5TH EUROPEAN CONGRESS OF THE EUROPEAN FEDERATION FOR COLPOSCOPY AND CERVICAL PATHOLOGY

Abstract Book

27 – 29 May 2010
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Congress President
Professor Dr. K. Ulrich Petry, Germany

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Friday, 28 May 2010, 08.30–10.05, Potsdam I/III

MA-01 Main Audience

Basic Science, Pathology

Chairs: T. Löning (Germany), C. Bergeron (France), A. Singer (United Kingdom)

MA-01-002

Update on Cytopathology

Christine Bergeron

Laboratoire Cerba, France

Objective: Human PapillomaVirus (HPV) is a highly infectious virus; most of infections are latent and regress spontaneously without intervention.

Method: The latent infection, even in case of the viral penetration in the epithelium, by definition, is not associated with morphological modifications. The productive infection is associated with the expression of the late viral genes L1 and L2 in the intermediate and superficial cells. It corresponds to a low-grade squamous intraepithelial lesion (LSIL) according to the Bethesda terminology (TBS). A LSIL diagnosis is reproducible if it is made on the presence of koilocytosis, the cytopathogenic effect of a productive HPV infection. LSIL represent on average 1% of the smears but is more frequent in women younger than 35. The transforming infection is associated with the expression of the early viral genes E6 and E7 in the basal cells. It corresponds to a high-grade squamous intraepithelial lesion (HSIL) according to the TBS. A HSIL diagnosis is the most reproducible and is based on the presence of abnormal basal cells, hallmark of a precancerous lesion.The mean percentage of HSIL may vary between 0.3 to 1% of the smears depending of the population. The surrounding grey area of equivocal squamous changes is described as atypical and borderline changes. In the TBS, the term „atypical squamous cells of undetermined significance" (ASC-US) is used for abnormal cytological changes that are suggestive of a LSIL, but lack criteria for a definitive interpretation. Even with this definition, the diagnosis of ASC-US is poorly reproducible and the percentage highly variable among readers of the same set of slides. The TBS suggests that not more than 3 % of the smears should have the designation of ASC-US. The term „atypical squamous cells not permitting exclusion of a high grade intraepithelial squamous lesion" (ASC-H) is proposed for those unconfirmed, although suspected of HSIL. The association with underlying cervical intraepithelial neoplasia (CIN) 2 and CIN 3 for ASC-H is lower than for HSIL, but sufficiently higher than for ASC-US to warrant consideration of different management recommendations. ASC-H should comprise 5%-10% or less of total atypical squamous cells.

Results: The current vaccines provide protection against 70% of cervical cancers. Also, they do not protect women who are already infected by HPV 16 or 18. If women are vaccinated between 10 and 15 years old, the time necessary to begin to see the impact on this vaccinated population on the incidence of cervical cancer will be at least 20 years. This impact will also greatly depend on vaccination coverage. The impact on cervical screening programme by cytology will be much earlier and depends of the catch up population concerned by the vaccination programme (16-25 years). The vaccination will decrease the percentage of abnormal smears with lowering the probability of high-grade lesions but not much low grade lesions or minor atypia. For the young vaccinated women, primary HPV testing with triage by cytology and prolonged screening interval would be probably the best scenario. Pap screening or primary HPV screening for older non vaccinated women remains a debate. HPV screening on self sampled material in women who have not routine Pap screening could become more important.

Conclusion: Cervical cancer prevention should be obtained in the future with the synergy of prophylactic vaccination for the young and adapted cervical cancer screening for the older women. Organized programme will permit to control the coverage, adapt the test to the age and follow appropriately the positive cases.

MA-01-003

Update on Histopathology

Thomas Löning

Albertinen-Pathology, Reference Centre of Gynecopathology and Cytology, Germany

Pathology is involved in diagnosis and perioperative management of patients with lower genital tract precancert and cancer. What pathologists have learnt over the last 3 decades is that true precancer is characterized by not only a malignant phenotype (structurally and/or at the level of individual cells, high suprabasal mitotic activity, atypical mitoses), but also a „malignant" genotype (aneuploidy, in case of cervical lesions often integrated high HPV and dysregulated HPV E6/E7 expression). The lessons taught especially by in situ methods (RNA in situ hybridization, surrogate markers as p 16) indicate that vulvar precancer and cancer segregate into HPV-associated lesions (basaloid and condylomatous VIN 3 and cancer) and non-HPV-associated lesions (differentiated „simplex" types of carcinoma in situ, differentiated squamous cell cancer, and -as unusual lesions- basal cell carcinoma, melanoma, and M. Paget), while cervical precancer and cancer is almost always HPV-associated and as a probable consequence most often of a low differentiated squamous phenotype, the major exception being the glandular (pre-) neoplasias. From molecular lessons it also became apparent that the former three-tiered classification need to be replaced by a dichotomous system with low grade lesions (e.g. condylomas and their variants, CIN 1) being self limited and often spontaneously regressing lesions, and high grade lesions (e.g. VIN 3, CIN 3, ACIS) representing bona fide precancer. Yet, still the former putative intermediate precursors of preneoplasia (VIN 2, CIN 2, glandular dysplasias), and even more the mimics of precancer give rise to considerable headaches in routine diagnostic workup. For these lesions, in situ hybridization to detect high risk HPV E6/E7 expression or even more sophisticated molecular studies to detect HPV integration were the gold standards for better definition of true precancerous lesions for some time. Today, however, these laborious methods are going to be replaced by surrogate markers of high risk HPV E6/E7 expression (i.e. especially combined p16/MIB1-immunohistochemistry). Our own studies show that p16/MIB1-immunohistochemistry allow to exclude certain CIN II lesions and particularly certain mimics of precancer (AIM, TEM) in 10-20% of cases formerly signed out as precancer by conventional morphological means. From these studies, however, it became also clear, that cancer and precancer of the cervix uteri is not only one entity especially when focussing on the glandular lesions. In that variety, non-HPV associated neoplasias occur which share the molecular signature of cancer of the tuboendometrioid phenotype often showing strong coexpression of p16 and p53 oncoproteins. On the eve of world wide HPV vaccination, and with the expectation of eradication or at least major decrease of HPV-associated (pre-) neoplasias, the fields of non-HPV associated cancer not only of the vulva, but also of the cervix uteri might get much more importance to gynecologic oncologist, and represent the future challenge to gynecologic pathology.

