTOR FOR UTERINE CERVICAL CANCER**

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**Objectives and Method:** Cervical cancer is the second most common type of cancer in women worldwide, after breast cancer. This cancer is preceded by precancerous lesions, which can be identified well before the development of full fledged cancer. Several epidemiologic risk factors have been identified for the development of cervical cancer. A risk about three times that of the general female population is found in women of low socioeconomic status, multiparous, those engaged in sexual activity at a young age or with multiple partners. A study was undertaken at our Institute in collaboration with Gynecology departments of major hospitals of Delhi. Epidemiological information was elicited after establishing thorough rapport with the patients attending the Gynae OPD’s of the collaborating hospitals. In the present communication the analysis is based on variables related with obstetric and hygienic practices.

**Results:** A total of 82 mild and moderate dysplasia (low grade lesions) and 112 cases of severe dysplasia and malignancy (high grade lesions) formed two case groups. A total of 210 control subjects were enrolled in order to carry out case control comparison. If any of the deliveries were conducted by untrained personnel, risk of development of neoplasia was almost two times higher in both groups. The detailed results would be presented and discussed.

**Conclusion:** Most women with cervical cancer experience a long asymptomatic period before the disease becomes clinically evident. Early recognition of abnormal cytologic changes through regular screening may prevent progression from preinvasive to invasive disease.

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**P-075**

**CERVICAL CANCER SCREENING: DEVELOPMENT OF IEC MATERIAL**

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**Background:** Screening methods are available for early detection and prevention of cervical cancer. In order to get a good coverage of the target population to be screened and its implication on cervical cancer control well planned IEC (information and education campaign) material is essential.

**Objective:** This paper attempts to discuss about the importance of health education material and present some example material for use in a cervical cancer screening project planned in a rural tehsil of Uttar Pradesh.

**Method:** Review of some existing material used for motivation of women for cervical cancer screening. The material was developed with suggestions received from the community based on a survey on community perspectives of screening. The material was reviewed by a board. The material was tested for adequacy of understanding the contents by gross root level health workers and the target women from the community.

**Results:** The extent of understanding of the message was evaluated and its adequacy was discussed. The material developed in terms of brochures and flip book was presented and discussed in the paper.

**Conclusion:** The information education and communication (IEC) material developed was found adequate for motivating the women to join in the cervical cancer screening project for an adequate coverage.
P-076

PRIMARY PREVENTION OF CERVICAL CANCER: DEVELOPMENT OF A PEER EDUCATION MODEL FOR LOW LITERACY RURAL COMMUNITIES IN INDIA

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Objectives: In India, there are over 130,000 cases of cervical cancer every year, and over 74,000 cervical cancer-related deaths. Though cervical cancer is the most common cancer among women and a leading cause of cancer-related deaths, rural Indian women lack the knowledge about prevention of cervical cancer. This study evaluates a communication skills training program on peer-educator’s knowledge, attitude and self-efficacy related to communication on prevention of cervical cancer in rural communities of Mysore, India.

Method: Between July and September of 2009, women from five villages in Mysore taluk were selected for peer-educator training based on their ability to act as peer-educators in their communities. Women were eligible to participate if they were 20-35 years of age, able to read and write Kannada, and members of self-help groups. In this pre-post-test intervention study, a three-day, 18-hour training program was developed and implemented. Pre- and post-test questionnaires were administered to assess the knowledge of the peer educator before and after the training.

Conclusion: Twenty-four women were selected from 5 villages to be trained as peer-educators. The median age was 30 years [range 23-35 years]. All the women were Hindus and their education ranged from grade 7-10. Participant’s knowledge increased from 34.4% before the intervention to 73.3% after the intervention. We found that training lay-community people on topics related to prevention of cervical cancer and in communication skills, improved their knowledge, changed some negative attitudes and enhanced assessment of their own ability as effective peer-educators.

P-077

PUBLIC KNOWLEDGE, ATTITUDE AND PRACTICE TOWARDS HUMAN PAPILLOMA VIRUS VACCINATION

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Objective: To determine knowledge, attitude and practice towards Human Papilloma virus (HPV) vaccination in the state of Haryana.

Method: Patients and their attendants visiting the Gynaecology Out Patient Department and admitted to the Department of Obstetrics and Gynaecology at PGI of Medical sciences, Rohtak were included in the study. A total of 650 participants aged 16-54 years were recruited from October through December 2009 and questionnaires were delivered to the participants. Questionnaire administration commenced with socio-demographic questions followed by an assessment of knowledge of HPV infection, cancer cervix and HPV vaccination. In-person interview was also taken at the same time.

Results: Only 7.4% of women had some knowledge of HPV infection, 6.8% knew about vaccination against HPV, 10.1% of women knew about a vaccine which could prevent cancer cervix. However 60.1% of participants were willing to take the vaccination themselves or were ready to get their daughters vaccinated when told about the vaccine. Only 16.6% agreed for vaccination at 10 to 12 years of age; however, all participants (60.1%) consented for 26 years of age.

Conclusion: The study confirms that there is a lack of information about HPV and more efforts are needed to raise awareness of HPV and HPV vaccination. Most of the people would accept the vaccination if it were offered. Possible side effects, efficacy, cost and the age group were highlighted as areas of concern.
**P-079**

**BELIEFS ABOUT CERVICAL CANCER AND ACCEPTABILITY OF HPV VACCINATION IN A PERI-URBAN AREA OF ANDHRA PRADESH, INDIA**

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Mediciti Institute of Medical Sciences, India

**Objectives:** To assess the knowledge about cervical cancer and HPV and to determine whether parents would accept HPV vaccination for their children.

**Method:** One hundred and twenty five parents of children aged 9-15 years were interviewed individually from six different peri-urban areas in Andhra Pradesh, India regarding the acceptance of an HPV vaccine for their children and their knowledge of HPV and cervical cancer. Interviews were transcribed and translated.

**Results:** HPV vaccination would be accepted by all the parents interviewed, though none of the women had heard of HPV and its mode of transmission. The main reasons for vaccine acceptance provided by all parents were to ‘prevent’ their child from cervical cancer. 49.6% of women were aware of the causal relationship of sexually transmitted infection and cervical cancer. Knowledge of HPV and cervical cancer, religion, age, education, marital status did not show any significant relation with HPV vaccine acceptance. Only 64% of women had a Pap smear once.

**Conclusion:** Acceptance of HPV vaccine was 100% even though knowledge of HPV and cervical cancer was low. Protection of their child was the main motivating factor for vaccinating their daughters. As only 64% of women had Pap smear, cervical cancer prevention should include strategies for regular cervical screening as well. Whether or not verbal acceptance would lead on to action to be vaccinated has yet to be tested.
**P-080**

**EDUCATION IN SCREENING FOR HUMAN PAPILLOMAVIRUS INFECTION PREVENTION, THE PSYCHO-SOCIAL IMPACT: MÉXICO**

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**Background:** All women should know the association of Human Papillomavirus with cervical cancer. Nevertheless, the disinformation even health professionals receive creates a malformation of ideas regarding the disease. Therefore, several emotional states occur altering the health of the person, couple, family or even the professional environment.

**Objectives:** To analyze the emotional response to the information and provide correct information to the patients, analyzing the psycho-social and the diverse altered emotional states that can occur when a patient is given screening report, whether positive for HPV or cancer.

**Method:** Every patient who attended the colposcopy clinic for the first time when her cytology and/or Hybrid Capture-II report was positive, received information and an orientation talk. Subsequently patients were interviewed for completion of a questionnaire.

**Results:** We observed that patients presented several emotional states, from confusion, doubt, desperation even depression and a mourning stage when the diagnosis of cancer was given. Present changes in your sexual behavior, feeling rejected, culpability, dirty or punished. They don’t realise that attitude lies with the couple. This situation sometimes is flattering for the medical personnel who project their personality aspects in the patients and at the same time to have repercussions on the treatment and managements.

**Conclusion:** Nowadays few experiences exist in the integral management of patients from multi-disciplinary environments and because of many factors, do not analyze psycho-social aspects in women with HPV infection, pre-cancer lesions or in situ cancer, from the perspective of gender in health is not done. Preventive screening is recommended including an educative program of information in the theme for the general population.

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**P-081**

**AWARENESS OF CERVICAL CANCER AND HUMAN PAPILLOMAVIRUS INFECTION AMONG SCHOOL CHILDREN IN INDIA: PARENTAL ATTITUDE TOWARDS ACCEPTANCE OF HUMAN PAPILLOMAVIRUS (HPV) VACCINATION**

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**Objectives:** To determine young adolescent’s knowledge of cervical cancer and HPV infection and parents’ attitude towards HPV vaccination acceptance.

**Method:** A total of 2500 adolescent college and school going girls and boys in the age group of 12-22 years completed a survey assessing demographic characteristics; knowledge of cervical carcinoma and HPV, acceptance of HPV vaccine and parents’ opinion about HPV vaccine.

**Results:** Two hundred and seventy five (11%) adolescents had heard of HPV and 375 (15%) had heard of cervical carcinoma. Students who lived in urban areas had significantly more knowledge of cervical carcinoma than those who lived in rural areas (p < 0.05). Only 162 (10.3%) of the female and 63 (6.8%) of the male participants were willing to accept HPV vaccination. Most parents, including teachers and principals, were of the opinion that school children were too young to understand and should not be exposed to this type of knowledge as it is related to sexual behavior. Some parents had the impression that vaccine might interfere with the fertility of their daughters and were doubtful about its safety.

**Conclusion:** Knowledge levels about HPV and cervical cancer were low. Only a small proportion would accept HPV vaccination but girls were significantly more willing to accept HPV vaccination. Acceptance of HPV vaccination seems to be affected by other, still unidentified factors. A large scale educational campaign has been initiated to cover knowledge about HPV, cervical cancer and belief and behaviors associated with the acceptance of vaccination.
**P-082**

**AWARENESS AND KNOWLEDGE OF HPV CARCINOGENESIS AND VACCINATION AMONGST MEDICAL STUDENTS IN INDIA**

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**Objective:** To assess awareness and knowledge of undergraduate medical students regarding HPV infection and primary prevention in cervical cancer.

**Method:** Medical students of 5th, 7th and 9th semesters of UCMS, Delhi, were administered a questionnaire comprising 35 questions on various aspects of HPV infection and vaccination. Questions assessed the knowledge regarding burden of cervical cancer in India, role of HPV in cervical carcinogenesis, mode of transmission, natural history and prevention of HPV infections. The questionnaire was also used to assess knowledge about the vaccine, its efficacy, safety, mechanism of action, dosage schedule and cost. The data was collated and assessed in percentages.

**Results:** 150 medical students (139 males, 11 females) completed the questionnaire. The majority of the students were aware that cervical cancer was very common and 96% implicated HPV as causative agent. They also knew that not all HPV viruses cause cervical cancer; 55% students said that transmission could be by both sexual and nonsexual route. However, none of the students knew time of progression to cervical cancer. 76% students were aware that HPV vaccination protects against cervical cancer in 60-80% but 90% did not know the vaccination schedule. 65% boys thought it was expensive for routine use and would take it themselves if cost came down while 88% of girls would vaccinate themselves.

**Conclusion:** Although awareness about HPV infection and vaccination was present some gaps in knowledge need to be addressed and integrated teaching regarding HPV carcinogenesis, vaccination and cervical cancer needs to be introduced.

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**P-083**

**SEXUAL PRACTICES, KNOWLEDGE AND ATTITUDE TO SEXUALITY AMONG YOUNG WOMEN IN DELHI, INDIA**

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**Objectives:** To assess sexual practices of female students and their knowledge about cervical cancer, its risk factors and preventive measures.

**Method:** An anonymous, self-administered 24-item survey of sexual practices and cervical cancer knowledge was completed by a convenience sample of 872 female undergraduate students enrolled in Delhi colleges.

**Results:** 10.2% of participants who were sexually experienced, 75.3% were monogamous, 50.6% used contraceptives. 23.3% participants had heard of cervical cancer but only 0.5% participants identified all risk factors, while 15.8% did not identify any risk factor correctly. The most identified risk factor was genital infection (52.2%). None of the participants was aware of HPV testing. Government school students’ mothers were less educated (39.2% vs. 84.8%, p<0.001). More government school students had sexual exposure at <18 yrs of age (13.9% vs. 5%, p<0.001), fewer were using contraceptives or had heard about Pap (4.1% vs. 9.3%, p<0.020); smoking was more prevalent in students of private schools (14.5% vs. 6.7%, p<0.004). Those who had heard of cervical cancer used contraception more (88.4% vs. 37.4%, p<0.004) while history of STI (0.0 vs. 7.8%, p<0.002), pregnancy and abortion rates (2.6% vs. 15.7%, p<0.043) were less, with better knowledge of Pap (82.4% vs. 0.0, p<0.006). The 783 sexually inexperienced students were less aware of cervical cancer and Pap (p<0.001).

**Conclusion:** Knowledge about HPV infection, cervical cancer risk factors and screening is poor among college students in Delhi. Education of STIs, contraception, safe sex and cervical cancer prevention should be linked, with special emphasis on Government schools.
AWARENESS AND ATTITUDE TOWARDS HPV INFECTION, CERVICAL CANCER PREVENTION AND VACCINATION

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Objectives: To develop an educational programme on cervical cancer prevention for adolescent school girls and evaluate its impact on knowledge.

Method: An educational program was developed as a Power point presentation on “cervical cancer prevention” in the local vernacular language, Hindi. Female students in the age group of 13 to 18 years old studying in class 6 to 12 of 4 local secondary schools in south Delhi were invited to participate. Self-administered questionnaires were used as pre- and post-test to evaluate the program effect. The program was approved by the institutional ethics committee and the school authorities.

Results: Two hundred and seventy five adolescent girls in the age group of (mean age 13.7 years, (SD 1.53) participated. After attending the program, participants’ knowledge on cervical cancer, HPV and HPV vaccination increased significantly. Knowledge of the role of sexual transmission of HPV increased from 32.4% to 82.1%. Knowledge of whether screening can prevent cervical cancer increased from 67.2% to 84%. Similarly, knowledge that cervical cancer can be prevented by vaccination increased from 69.5% to 87.6%. Overall, approval for accepting the HPV vaccination in adolescents increased to 83.3% of the participants in the post test compared to 33% in the pre-test. This school-based educational program was well received by the participants and teachers.

Conclusion: Awareness about cervical cancer and vaccine for cervical cancer, the role of HPV in cervical cancer and the availability of HPV vaccination can be improved by simple interventions among the school going adolescent girls in India.

CARCINOMA CERVIX: ATTITUDE AND BEHAVIOUR OF GYNAECOLOGISTS TOWARDS SCREENING PRACTICES

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Introduction: Cervical cancer is the most common cause of cancer mortality among women worldwide, but this is largely preventable.

Objective: To study the attitude and clinical practices of gynecologists towards screening of cancer cervix.

Method: Cross sectional analysis based on a questionnaire given to 300 gynecologists practicing in various regions of Delhi and NCR was done and data analyzed.

Results: In our study it was found that there is a varied approach of various gynecologists towards screening. Very few doctors have an attitude towards opportunistic screening and VIA and VILI are rarely used, though they have adequate screening facilities.

Conclusion: A focused and concerted drive is urgently needed for all gynaecologists, with special attention to the practice of opportunistic screening, in order to achieve a near total secondary prevention of these cancers.
**P-086**

**HUMAN PAPILLOMA VIRUS TESTING BY SELF SAMPLING: ACCEPTABILITY ISSUES**

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**Objective:** To compare the acceptability of supervised self-sampling with provider-sampling for HPV testing in a cancer screening study.

**Method:** 220 women performed a supervised HPV self test, then a doctor took a cervical sample for cytology and HPV test. Later they answered a questionnaire to assess comparison between the self and physician test method.

**Results:** A total of 220 women participated. The majority (92%) were between 30-40 years, most (41%) were illiterate. When questioned before self-sampling, 90/220 women said they were apprehensive due to: embarrassment (74.4%), fear of injury (66.7%), fear of inadequate sampling (57.8%) and procedure unclear (17.8%). More (82.7%) women were apprehensive before the clinician-collected sampling. 87.7% women were afraid of pain as compared to 50% women for the self-sampling. Other reasons for apprehension in physician sampling were: embarrassment (80.4%), fear of injury (64.5%) and fear of bleeding (48.6%). When questioned after the procedures, 124/220 women (56.4%) preferred the self sampling while 86 (39.1%) preferred the physician sampling. Ten preferred both. Self-sampling was preferred for more privacy and easier (99.2% each) and less painful in 97.6%. Of the 86 (39.1%) women who preferred clinician sampling the reasons were: more likely to be adequate (64%) less painful (97.7%), while the self sampling procedure was unclear in 58.1%.

**Conclusion:** Self-collected sampling for HPV DNA is comparable to physician-collected sampling, is acceptable to the majority and is a good alternative in low resource situations and for women who wish to avoid pelvic examination.

**P-087**

**FACTORS INFLUENCING HPV VACCINE INTRODUCTION IN INDIA : A POLICY ANALYSIS,**

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**Objectives-Methods:** Elucidation of the burden of cervical cancer (CaCx) in relation to other diseases in the Indian context. Determination of the health spending contributed by public vs private sectors in India per capita GDP. Requirement of screening in addition to vaccination. Assessment of logistical barriers to vaccine implementation programs. Methodology followed included review and analysis of available published literature.

**Results:** Cancers have a lower-priority in the Empowered Action Group States plus Assam (EAGA States; rank 10) compared to other states (rank 3). India’s public investment in health care is much less than most countries with a similar GDP (currently 1.2%). Moreover, the immunization trend for EPI vaccines is only 44% nationwide, as well as a severe shortfall in public health service facilities, such as, Community Health Centres (CHCs), Primary Health Centres (PHCs) and Subsidiary Health Centres (SHCs). Infrastructure deteriorates as one goes down the ladder. Screening will be required in addition to vaccination. Logistical barriers having a bearing on vaccine acceptability need to be addressed.

**Conclusions:** There is a need for increased public spending in health sector (at least 2% of GDP by 2012, as pledged). Once-in-a-lifetime screening for adult women should be started using visual inspection methods. Vaccination strategies targeting school-level girls should be planned for high-risk states. The topic of CaCx should be incorporated into the sex education curricula in schools. There is an urgent need for more studies to address vaccine-acceptability issues.
**P-088**

**CERVICAL CANCER SCREENING: COMMUNITY PERSPECTIVES IN A RURAL TEHSIL OF NORTH INDIA**

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**Background:** Cervical cancer is a second major cancer site in terms of high incidence among Indian women. Screening methods are available for early detection and prevention of this cancer. Successful planning and organization of screening programs for the prevention necessitate community perspectives.

**Objectives:** This paper attempts to study community perspectives and present an approach of organizing a cervical cancer screening programme.

**Method:** Data on 450 women from a rural community of Uttar Pradesh were collected to assess the awareness of cancer and cervical cancer, their beliefs, risk factor prevalence and community view point for responding to a screening programme if organized in the community.

**Results:** Knowledge of cancer of the uterine cervix has been found to be very low while cancer in general is known to the community. The magnitude of awareness, risk factor prevalence, community perspectives of screening are discussed in the paper.

**Conclusion:** The extent of awareness, likely acceptance of screening facilities by the community, assessment of adverse beliefs in the community help in development of information, education and communication (IEC) material, other protocol procedures and the organization of screening programmes.

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**P-089**

**ADVOCACY PROJECT ON HOSPITAL/PHC SURVEY FOR ASSESSING DOCTORS’ AWARENESS ON CERVICAL CANCER PREVENTION AND FACILITIES AVAILABLE FOR SCREENING AND TREATING CERVICAL CANCER**

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**Background:** Cervical cancer is the second most common cancer in women, with an estimated five lakh new cases detected annually worldwide. Unfortunately, out of about 2.5 lakh deaths occurring worldwide due to cervical cancer each year, 0.8 lakh women are from India alone. Women with treatable precancer lesions in the cervix remain undetected till the disease becomes fatal. The major limiting factor for carrying out any concerted, large-scale cervical cancer screening in India is the country’s low resource setting coupled with widespread inequity in healthcare.

**Objectives:** This survey aims to evaluate the knowledge of primary healthcare professionals about cervical cancer and to assess their practices on screening, managing and counseling women on cervical cancer.

**Method:** This health education drive would include information dissemination on cervical cancer screening and precancer treatment in the early stages besides advocating the importance of HPV vaccination in adolescent girls. The survey would assess doctors’ awareness on cervical cancer prevention and facilities available for screening and treating cervical cancer at various primary health centres (PHC’s) in the National Capital Region. About 200 PHCs would be visited and through a questionnaire, various assessments would be made on the following topics: physicians’ socio-demographic characteristics; cervical cancer etiology and screening protocols; HPV diagnosis and management; HPV vaccination; and practices regarding patient counseling on HPV. The data collected shall be statistically analyzed using APM.4 software. Besides, pamphlets and posters will be distributed to patients in waiting rooms for creating awareness about cervical cancer. The materials developed for this will be presented.
P-090

ACCEPTABILITY OF CERVICAL SMEAR AND SHORT TERM PSYCHOLOGICAL CONSEQUENCES IN ABNORMAL SMEAR

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Objectives: Pilot study to see acceptance rate of cervical smear in urban women in a private setting and also its psychological consequences.

Method: Women aged 25-64 attending gynaecological outpatient department in a private setting counseled for cervical smears and follow up for two and a half years.

Results: Twenty six percent of women accepted the test. Ten percent had abnormal smears. Eighty percent had worries about the test.

Conclusion: Increased awareness is required regarding cervical screening and structured counseling is needed to reduce post-test stress-related worries.

P-091

STUDY OF SOCIO-BEHAVIOURAL ASPECTS IN PATIENTS OF RTI’S AND STD’S

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Objectives and Method: Reproductive tract infections account for a large portion of reproductive ill health. In resource-poor settings, RTI’s are extremely common along with their sequelae. Women are generally affected because of synergistic effects of infection, malnutrition and reproduction. The objective of the study is to assess the socio-behavioural problems following HIV infection. The data were collected from Lok Nayak Hospital attached to Maulana Azad Medical College, Delhi, through a specially designed proforma seeking information on socio-behavioural problems and information regarding STDs and RTI’s, HIV infection, condom use and partner relationship.

Results: The present study found 96 male STD’s in the age-range of 16-60 years (27.35 + 7.69) and 37 female RTI’s in the age group 15-45 years (26.94 + 6.82), 10% males reported condom usage sometimes, despite reporting risky behaviour with multiple sex partners. About 32% of them were uneducated. Among STD’s male HIV positive 5.2% and 8.1% of female RTI’s patients were found positive for either HIV1 or HIV2 by ELISA and Western Blot Test. As a result of health education and counseling, 42% started using condom regularly.

Conclusion: Behavioural problems such as mood disturbance with anxiety and depression, maladjustment, emotional distress and loss of self confidence, fear of loss of job lead to complete break-down of all familial, social and behavioural norms and bonds. There is need for social, mental and behavioural rehabilitation of patients through educational counseling and intervention programs among HIV, RTI and STD patients.
VISUAL INSPECTION OF CERVIX WITH LUGOL’S IODINE AS A SCREENING TEST FOR PREMALIGNANT AND MALIGNANT LESIONS OF CERVIX

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Objectives: To screen for carcinoma cervix and its precursors by Visual Inspection with Lugol’s Iodine (VILI), Visual Inspection with Acetic Acid (VIA) and Papanicolaou smear and to analyse the sensitivity and specificity of VILI as a screening test for carcinoma cervix.

Method: 350 women with complaints of vaginal discharge, intermenstrual bleeding, postcoital bleeding, clinically suspicious cervix and blood stained discharge were subjected to Pap smear, visual inspection with acetic acid, visual inspection with Lugol’s Iodine and colposcopy. Cervical biopsy and endocervical curettage were taken from patients positive on any screening test and from 10% of screen negative cases. Sensitivity, specificity and positive predictive values of various screening methods used were analysed using colposcopic directed biopsy as reference.

Results: Mean age of patients was 34.1 years and mean parity 2.4. Commonest complaint was vaginal discharge in 90.6% patients. Commonest abnormality on per speculum examination was ectopy (25.4%). Pap smear was abnormal in 3.7%, including 2.9% LSIL and 0.9% HSIL. 13.1% patients were positive on screening by VIA and 11.7% patients were positive on VILI. Sensitivity for VIA, VILI and Pap smear was 89.5%, 100% and 52.6% respectively while the specificity for VIA, VILI and Pap smear was 91.2%, 93.3% and 99.1% respectively.

Conclusion: VILI had the highest sensitivity to detect any grade of dysplasia and its specificity was also good. In low response settings, usual methods of screening like VIA which are cost-effective and feasible can be used as a primary screening modality.

AGGRESSIVE ANGIOMYXOMA OF VULVA AND VAGINA: DIAGNOSTIC DILEMMA

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Background: Aggressive angiomyxoma is a benign tumor affecting the pelvis and perineum. It is a vulvovaginal mesenchymal neoplasm with a marked tendency to local recurrence but which usually does not metastasize. Because of its variable presentation as a soft mass in the vulva, perianal region, buttock, or pelvis, the tumor is often clinically misdiagnosed. The recommended treatment is wide excision.

Case Report: Two patients, one with a vaginal and the other with a vulvar mass, underwent surgical intervention with different preoperative diagnoses; the former as vaginal cyst and the latter as lipoma. Diagnosis and management will be discussed.
OUTCOME OF INDIVIDUALIZED APPROACH TO VULVECTOMY IN CASES OF VULVAL LESIONS

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Objective: To assess outcome in terms of wound dehiscence, recurrence and survival, in cases of vulval malignancies having individualized approach to vulvectomy.

Method: Nineteen preinvasive and invasive vulval neoplasms were operated. Individualized approach was done for vulvectomy. Radical vulvectomy was performed by triple incision and patients’ outcome assessed in follow-ups.

Results: There were 15 invasive malignancy, 3 VIN and one verrucous hyperplasia without atypia. Mean age was 51 years (40-77 years). Mean duration of symptoms was 16 months (4-48 months), with history of itching in 14 (70%), pain in 8 (40%) and growth in 19 (100%) cases. Mean size of lesion was 5.1 cm (0.5 – 8cm). Radical vulvectomy with triple incisions was performed in 15 cases, wide local excision in 3 cases and simple vulvectomy in 1 case. Conservation of vulva was possible in 2 cases. Urethral resection was required in 5 cases and abdomino-perineal resection of rectum was required in 1/2 cases of anal sphincter involvement. Histopathology was squamous cell carcinoma in 13, basalogic carcinoma in 1 and melanoma in 1 case. Three patients were in stage I, 5 were in stage II, 4 were in stage III and 3 patients were in stage IV. One patient received pre-operative and 7 received post-operative radiotherapy. In post operative period, wound dehiscence occurred in 6 cases- complete dehiscence in 2 and superficial in 4. One case had recurrence at pubic bridge which responded to radiotherapy. Survival rate was 17 (90%).

Conclusion: Individualized approach is ideal in cases of vulval malignancies. Triple incision is a good option even in advanced stage.

Rhabdomyosarcoma: childhood cancer

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Background: Rhabdomyoblasts can give rise to several different types of neoplasm that are classified as embryonal, botryoid, alveolar or pleomorphic. Botryoid represent 10% of rhabdomyosarcoma, the most common form of rhabdomyosarcoma encountered in gynaecology. Eighty percent of patients present either with mass protruding from vagina or bleeding. The polypoid appearance, due to location of embryonal type cells under the mucus membrane, allows for early detection.

Case Report: A 14-year old adolescent girl, who attained menarche 2 years ago, complained of bleeding per vaginum in intermenstrual period. Initially she was treated by her family doctor with antibiotics and haemostatic drugs for 5 days. Continued blood stained discharge per vaginum forced the patient to visit the gynaecologist, who performed examination under anaesthesia and an excision biopsy of a mass 6x4x3cm, friable, white in colour. Histopathological examination revealed a diagnosis of rhabdomyosarcoma. After detailed investigations, CT scan, sonography and X-ray, the patient’s disease was staged as stage-1. Chemotherapy was started with Vincristine, Actinomycin-D, Cyclophosphamide at 3 weekly intervals. After three courses of chemotherapy, the patient was again evaluated by CT scan, sonography, X-ray chest, examination under anaesthesia and found to be free from macroscopic disease. She is on regular follow-up, leading a fairly normal life, planned to continue chemotherapy for 3 more cycles.

Discussion: The survival rate for stage-1 is 90%. Long term outlook for a child with rhabdomyosarcoma depends on extent of disease, site, presence or absence of metastasis, response to therapy, age, general condition and tolerance to medication. Young girls have a good prognosis.
**P-096**

INTERESTING CASE OF VULVAL LYMPHANGIECTASIA FOLLOWING TUBERCULAR LYMPHADENITIS

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**Case Report:** A 30 year old presented with tubercular cervical lymphadenitis for which she took ATT for 8 months. After 1 month of completion of ATT, she developed vulval oedema and discharge. She was investigated for STDs and lesions were biopsied. HPE report confirmed lymphangiectasia. Steroid therapy gave her only temporary relief so she was referred from STD clinic to us. On examination bilateral labia was swollen and tender with multiple pustules. Simple vulvectomy was done. HPE report confirmed acquired lymphangiectasia of vulva. Two years follow up of the patient has shown no recurrence of the disease.

**Discussion:** Vulval acquired cutaneous lymphangiomata pose diagnostic and treatment dilemma. Acquired lymphangiectasia is dilatation of lymphatic channels secondary to increased intra-lymphatic pressure due to damage to previous normal deep lymphatics. Causes of acquired lymphangiectasia include post-surgical scarring, recurrent cutaneous infections, scleroderma, tuberculosis, malignancy, radiotherapy. Vulva is an uncommon site for development of lymphangiectasia with only 31 cases reported in literature so far.

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**P-097**

IMIQUIMOD FOR THE TREATMENT OF POST-SURGICAL RECURRENT VULVAR INTRAEPITHELIAL NEOPLASIA: A REPORT OF 3 CASES

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**Introduction:** Management of HPV related Vulvar intraepithelial neoplasia (VIN) is a clinical challenge. Current treatments are suboptimal with high failure rates. Surgery also does not eliminate HPV infection, and disease recurrence is common. Use of 5% Imiquimod is showing promising results as first line treatment in young women and small sized lesions of VIN.

**Objective:** To evaluate the effect of topical application of 5% Imiquimod cream in post surgical recurrent VIN patients.

**Method:** Three patients who underwent simple vulvectomy and wide local excision for VIN with local recurrence within 12 months were treated with local application of 5% Imiquimod cream thrice a week for 3-4 months. Close clinical and vulvoscopic follow up was done for 12 to 18 months.

**Results:** Two women with local recurrence of VIN after surgical treatment had good clinical response with topical Imiquimod and there is no further recurrence or expanding lesions were noted on follow up for up to 18 months. Another woman who showed clinical signs of possible early recurrence at 3 months after wide local excision also did not show any further progression or expanding lesion with Imiquimod usage. All patients had symptomatic relief also.

**Conclusion:** Imiquimod can be used as an adjunctive in post surgical excision VIN recurrences as Imiquimod treatment was also observed to be effective in clearing HPV infection. Its exact role as an adjunctive to surgical treatment with long term follow up and duration of treatment needs to be further evaluated on more patients.
**P-098**

**RECURRENT VULVAL CONGENITAL LYMPHANGIOMA CIRCUMSCRIPTUM - A CASE REPORT**

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**Case Report:** A 35 years old para 2 female presented with recurrent vulval growth for past 20 years despite previous three surgical excisions performed elsewhere. The patient presented with huge vulval growth causing difficulty in walking. Swelling was non tender, covered with hyperkeratotic skin with peach / orange appearance. A careful preoperative planning was done. Vulvectomy was performed with wide margins liberally using electrocautery at the depth of incision to excise sequestrated lymphatic cisterns lying in deep dermis. Postoperative course was uneventful with no recurrence at 1 year follow up.

**Discussion:** Lymphangioma circumscriptum (LC) is a vulval tumor occurring due to developmental defect of lymphatics in deep dermis and subcutaneous tissues. It is an extremely rare and unusual cause of vulval growth. Its various clinical mimics and treatment dilemma confront an unsuspecting surgeon leading to multiple recurrences. Wide excision of normal margins and liberal use of electrocautery at depth of dermis and attempt made to remove all lymphatic cistern in deep subcutaneous tissue is recommended as the preferred surgical procedure.

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**P-099**

**A RARE CASE REPORT OF TUBERCULOSIS OF THE CERVIX AND VULVA**

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Tuberculosis of the vulva is a rare form of genital tuberculosis. It may be presented as isolated chronic ulcerative lesions in the external genital without the tuberculosis of the upper urogenital system, thus the diagnosis of this type of tuberculosis may be delayed. The present case is a tuberculosis of vulva in a 73-year-old woman with chronic external genital ulcers whose treatment with different drugs was failed. In the clinical study and laboratory evaluation tuberculosis of vulva and cervix was detected and after starting anti-tuberculosis therapy the ulcerative lesions were healed.
UMBILICAL SURGICAL SCAR AND VULVAL METASTASES SECONDARY TO ADVANCED CERVICAL SQUAMOUS CELL CARCINOMA: A REPORT OF TWO CASES

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Objective: Association of cutaneous metastasis with cervical carcinoma is a rare finding, with only a few case reports in literature. Herein, we report two cases of cervical squamous cell carcinoma, who later presented as skin metastases on the surgical scar and vulval metastasis as an initial sign of recurrent disease.

Case Reports: Case 1: A 45 year old multiparous female, known case of cancer cervix FIGO stage IIA, underwent Wertheim’s hysterectomy. Six months following surgery, she developed a painless abdominal periumbilical nodule with blood stained discharge at the site of previous surgical scar.

Case 2: A 39 year old para one presented with vulval metastasis six years after a Wertheim’s hysterectomy for FIGO stage IIA cancer cervix at a private hospital elsewhere followed by chemoradiation.

Conclusion: Cervical cancer is the commonest gynaecological malignancy in Indian females and the number one cancer killer of women worldwide. Cutaneous metastasis in women with pelvic gynaecological malignancies has been reported after paracentesis or laparoscopy or laparotomy or no scar (Sister Mary Joseph Nodule). Vulval metastasis has been seen less frequently as a site of spread in cervical malignancy than surgical scar. Occurrence of cutaneous metastasis (nodules, plaques or inflammatory telangiectatic lesions) carries a poor prognosis with a mean survival of approximately 9 months and is considered to be a preterminal event. To conclude, incisional cutaneous and vulval metastasis is a rarity with cancer cervix and is considered as an ominous prognostic sign with a short survival after diagnosis.
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SUBCUTANEOUS METASTASIS FROM CERVICAL CANCER

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Objective: Case-report of rare manifestation of HPV type 58 cervical cancer

Case Report: A 69 year old women visited the gynecologist in Gynecological Division, National Cancer Institute, Thailand with abnormal vaginal bleeding. She had an exophytic tumor of ectocervix 6cm in size. The tumor extended to parametrial and pelvic wall. Results of intravenous pyelography, cystoscopy, sigmoidoscopy and chest film were within normal limit. Cervical biopsy presented non-keratinizing moderate differentiated squamous cell carcinoma. The definite staging was FIGO Stage IIIB. She received concurrent chemoradiation therapy. Seven months after complete irradiation, she had two asymptomatic squamous cell carcinoma subcutaneous nodules at mid-abdomen and supraclavicular lymph node metastasis only. The subcutaneous nodules were tested for HPV. HPV DNA was detected by Hybrid Capture II method (Digene Co.) and show 242,903 in relatively light unit (cut off value was 432 relatively light units) of high-risk HPV type. HPV typing was performed using a general primer-mediated GP5+/6+ polymerase chain reaction enzyme immunoassay, shows this patient had single type of HPV infection, type 58. The patient underwent multimodality treatment with complete excision, radiotherapy and combination of chemotherapy.

Conclusion: This patient is a rare presentation of HPV type 58 cervical cancer with a more aggressive course of disease and risk of treatment failure. In this type of HPV it may needed to use multimodalties treatment and closer follow-up may be indicated.

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ONE CASE OF VULVAR METASTASIS FROM SQUAMOUS CELL CARCINOMA OF CERVIX

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Metastasis to the skin occurs rarely in gynecologic cancer. Although carcinoma of the cervix is the fifth most common malignancy in Korean women, cutaneous involvement originating from cervical cancer is unusual. Common pattern of occurrence is multiple nodule in abdomen, vulva, lower extremities.

We report a case of metastasis from squamous cell carcinoma of cervix to vulva. The patient was diagnosed with cervical cancer IIA. The extensive skin lesion on the vulva occurred 3 months after neoadjuvant chemotherapy, radical hysterectomy and concurrent chemoradiation therapy. We experienced such a case and report the case with brief review of literatures.
COMPARISON STUDY OF OUTCOME OF LARGE LOOP EXCISION OF TRANSFORMATION ZONE (LLETZ) PERFORMED UNDER GA VS LA

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Objective: Large loop excision of transformation zone (LLETZ) is a commonly performed procedure for treatment of cervical intraepithelial neoplasia (CIN). Although in the past it was performed under general anaesthetic (GA), recent NHS cervical cancer screening guidelines suggest that 80% of women should be treated with outpatient procedures, under local anaesthetic (LA)¹. We audited and present the results in our UK general hospital.

Method: We performed a retrospective analysis for all patients who underwent LLETZ between January and December 2008. Following an abnormal smear and a cytological, histological or colposcopic diagnosis of CIN, patients underwent LLETZ for treatment. 133 consecutive procedures were performed, 60 under GA and 73 under LA.

Results: Under GA, 23% patients had a complete excision of margins, 65% had a normal post procedure smear while 20% had an abnormal smear. 90% of the patients who had a Human Papilloma Virus (HPV) test of cure performed were negative. Under LA, 32% had complete excision of margins, 60.8% had a normal smear post procedure, with no positives for the HPV test of cure. We also analysed the indications for procedure and compared complication rates and volumes in each group to judge statistical significance. Data were also compared for patients who had a repeat procedure within 2 years.

Conclusion: LLETZ under LA is a safe and viable alternative to GA. The practice in our hospital is commensurate with national guidelines and we recommend its adoption internationally.

PRIMARY LYMPHOMA OF THE CERVIX: A DIAGNOSTIC DILEMMA

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Primary lymphoma of the uterine cervix is a very rare gynecologic malignancy. This is a case report of a 45 year old lady with primary non Hodgkin’s lymphoma of the cervix. Diagnosis was confirmed by immunohistochemical staining of deep cervical biopsy. She was treated with 4 cycles of CHOP rituximab with local radiation. While reporting (sixteen months after the treatment), she had no evidence of disease recurrence.
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CONSERVATIVE MANAGEMENT FOR STAGE IA1 SQUAMOUS CELL CARCINOMAS OF THE UTERINE CERVIX WITH POSITIVE RESECTION MARGIN AFTER CONIZATION

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Objective: To evaluate the efficacy of cold knife conization with electrocauterization followed by conservative management in patients with stage IA1 uterine cervical carcinoma.

Method: Medical and histopathological records were reviewed retrospectively. One hundred eight patients with stage IA1 uterine cervical carcinoma were treated by cold knife conization with electrocauterization only or followed by hysterectomy. Disease recurrence was defined as a histologic diagnosis of cervical intraepithelial neoplasia (CIN) II or higher grade lesions.

Results: Forty patients underwent conization followed by hysterectomy and 14 (35%) out of these had residual lesion at cervix. The other sixty eight patients underwent conization only without further surgical intervention. Forty patients had clear resection margin without recurrence. Twenty eight patients had involved resection margin. (Ectocervix (+) : 11 cases, Endocervix (+) : 17 cases) There were seven cases of recurrence; one case in Ectocervix (+), six cases in Endocervix (+)

Conclusion: Cold knife conization with electrocauterization appears to be safe treatment option for patients with stage IA1 cervical squamous cell carcinoma, if careful follow-up is guaranteed in patients having CIN III at ectocervical resection margins. However, patients having CIN III at the endocervical resection margin should be managed surgically (reconization or hysterectomy).
FACTORS AFFECTING RESIDUAL LESION IN WOMEN WITH CERVICAL ADENOCARCINOMA IN SITU AFTER ELECTROSURGICAL CONIZATION

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Objective: This study was undertaken to evaluate the factors affecting residual lesion in women with adenocarcinoma in situ (AIS) on electrosurgical cervical conization specimens.

Method: The medical records of 30 women with AIS (1995-2008) who had no associated invasive carcinoma after loop electrosurgical excisional procedure (LEEP) underwent subsequent hysterectomy were reviewed. The mean age was 45.2 years (range, 30-66 years).

Results: Twelve (40%) women presented with AIS on Pap smear. All underwent loop electrosurgical excision procedure. Twelve (40%) women had mixed lesions of AIS and squamous intraepithelial lesion on cervical specimens. Surgical cone margins were clear in 15 (50%) women. Twelve (40%) and 3 (10%) women had involved and non-evaluable cone margins, respectively. Residual lesion was noted in 10 (33.3%) hysterectomy specimens. There was no residual lesion in women with clear cone margins while 80% and 75% of women with involved and non-evaluable cone margins had residual lesion, respectively. These differences were statistically significant. No significant association between the ECC results and the residual lesion was noted.

Conclusion: Approximately one-third of women with AIS on cervical conization have residual lesion on subsequent hysterectomy specimens. Only cone margin status is a significant predictor for residual lesion. Therefore, conservative management in these patients seems to be feasible but careful surveillance is required. However, positive resection margin carries a higher risk for residual AIS or occult invasive adenocarcinoma, warranting additional hysterectomy in these patients.

MAGNETIC RESONANCE IMAGING FOR CARCINOMA CERVIX – A USEFUL ADJUNCT TO FIGO STAGING

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Objective: To evaluate the role of MRI in staging and management of Carcinoma cervix.

Methodology: In this prospective study, confirmed cases of cancer cervix were subjected to MRI after clinical FIGO staging. Sagittal, axial and coronal images were taken using 0.05T superconductive magnet and gadolium contrast was used when required. Additional information gained by MRI was analyzed and MRI staging was compared with FIGO staging.

Results: A total of 31 cases were included. Clinical FIGO staging correlated with MRI staging only in early stages up to II B in 42% of the cases. MRI was better in delineating the disease extent in advanced cases in stage III and beyond. MRI showed bladder and rectal wall invasion without mucosal involvement. In addition some prognostic factors such as tumor volume, uterine corpus involvement, and pelvic lymph node infiltration was made out by MRI. The only limiting factor was the cost factor.

Conclusion: MRI assisted FIGO staging is useful in selecting optimum treatment and follow up of cervical cancer patients. It is noninvasive and provides objective images which may even assist in future to focus radiotherapy.
**P-110
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**DO HEALTH CARE PROVIDERS HAVE A LOWER PREVALENCE OF ABNORMAL PAP SMEAR THAN THE GENERAL PUBLIC?**

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**Objective:** This study compares the prevalence of abnormal Pap smears between samples from healthcare providers (HC) and non-healthcare providers (NHC) by using liquid-based Pap smear (LBP) processing at Thammasat University Hospital’s pathology department, Thailand.

**Method:** Both HC and NHC from the outpatient clinic, Thammasat University Hospital, were screened for cervical cancer by using LBP. All subjects who had abnormal cytology more than atypical squamous cells or atypical glandular cells were counseled to perform colposcopic directed biopsy for pathological confirmation.

**Results:** Both HC and NHC group are similar in number, age, religious, income and education level in general. Prevalence of abnormal Pap smears was 9.8% in HC and 9.3% in NHC (p value = 0.90). HC showed atypical change (ASC, AGC), low-grade squamous intraepithelial lesions (LSIL) and high-grade squamous intraepithelial lesions (HSIL) at 0.8%, 1.6% and 7.4%, respectively. While NHC showed atypical change, LSIL and HSIL at 0.8%, 0.8% and 7.8%, respectively. HC showed equal abnormal Pap smear prevalence to NHC. Further, the percentage of HC and NHC groups with histological confirmed cervical intraepithelial neoplasia (CIN) were no significantly different (4.92% vs. 6.25%, p value = 0.70), likewise CIN 2/3 (1.64% vs. 1.56%, p value = 1.00). According to our study equal rate of abnormal Pap smears occur in both healthcare providers and clients.

**Conclusion:** The prevalence of abnormal Pap smears in healthcare providers was statistically equivalent to their client.

**P-111
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**THE FRACTIONATION OF HDR BRACHYTHERAPY MAY DETERMINE THE RESPONSE IN LOCALLY ADVANCED CERVICAL CANCER**

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**Objective:** The present study was undertaken to compare once a week versus twice a week HDR brachytherapy in carcinoma of the uterine cervix in terms of its efficacy.

**Method:** Eighty two previously untreated patients of locally advanced carcinoma uterine cervix were enrolled into this study. Patients in FIGO stage IB-IIIB were included in the study. They were divided into 2 groups, Group-I (control arm) of 40 patients and Group-II (study arm) of 42 patients. Patients of both groups received concurrent chemoradiation in the form of carboplatin 150 mg IV weekly for 5 weeks during the external beam radiotherapy. In all patients the total dose of EBRT was 50 Gy to whole pelvis in 25 fractions over 5 weeks. Patients of Group-I were administered 7 Gy weekly for 3 weeks and patients of Group-II were administered 4 Gy twice a week for 3 weeks by HDR brachytherapy.

**Results:** The acute effects observed were more or less similar in both groups. Patients with carcinoma cervix stage IIIB showed better local control rate with twice a week HDR brachytherapy schedule as compared to once a week, although the difference did not reach statistical significance. Late toxicities were a little less (though not statistically significant) in the study group.

**Conclusion:** This study has found that the twice a week brachytherapy schedule of HDR brachytherapy is better than once a week brachytherapy in treatment of carcinoma cervix.
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RANDOMISED CONTROLLED STUDY TO EVALUATE THE ASSOCIATION OF HUMAN PAPILLOMA VIRUS WITH CARCINOMA CERVIX AND TO STUDY THE EFFECT OF EXTERNAL RADIOTHERAPY ALONG WITH BRACHYTHERAPY ON HPV TITRE IN CARCINOMA CERVIX

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Objectives: The aim of this study was to evaluate the association of HPV with carcinoma cervix and to analyse the effect of radiotherapy on HPV titre.

Method: Seventy one patients of locally advanced carcinoma cervix were studied. Pre-treatment cervical biopsies were taken and HPV DNA typing and estimation of titre was done. Patients received EBRT in dose of 4600 CGY/23 fr in 4.5 weeks to pelvis and ICRT in dose of 650 CGY weekly for 3 weeks. After 6 months of completion of RT 38 patients were followed in whom HPV typing was done and titre was measured by real time PCR in Pap smear specimen.

Result & Conclusion: Among 71 patients, 35 (49.3%) patients were HPV-16 positive, 5 (7.0 %) patients were HPV-18 positive, 13 (18.3%) patients were HPV (16 and 18) positive and 18 (25.4%) patients were HPV positive. Thirty eight patients were followed. HPV titre was measured before RT and 6 months after RT and there was significant decrease in the titre after RT. HPV titre ranged from 0.00145 to 7090 before RT and from 0.0064 to 71.7 in ng/ml 6 months after RT (P Value < 0.001). The clinical, histopathological and cytological correlation of HPV titre was also done. RT is effective in decreasing the HPV titre. A reduction in titres of their baseline values at the end of RT is also associated with better survival outcomes. Long term disease survival is under assessment.

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PREVALENCE OF UROLOGICAL PROBLEMS IN WOMEN WITH CARCINOMA CERVIX TREATED WITH RADIOTHERAPY

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Objectives: To find out the prevalence of various urological problems in women with advanced stage carcinoma cervix treated with radiotherapy.

Method: A questionnaire incorporating various urological problems was prepared and administered to 40 women with advanced carcinoma cervix treated with radiotherapy attending Gynaecology clinic/IRCH, All India Institute of Medical Sciences, New Delhi from October 2008 to January 2009. It included demographic data of the women, parity, presenting complaints, urinary symptoms and examination findings in relation to urological problems.

Results: The age ranged from 35 to 68 years with mean of 50.8 years. The mean parity was 4.1. Most women were from low socioeconomic status and presented with post menopausal bleeding (42.5%), discharge per vaginum (30%), menometrorrhagia (15%), post coital bleeding (12.5%). The urological symptoms were nil (15%), increased urinary frequency (25%), burning micturition (25%), hematuria (15%), nocturia (10%), urinary incontinence (7.5%), urinary hesitation (2.5%). Cystoscopy revealed normal findings (65%), cystitis (17.5%), bullous oedema (10%), growth (7.5%). Treatment given for urinary symptoms were assurance along with oral hydration (45.5%), urinary antibiotics along with alkalisers (35%), admission along with saline irrigation plus alum irrigation (19.5%).

Conclusion: There is a high prevalence (85%) of urological problems in women with advanced carcinoma cervix following radiotherapy.
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RADIATION SPARING MANAGEMENT FOR LOCALLY ADVANCED CERVICAL CANCER

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Background: Cervical cancer is still the most common cause of cancer related morbidity and mortality in our country. Due to lack of organized screening programs, a majority of the patients present in advanced stages with large growth. Results of treatment of early stage disease are satisfactory, however treatment of locally advanced cervical cancer is still a matter of controversy. Till recently, radiotherapy was the only option with little improvement in survival in last 50 years and extensive morbidity we are all aware of. Current standard of care in locally advanced cervical cancer is chemoradiation, however other options are being explored to further improve survival and to reduce morbidity. In many developing countries radiotherapy facilities are not widely available and in some African countries no radiotherapy facilities are available at all, hence the need for radiation sparing management options.

Method: Neoadjuvant chemotherapy followed by radical hysterectomy in locally advanced cervical cancer has been studied widely in phase II and III trials in the last two decades. Results of phase II trials are in favour of NACT for locally advanced cervical cancer. Results of randomized phase III trials are awaited.

Results and Conclusion: In our study, retrospective analysis of patients who have been treated with NACT followed by radical hysterectomy was done and results suggest that in at least 40-50% of patients radiotherapy was not needed.

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RETROSPECTIVE STUDY OF LOCALLY ADVANCED CANCER CERVIX (LACC) AFTER NEOADJUVANT CHEMOTHERAPY (NACT) AND RADICAL SURGERY

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Objectives: Chemoradiation is standard treatment of LACC with 30-50% reduction in death. However, NACT is being used to downstage and make LACC resectable. Efficacy of NACT and radical surgery was studied in 49 LACC patients, in terms of optimal pathological response, need of adjuvant radiation for adverse histopathology, pattern of disease relapse, and disease-free survival.

Results: Stage 2b patients were 24 (48.98%) while 11 (22.45%) were stage 3b and 2 were stage 4a. Squamous carcinoma was seen in 91.83%. Median follow up was 14 months (range, 0.5 - 62.9). Complete response (CR) with no microscopic disease was seen in 8 (16.3%) while 7 had near CR with CIN or microinvasive cervical disease. Adjuvant radiotherapy was given to 34 (69.4%) patients as they had partial pathological response (PR). Eleven (22.4%) recurrences occurred, all in PR patients with their median disease free interval (DFI) being 28.7 months. Patients with optimal pathological response had no relapse during their median follow up of 18.46 months. In patients who relapsed, mean DFI was 6.5 months (range, 1-14). Five (20.8%) of stage 2b, 4 (36.4%) of stage 3b, while 2 (100%) stage 4a patients recurred. Three pelvic recurrences involved trigone in one, psoas in another, and vault in third. Of 8 distant failures, one had liver and another vertebral metastasis, while 2 developed metastatic supraclavicular nodes. Rest had obstructive uropathy consequent to paraaortic lymphadenopathy.

Conclusion: This study suggests that postoperative radical radiotherapy is needed in the majority of LACC patients, especially so with more advanced stages, hence efficacy of NACT in LACC is inconclusive.
Phase II Trial of Sequential Combination of Cisplatin After Topotecan in Persistent or Recurrent Cervical Cancer

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Objective: Combination chemotherapy of cisplatin on day 1 and topotecan on day 1-3 has been well known for recurrent or persistent cervical cancer treatment. The aim of this study is to evaluate the efficacy and toxicities of combination chemotherapy of cisplatin on day 3 after topotecan on day 1-3 administration in persistent or recurrent cervical cancer patients.

Method: Topotecan 0.75 mg/m² was administered as a 30-minute infusion for 3 consecutive days and cisplatin was given at a dose of 50 mg/m² intravenously (IV) over 1 h on day 3, every 21 days. Tumor response and regimen toxicity were assessed using established GOG criteria.

Results: Twenty-four patients were evaluable for tumor response and toxicity. A total of 92 cycles of chemotherapy were administered during the study period. An overall response of 29.2% (7 of 24 patients) was found which consisted of 4 CR and 3 PR. Five patients (20.8%) had SD. Treatment delays of more than 7 days occurred in 16.7% of courses. There were 59 days of delays in treatment in 21 of 92 (22.8%) cycles and 2 episodes of dose reduction in 2 patients. Overall, grade 3/4 anemia, thrombocytopenia, and neutropenia were experienced in 13.1%, 1.1%, and 18.5% of the courses, or 33.4%, 4.2%, and 45.8% of the patients, respectively. Non-hematologic toxicities were generally mild.

Conclusion: We observed that the combination chemotherapy of topotecan following cisplatin showed modest activity and relatively low rate of hematologic toxicities in recurrent or persistent cervical cancer patients.
ANATOMICAL AND HISTOLOGICAL BASIS OF COLPOSCOPY

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Squamous cancer of the cervix almost always arises within the cervical transformation zone. Knowledge of the anatomy and histology of the cervical transformation is the basis for understanding the practice of colposcopy.

In the pre-pubertal cervix, the endocervix is lined by columnar epithelium, a single cell lined epithelium that overlies cervical stroma. The ectocervix and vagina are lined by a multilayered squamous epithelium which is adapted to withstand the potential trauma of intercourse and childbirth. The two types of epithelium meet at the anatomical external os.

At puberty there is a change in structure of the collagen of the cervix which results in an eversion of the lower endocervical canal (ectropion) exposing the columnar epithelium to the low pH of the vagina. As a result there is reserve cell hyperplasia and a new squamous epithelium replaces the exposed columnar epithelium, produced by the process of squamous metaplasia. Originally the metaplasia is immature, and then matures. At the climacteric the collagen fibres change again, this time the transformation zone is withdrawn within the endocervical canal. At different times in a woman’s reproductive life and under different hormonal influences, therefore, the site of this metaplasia – the transformation zone – may be sited at different locations.

Original squamous epithelium is a smooth, pink featureless epithelium originally established on the cervix and vagina. There are no remnants of columnar epithelium identified, such as mucus-secreting epithelium, cleft openings, or Nabothian cysts. The epithelium does not stain white after the application of a dilute solution of acetic acid; it stains brown after application of Lugol’s iodine.

Columnar epithelium is a single layer, mucus-producing epithelium that extends between the endometrium cranially and either the original squamous epithelium or the metaplastic squamous epithelium caudally. At colposcopy after application of acetic acid the area has a typical grape-like structure. Columnar epithelium is normally present in the endocervix and may be present on the ectocervix (ectopy) or, on rare occasions, in the vagina.

The transformation zone (TZ) is the area between the original squamous epithelium and columnar epithelium within which varying degrees of maturity may be identified. Immature metaplastic epithelium may stain slightly white after the application of acetic acid and partially brown after the application of Lugol’s iodine. Components of a normal transformation zone may be islands of columnar epithelium surrounded by metaplastic squamous epithelium – cleft openings and Nabothian cysts. The mean depth of clefts in the cervix from the surface is 1.2 mm but clefts may extend to a depth of 5.6 mm.

- **Type 1** TZ - completely ectocervical and fully visible, may be small or large
- **Type 2** TZ - endocervical component that is fully visible, and an ectocervical component, may be small or large
- **Type 3** TZ - endocervical component is not fully visible, may have an ectocervical component that may be small

In a few women the TZ may extend caudally onto the upper vagina, usually with an anterior and posterior triangle or tongue.

- An unsatisfactory colposcopy examination occurs when the squamocolumnar junction cannot be visualised. It may also occur if associated trauma, inflammation, or atrophy preclude a full colposcopic assessment, or when the cervix is not visible.

Colposcopy involves examining the cervix, notably the TZ under magnifications of x6 and x10 using solutions of saline, dilute acetic acid and lugol’s iodine.

Acetowhite epithelium: After application of 3-5% acetic acid, areas of high nuclear density appear white. Generally the denser the acetowhite change, the faster the change becomes apparent and the longer the epithelium holds the change, the more severe the lesion may be. Dense acetowhite change within columnar epithelium may indicate glandular disease.

**Punctuation:** A focal colposcopic pattern in which capillaries appear in a stippled pattern. The finer the punctuation, the more likely the lesion is to be low-grade or metaplasia; coarser punctuation is more likely to be a high-grade lesion.

**Mosaic:** A focal colposcopic appearance in which new vessel formation appears as a rectangular mosaic pattern. The smaller the mosaic, the more likely the lesion is low-grade or metaplasia. The coarser, wider, and more irregular the mosaic, the more likely the lesion is to be of major grade.

**Iodine negativity:** After application of Lugol’s iodine, mature squamous epithelium, which contains glycogen, will stain deep brown. Iodine negative areas may represent immature metaplasia, CIN or low oestrogen states (ie, atrophy). A speckled appearance in an area with slight acetowhite change may represent immature metaplasia or low-grade intraepithelial neoplasia. Complete iodine negativity, a yellow staining in an area that has appeared strongly acetowhite, is highly suggestive of high grade intraepithelial neoplasia.

**Atypical vessels:** A focal abnormal colposcopic pattern in which the blood vessel pattern appears not as punctuation or mosaic or as the finely branching capillaries of a normal epithelium, but rather as irregular vessels with an abrupt and interrupted course appearing as commas, corkscrew capillaries, or spaghetti-like forms.

Colposcopic features suggestive of metaplastic change:
- A smooth surface with fine, uniform-calibre vessels.
- Mild acetowhite change.
• Negative or partial positivity with Lugol’s iodine
Colposcopic features suggestive of low grade disease (minor change)
  • A smooth surface with an irregular outer border.
  • Slight acetowhite change, slow to appear and fast to disappear.
  • Mild, often speckled iodine positivity
  • Fine punctation and fine regular mosaic
Colposcopic features suggestive of high grade disease (major change)
  • A generally smooth surface with a sharp outer border.
  • Dense acetowhite change, that appears early and is slow to resolve; it may appear oyster white.
Iodine negativity, a yellow appearance in a previously densely white epithelium.
  • Coarse punctation and wide irregular mosaics of differing size.
  • Dense acetowhite change within columnar epithelium may indicate glandular disease.

W.1.4
PITFALLS OF COLPOSCOPY
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Traditional colposcopy for the detection and treatment of cervical precancerous lesions has a long and established history, and remains the main examination technique for the investigation of screen-detected cervical abnormalities. There are several situations which complicate the colposcopic examination, usually because they result in changes in the appearance of the cervix, thus making the task of identifying cancer precursors more difficult. This lecture will explore some of these situations and will include colposcopy of glandular lesions, pregnancy, the congenital transformation zone and atrophy.
THE ROLE OF COLD COAGULATION IN THE TREATMENT OF CERVICAL INTRAEPITHELIAL NEOPLASIA (CIN)

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The treatment of cervical intraepithelial neoplasia (CIN) is carried out with a variety of surgical methods leading to the destruction or excision of the entire transformation zone (TZ) bearing the CIN and potentially at risk for cervical neoplasia. It is the general consensus that a method of destroying the TZ will be as successful in treating women with CIN as are the excision techniques, when the lesion is entirely confined to the ectocervix (without endocervical extension) and the TZ is fully visible. Currently, cryotherapy is the most widely used destructive treatment method for CIN. The histological nature of the lesion chosen for destructive therapy can be established by biopsies directed before the treatment. Among the other two destructive treatment methods, laser is not feasible in low-resource settings due to the expensive equipment required and the high-level of expertise needed for the providers. On the other hand, cold coagulation is a feasible alternative to cryotherapy in such settings as it uses a light weight (3 kg), portable electrical generator to heat a probe to 100-120°C that is applied on cervix for 40-60 seconds to destroy the TZ. Cure rates of CIN following cold coagulation reportedly vary from 93-99%, depending upon the size of the lesions, histological grade and number of treatment applications and has been shown to be a safe and acceptable form of treatment. Results in terms of cure rates, safety and acceptability will be discussed in detail.

HPV DETECTION AND GENOTYPING IN TRIAGE OF ASC-US

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Cervical cancer can be prevented by cervical cytology screening which can detect the cancer cells and its precursors. The most common abnormal cytological finding encountered in screening program is “atypical squamous cells of undetermined significance (ASC-US)”. Human papillomaviruses (HPV) have been recognized as etiologic agents of cervical cancer. HPV DNA testing has been reported to be an option in the triage of women with ASC-US since ASC-US cases carrying high risk type HPVs were found to have markedly higher risk of harboring high grade cervical cancer precursors. Under current guidelines in most developed countries with available HPV test, women with ASC-US found to be positive for HPV can be referred for colposcopy directly while women who are HPV negative can be reassured and asked to rejoin cytology screening 12 months later. Prophylactic vaccines against HPV 6, 11, 16 and 18 have been adopted for protection against cervical cancer and genital warts. It is likely that the incidence of abnormal cervical cytology caused by vaccine type HPVs can be reduced leading to socioeconomic benefit. Since the immunity conferred by vaccines is type-specific, it is important to understand the prevalence of HPV genotypes in ASC-US to better predict the impact of HPV vaccine on possible change in prevalence of the disease in the community.
LIQUID BASED CYTOLOGY AND REFLEX HPV TESTING

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Liquid based cytology has revolutionized the practice of cervical smear cytology because of automation and high degree of quality assurance regarding processing and staining. Because the specimen is obtained in a preservative solution, it lends itself easily to application of multiple tests being performed on the same sample, including cytology and HPV testing. The purpose of cervical sampling is early detection of high grade squamous intraepithelial lesions (HSIL) which are subjected to ablative treatment to prevent progression to cancer.

Cervical smear cytology has the advantage of high specificity but poor sensitivity. Testing for high risk HPV by Hybrid Capture II (HCII) has very high negative predictive value, since patients without HSIL are invariably negative for HPV by HCII. However the positive predictive value is poor, since high risk HPV which is not causing HSIL are also detected in close to 12-16% of the screened population.

Optimum combination of cytology and HPV testing by HCII was established in the ALTS trial, where it was determined that all patients should be screened with cervical smear cytology. Patients diagnosed on cytology to have HSIL or ASC-H undergo a straight colposcopy directed biopsy to confirm HSIL followed by ablative therapy. Patients diagnosed on cytology to have LSIL or ASC-US need triage with HPV testing by HCII. Patients with HCII negative are followed up. Patients who are HCII positive are subjected to colposcopy directed biopsy for evaluation of the cervical lesion. Those detected to have HSIL on biopsy undergo ablative treatment while patients with biopsy negative for HSIL are followed up.

This triage procedure for LSIL and ASCUS can be done by “reflex HPV testing” in which the liquid based cytology specimen is stored after processing for cytology. In patients having an abnormal cytology, the sample is tested for HPV by HCII. By this means, there is no necessity for recall of patients for re-sampling to undertake the HPV test. This has now become the standard of care for cervical smear cytology and HPV testing.

TYPES OF HPV DNA TESTS AND THE ROLE OF HPV GENOTYPING

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More than 100 types of human papillomaviruses (HPVs) are known. Mucosal HPV are classified as high-risk (HR) and low-risk (LR) types depending on the associated disease risk. Specific aetiological diagnosis of HPV types is possible only by molecular methods, since the virus is not routinely cultivable and serological methods are not reliable.

Various methods for HPV DNA detection that have been used in the diagnosis of cervical (and other) cancers, with or without genotyping, include those based on nucleic acid hybridisation (Southern blot) without prior amplification, hybridization in liquid phase with signal-amplification and immunoblot-based detection using an antibody specific for RNA-DNA hybrids (e.g., Hybrid Capture assays) and a variety of target-amplification methods like those based on the polymerase chain reaction (PCR), often followed by genotyping by hybridization to immobilized HPV type-specific probes e.g., reverse line blot (RLB, which can detect as many as 37 high and low risk HPV genotypes) or line probe assay (LiPA). Other techniques for HPV detection include the use of a reverse transcriptase (RT) PCR for mRNA transcripts of specific genes, real-time PCR (which is quantitative and may designed to be HPV type-specific or multiplexed to detect and quantify multiple genotypes) and nucleic acid array-based methods (which have the advantage of high throughput).

Both HPV DNA detection and HPV genotyping can enhance current cervical cancer screening programmes. The current FDA-approved high-risk HR-HPV DNA diagnostic tests are capable of detecting 13 or 14 high-risk HPV genotypes out of HPV- 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66 and 68. The 2006 ASCCP Consensus Conference determined the clinical role of HPV genotyping assays and recommended that in cytology negative women 30 years and older who are HPV DNA positive by these, molecular genotyping assays that specifically detect HPV 16 and 18 would be clinically useful for determining which women should be referred for immediate colposcopy, and which could be followed-up with repeat cytology and HR-HPV testing in 12 months.

Subsequently, FDA has approved HPV genotyping tests for assessing the presence or absence of specific HR-HPV genotypes 16 and 18 to be used adjunctively with HPV DNA tests in patients with atypical squamous cells of undetermined significance (ASC-US) in cervical cytology. The results of these tests are not intended to prevent women from proceeding to colposcopy.

However, to prevent over-testing and unnecessary, current ASCCP guidelines do not recommend HPV DNA tests and HPV genotyping for
Numerous studies have established that testing for HPV is significantly more sensitive than Pap cytology for detection of CIN 2+. There are also indications that testing for HPV might be the most effective method of cervical cancer screening in developing countries. Moreover, HPV testing would be warranted as a primary screening tool in the era of HPV vaccination. Both HPV DNA and mRNA-based tests are available to detect high-risk oncogenic HPV types. Due to the ubiquitous and transient nature of HPV infection in women, the specificity and PPV value of DNA-based tests tend to be low. Since the oncogenic process is initiated by persistent HPV infection and mediated by the up-regulation of E6/E7 oncoproteins, testing for E6/E7 oncogene activity could be more specific and a better predictor of cervical cancer risk than the detection of HPV DNA. Detection of E6/E7 oncogenic activity can be achieved by testing for E6/E7 mRNA transcripts.

The Hybrid Capture 2 (HC2; Qiagen) test detects DNA of 13 high-risk oncogenic HPV types, has been extensively validated, and is recommended as a reference test to evaluate any newly developed HPV tests. The clinical performance of the following HPV DNA and RNA-based tests for the detection of CIN 2+, compared with HC2, may be summarized as follows: The AMPLICOR HPV test (Roche) detects DNA of 13 HR types, and is slightly more sensitive but less specific than HC2. The Cervista HPV HR test (Hologic) detects DNA of 14 types and has similar performance as HC2. The PreTect HPV-Proofer (Norchip) test detects E6/E7 mRNA of 5 HR types, and is less sensitive but more specific than HC2. The APTIMA HPV assay (Gen-Probe) detects E6/E7 mRNA of 14 HR types, and has similar sensitivity but higher specificity than HC2. While E6/E7 mRNA-based tests appear to have the potential to identify CIN2+ lesions that are likely to progress into cervical cancer more so than DNA-based tests, large scale population based studies are required to fully assess the predictive values and clinical utilization of these tests. The relevance of prevalent genotypes in cervical precancer and cancer in HPV-based screening and triage, and some screening algorithms incorporating HPV testing will be presented and discussed.

In addition to the clinical role of HPV genotyping, various scientific and epidemiological justifications exist for the application of these methods. Multiple HPV types are found in about 20–30% of HPV infections and quantitative genotyping-based methods are necessary to determine the contribution of each genotype. Background information on the geographical distribution of HPV genotypes and their associated diseases is required for designing prophylactic immunization programmes and to monitor changes in distribution and prevalence of genotypes after initiation of such programmes. Recurrent infection can be identified by genotyping methods for specific HR-HPV genotypes. Novel strains can be identified if a comprehensive genotyping method is unable to type the strain into one of the known HPV genotypes, despite being positive by an HPV consensus group-specific PCR.

The role of HPV genotyping is expected to expand as newer generations of HPV genotyping tests are developed and licensed. For this, a continuing process of reappraisal of guidelines would be necessary in the future.
MOLECULAR BIOMARKERS IN CERVICAL CYTOLOGY: SCREENING AND TRIAGE
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Cervical cytological examination is a widely applied screening method for cervical cancer and its precursors. Liquid based cytology, besides produce good quality cervical cytology preparation, allows the use of ancillary laboratory techniques to improve the efficiency of cancer detection. Besides the commonly applied Human papilloma virus (HPV) tests, cervical cytology samples can also be used for genetic and epigenetic studies such as mutation and gene promoter methylation analysis as well as assessment of telomerase activity. The ploidy of epithelial cells, the copy number and the expression of genes can also be assessed with an intact morphological background by immunocytochemistry and in situ hybridization. p16 immunocytochemical study on liquid based cytology has been reported to have a high positive predictive value in detection of cancer cells and their precursors. We have earlier applied chromosome in situ hybridization (ISH) as well as Ki-67 and telomerase immunocytochemistry in liquid based cervical cytology as attempts to assist the detection of carcinoma cells and high grade squamous intraepithelial lesions (HGSIL). Recently, we reported p63 and p73 immunocytochemistry to be potential good markers for detection of carcinoma and HGSIL in cervical cytology samples from screening population. Significantly higher p63 and p73 indices were found in HGSIL or carcinoma. Among atypical squamous cells of undetermined significance (ASC-US) and LGSIL, p63 and p73 indices of cases that subsequently progressed to HGSIL were significantly higher than those that did not. p63 and p73 immunocytochemistry was therefore useful for triage management of women with ASC-US and LGSIL. Amplification or deletion of genes has been identified in cervical cancers and their precursors by comparative genomic hybridization, real time PCR and ISH. Actually, evaluation of copy number of such candidate genes can be applied in cervical cytology samples by in situ hybridization. Combined cytopathologic evaluation and application of molecular markers in cervical cytology can facilitate reliable detection of cervical cancer and to allow triage of equivocal diagnoses based on a single clinical collection.

EXTERNAL AND INTERNAL QUALITY ASSURANCE FOR HPV TESTING LABORATORIES
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Objective: To explore opportunities and processes for quality assurance of HPV testing. Internal quality control and external quality assurance should exist in all laboratories which provide HPV results used for clinical management or for surveillance which influences healthcare decisions and policy.

Methods: We first developed a system of regular provision of well-characterised materials and reproducibility testing in the English HPV/LBC pilot study in 2003-2004. Thereafter we provided clinical materials for 3 pilot distributions for HPV testing through UK National External Quality Assessment Service (UKNEQAS) in 2007-08, followed by a scheme in 2009. Several external quality assurance panels have been developed to assess analytical sensitivity, e.g. QCMD and WHO HPV LabNet, and are particularly useful for surveillance. HPV standards for HPV 16 and 18 have been recently produced by the UK National Institute for Biological Standards and Control (NIBSC).

Comments: Laboratories doing significant HPV testing must develop their own internal quality control samples for regular use and make use of available standards to assess their own performance. Participation in robust EQA of HPV molecular testing is essential for understanding population needs in relation to HPV disease control, monitoring the impact of vaccine and making use of HPV results to inform clinical management. All elements are necessary to ensure high quality, reproducible and comparable results from around the world. This presentation will concentrate on principles and processes for development and use of control materials and external panels based on experience in the Scottish HPV Reference Laboratory.
Pre-neoplastic lesions are important to recognize at an early stage for appropriate therapy and prevention of their progression to invasive malignancy. In the female genital system, the cervix has been the main focus of screening programmes for detection of pre-neoplastic lesions (cervical intraepithelial neoplasia, CIN). A similar spectrum of lesions also involves the vulva and vagina (vulvar intraepithelial neoplasia, VIN and vaginal intraepithelial neoplasia, VAIN respectively). The traditional categorization of vulvar lesions into Bowen’s disease, and bowenoid papulosis has recently been grouped under VIN as bowenoid dysplasia. As with cervix, lesion of VIN of Bowen’s disease type have shown a strong association with HPV-16 and occur in younger age group that invasive squamous cell carcinoma (SCC). VIN is classified using three-tier system into VIN I, II and III, which differ in the thickness of the involved epithelium. The therapy of VIN depends on age of patient and characteristics of the lesion and ranges from wide local excision to skinning vulvectomy. Apart from VIN, lichen sclerosus of vulva also progresses to squamous cell carcinoma in a small proportion of patients. VAIN or vaginal intraepithelial neoplasia, usually occurs concomitantly with neoplasms of lower genital tract. It most commonly involves upper third of vagina in continuation with the cervical lesions. In diagnosis of VAIN, transitional cell metaplasia needs to be kept in mind to avoid overdiagnosis.
Cervical histopathology remains the gold standard for final diagnosis of cervical pathology. A wide variety of benign and malignant tumours, as well as non-neoplastic tumour-like conditions, can be diagnosed by light microscopic examination. In recent years, immunohistochemical techniques have been found useful to assist in the differential diagnosis of cervical lesions. For histological typing of cervical tumours, certain lineage markers are useful in the differential diagnosis of lesions of epithelial, stromal, smooth muscle, lymphoid, melanocyte or trophoblastic origins. Immunohistochemistry is particularly valuable in distinguishing metastatic and primary carcinomas in the uterine cervix and ascertaining origin of metastatic carcinoma in difficult clinical scenarios involving the uterine cervix.

Immunohistochemical markers, such as oestrogen receptor, carcinoembryonic antigen and p16, help distinguish between a cervical adenocarcinoma and an endometrial adenocarcinoma of endometrioid type. The distinction between a large cell neuroendocrine carcinoma and a poorly differentiated squamous or adenocarcinoma may be problematic. Markers for neuroendocrine differentiation, such as chromogranin, synaptophysin, and CD56 may be useful. On the other hand, p63 is useful in distinguishing small cell neuroendocrine carcinoma from small cell squamous carcinoma and in confirming that a poorly differentiated carcinoma is squamous in type.

The diagnostic and prognostic value of protein products of oncogenes and tumour suppressor genes, as well as proliferation and apoptosis markers is also gaining importance. MIB1 and p16 are particularly useful in the assessment of pre-invasive cervical squamous and glandular lesions. CD10 is suggested to be a marker of mesonephric lesions.

Since molecular targeted therapy of cervical cancer is relatively less established compared with other gynaecological cancers, the role of immunohistochemistry in such clinical application is less explored. On the other hand, diagnosis of an infectious disease in the uterine cervix is also important. Besides special histochemical stains, antibodies against viral protein including human papilloma virus and cytomegalovirus have been found useful to assist diagnosis. Such information will permit greater diagnostic accuracy and tailoring of treatment regimens in an individual patient. Pathologists and gynaecologists should bear in mind that no marker is specific and interpretation of any findings derived from adjunct laboratory techniques must be employed in conjunction with the morphologic and clinical findings.
HPV prophylactic vaccination is favourably viewed by most with great promise for the elimination of cervical cancer based on a particularly powerful linkage, namely that cervical cancer arises secondary to 10+ year infection by carcinogenic HPV in virtually 100% of cases. It is obvious that complete control of the disease, in theory at least, may be accomplished by global HPV vaccination programs. There are some important questions remaining, among these are: the real world effectiveness of the HPV vaccine; the timeframe to realize this effectiveness; how to maintain a steady state of control; and how much it will cost. The best way to screen post-vaccination is not yet obvious as there is a dearth of data and as with most areas of public health, simplistic scenarios often become entangled in the complex details. It appears obvious to many epidemiologists that HPV DNA screening should become the new partner of HPV vaccination. Carcinogenic HPV types cause the cancer, established HPV present before vaccine administration is likely to persist and waning immunity will allow breakthrough of new infections in genital epithelia. Tests for HPV DNA are remarkably sensitive and are becoming less costly every year, thus follow-up tests for HPV are the logical choice. The legitimate role of cervical cytology in a post-vaccine era will be limited to triage of HPV screening tests and possibly in combination with HPV to assess efficacy of surgical treatments.

In the USA today and in many European countries the HPV vaccine has been administered to only a small fraction (less than 30%) of the target group of adolescent girls and to only a minuscule percentage of females outside the target ranges. In most of Asia and Latin America the vaccination of some populations has started but generally gingerly and amid concerns of affordability and effectiveness. In a nutshell the post-vaccination era will arrive slowly and thus screening scenarios must evolve in tandem over a period of 20-30 years or longer. There are important details of HPV tests to be worked out and in the absence of data one must speculate on the general attributes of these tests. Current HPV tests are initially suitable for vaccinated women but there is already a growing importance for ultrasensitive genotype-specific tests to detect very low levels of vaccine targeted HPV to demonstrate clearance. Continued screening of vaccinated women will be necessary but at long intervals (10 years or longer) with ultrasensitive HPV tests and additional followup (HPV genotype, persistence, RNA expression or abnormal cytology) for positive screening results. We must not forget the 15 to 20% of cervical cancers caused by HPV types not effectively controlled by current vaccines. It is advisable in fully vaccinated populations for all women to receive a broad genotype spectrum HPV screen at least once every ten years starting at age 30 to 35 until age 55 or 60 at which point screening can stop in HPV negative women.
LAPAROSCOPIC RADICAL HYSTERECTOMY

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Worldwide, cervical cancer is the second major cause of death in women of reproductive age. An effective strategy to decrease mortality is screening and early detection for maximum therapeutic benefit. Treatment options vary from surgery alone or concurrent chemoradiation or combinations of these, depending on the FIGO stage. The role of neoadjuvant chemoradiation is still under trial. Surgery for cervical cancer ranges from conisation to radical hysterectomy, younger patients may even opt for radical trachelectomy. Previously surgical procedures were more invasive with more intra- and post-operative complications and a longer hospital stay, but now in the modern era of minimally invasive surgery this radical procedure can be done laparoscopically with promising results in terms of fewer complications, shorter hospital stay, minimal blood loss and a faster postoperative recovery. The magnification that laparoscopy provides is advantageous in that it helps in better visualization of important and vital structures like the ureter which can be dissected and traced in its entire pelvic course. Similarly the pelvic vessels can be visualized more clearly facilitating a more precise and extensive pelvic lymphadenectomy. Dissection in more depth helps more complete removal of the parametria and lymphatics. The tissues heal faster due to early ambulation. This surgery however depends on the surgeon’s expertise in this procedure. It can be safe only in the hands of a surgeon who is well versed with laparoscopic planes of dissection, suturing and the intelligent use of appropriate tissue desiccating devices. The procedure may take about 3-4 hours, but this improves with expertise.

The procedure involves a careful dissection of the ureter in its entire course from the pelvic brim to insertion in the bladder. Prior to the ureteric tunnel dissection the rectum is separated from the vagina and pararectal spaces are created, the utero-vesicular fold is opened and the bladder is dissected down after creating the paravesicular spaces. The uterine arteries are ligated at the origin from the internal iliac arteries, following this the ureter is dissected from the ureteric tunnel till its entry into the bladder. The specimen is then removed after resecting around 3-4cm of vagina and detaching the infundibulopelvic ligaments. The details of the procedure will be shown in the video.

Laparoscopic radical hysterectomy will soon be established as a gold standard for the treatment of early stage cervical cancer especially in young women who are unfortunate to be affected by this disease.

SENTINEL NODE EVALUATION IN CERVICAL & VULVAR CANCERS

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Background: Sentinel lymph node is the first echelon lymph node or first station of lymph node to drain the primary tumor site and the first to receive metastatic cells from the primary site. It is postulated that if this first echelon SLNB is negative for metastasis, the remaining lymph nodes draining the primary site are also negative and hence unnecessary systematic lymphadenectomy and resultant complications and morbidity like lymphorrhoea, lymphoedema and neuralgic pain can be avoided. The role of sentinel node biopsy in the management of gynaecologic malignancies is not well established. In view of the lower incidence (10-15%) of pelvic lymph node metastasis in early cervical cancer, sentinel lymph node mapping and biopsy could be a useful technique to avoid unnecessary lymphadenectomy. Especially in vulval cancers, SLNB is highly useful since these are the women who are usually in the 7th-8th decade with associated co-morbidities. In the surgical management of vulval cancers, the morbidity of surgery from bilateral groin dissection is more than the primary resection per se. It is highly useful in these old women in avoiding these complications and improving the quality of life.

Method: Biopsy proven early stage cervical cancer (FIGO Stage IB1, IB2) and vulval cancers were subjected to intra-operative sentinel lymph node mapping using a hand-held gamma probe (hot nodes) and identification of the blue nodes was done following peritumoral injection of radioactive colloid and methylene blue preoperatively. Definition of SLNB is the deep blue stained lymph node identified intraoperatively or the hottest node detected with hand-held gamma probe with 1:20 ratio of activity in comparison with primary activity and all nodes 1:10 activity in comparison with highest activity primary node. My talk shows a video presentation of the technique of SLNB using combination of blue dye and Radonon colloid and use of hand-held gamma probe, the detailed procedure.

References:
Towards Eradication of Cervical Cancer

W.3.12

LAPAROSCOPIC GROIN DISSECTION

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Inguino femoral dissection is indicated for all surgically managed cancers of the vulva and lower half of the vagina. In clitoral and lower vaginal cancers, bilateral (lower) dissections are required and pelvic lymphadenectomy is recommended. Videoadsincopic groin dissection has the same indications and should not be performed in the presence of obvious metastatic involvement. If nodal involvement is detected during the procedure, conversion to open technique is recommended. Dargent performed 15 dissections using video endoscopic technique combined with liposuction between July 1994 and July 1996.

We have performed video endoscopic inguinal femoral dissection in 15 cases since Feb 2006. After studying the pioneer work of Tobias et al. Showcasing here the simple video endoscopic technique of inguino femoral dissection used by us and the results obtained thereof we learnt that even though the technique has a longer operating time (120-160 minutes), complications such as induration and skin flap necrosis are markedly reduced.

Surgical Technique: The video endoscopic inguinal lymphadenectomy (VEIL) technique was standardized in the following surgical steps:
1) Positioning of the inferior member extended in abduction, 2) Introduction of 3 work ports distal to the femoral triangle, 3) Expansion of the working space with gas, 4) Retrograde separation of the skin flap with a harmonic scalpel, 5) Identification and dissection of the long saphenous vein until the oval fossa, 6) Identification of the femoral artery, 7) Distal ligature of the lymph node block at the femoral triangle vertex, 8) Liberation of the lymph node tissue up to the great vessels above the femoral floor, 9) Distal ligature of the long saphenous vein, 10) Control of the saphenofemoral junction, 11) Final liberation of the surgical specimen and endoscopic view showing that all the tissue of the region was resected, 12) Removal of the surgical specimen through the initial orifice, 13) Vacuum drainage and closure of the incisions.

Conclusion: The VEIL technique is feasible and allows the radical removal of inguinal lymph nodes in the same limits of conventional surgery dissection. The main anatomic repairs of open surgery can be identified by the endoscopic view, confirming the complete removal of the lymphatic tissue within the pre-established limits. Preliminary results suggest that this technique can potentially reduce surgical morbidity. Oncologic follow up is yet premature to demonstrate equivalence on the oncologic point of view.

W.3.15

LAPAROSCOPIC RADICAL HYSTERECTOMY WITH ROBOTIC ASSISTANCE

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Since mid-2008, we have started to perform Laparoscopic Radical Hysterectomy with Robotic Assistance (Da Vinci). The advantages of the Da Vinci Robots over conventional laparoscopic radical hysterectomy include (1) better vision: with a 3 D camera; with easy manipulation of the video camera which can be put deep into POD and still maintaining a good angle of vision; with full control by the operator; without tremor despite long hours of operation leading to fatigue of assistant holding onto the camera and better control on the intensity of the light. (2) better instruments: with the 270 degree wrist like movement of the instruments that can manipulate or operate on tissues deep in the pelvis at angles normally difficult to reach with conventional straight or slightly curved but fix instruments; the third arm for holding allows for firm and stable grasp and also at position as desired by the operator; easier and more precise in dissection and suturing. (3) better ergonomics for operator and assistants: everybody can sit down with less stress on legs and backs; easier to assist with good view and no need to hold the camera. The video will try to demonstrate these advantages by showing different steps in the laparoscopic radical hysterectomy using the Da Vinci.
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