Friday, 28 May 2010, 10.35–12.15, Potsdam I/III

MA-02 Main Audience

Screening in Europe in 2010

Chairs: E. Diakomanolis (Greece), K. U. Petry (Germany), M. Arbyn (Belgium)

MA-02-001

4 Short reports from different European regions - Sweden

Bengt Andrae

Sweden

Swedish Society of Obstetricians and Gynecologists (SFOG) Guidelines for the Management of Cervical Intraepithelial Neoplasia 2010 National Board of Health and Welfare recommends organised scree-

ning for cervical cancer. SFOG provides guidelines, systematically developed recommendations for prevention of cervical cancer and decision making regarding the management of abnormal tests found in the screening. Cervical cancer screening is computerised and linked to population and morphology registers. Invitations are issued three years after the last smear recorded, organised or opportunistic, to all women age 23-50 and after five year at ages 51-60. Screening tests are taken by midwives. Reminders are sent out to non-responders. Normal smear results are reported from the laboratory directly to the woman. The next invitation is issued after three or five years has elapsed. If a woman chooses to have an opportunistic smear earlier, next invitation will be postponed to avoid testing the already tested. Abnormal findings are referred to a gynaecologist for colposcopy. Statements in the guidelines Regional multidisciplinary boards are responsible for coordinated implementation and monitoring. HPV DNA-testing is introduced in the triage of ASC-US and CIN1 and the follow up after treatment of CIN2/3 and AIS. Registration of HPV testing results is according to a standardised protocol developed for the implementation of HPV in the screening programs. Regional and nationwide registers to monitor and audit the outcome of cervical cancer prevention measures, including HPV testing and vaccination. On-line re-scheduling systems help the individual woman to adjust their appointment to the time and place that suits her. The screening test should be free of charge. Extended follow up after treatment of dysplasia within the framework of the screening programme. Colposcopy training courses are mandatory to evaluate and treat dysplasia. Management of atypical smears in screening CIN1 or ASC-US are referred to colposcopy or triaged with HPV DNA testing, preferably by LBC reflex testing. If triage is negative the woman returns to routine screening after one negative smear at 12 months. Repeat cytology only is not adequate. CIN2-3, ASC-H, Glandular atypia and AIS is always to be referred to colposcopy. Management in young women should be more restrictive and tailored according to the risk of progression, the age of the patient, and her wish to maintain fertility. CIN1 lesions under the age of 40 should be managed expectantly under supervision, as well as selected very young women with CIN2. Symptoms suspicious for invasive cancer: Immediate referral to gynaecologists. Follow up after treatment of CIN1: Return to routine screening after assessment/treatment followed by three negative smears. Follow up after treatment of CIN2-3 or AIS: After three negative smears or two negative smears and a negative HPV test at 12 months the women should be referred to follow-up bi-annually within the organised screening programme for at least 25 years continuing past the 60 year age limit. Pregnant women should be offered a test unless a test is taken within 2,5 years, and be referred to experienced colposcopists to exclude invasive cancer in case of an abnormal screening test. Treatment, however, should be postponed until after delivery, if possible. Immunocompromised women should be cared for by subspecialised experienced gynecologists. Non-attenders to screening should be offered tests when visiting midwives or physicians for other gynaecological reasons including antenatal care or family planning, and including older women not tested to age 60 School based HPV vaccination programme offering all 11 year old girls free vaccination starts September 2010. In addition, catch up HPV vaccination planned to girls born 1994-1998. Sweden: Population 9 million. 660000 smears taken annually. 450 cervical cancer cases and 135 deaths.

MA-02-002

4 Short reports from different European regions - Georgia

Tamar Alibegashvili
GSCPC, Georgia
R. Gvamichava

Objective: To analyse the first results of pilot Cervical Cancer Screening Program in Georgia.
Method: The retrospective analyses of examination of 27000 women participated in Screening Program in 2008-2009.
Results: In 2008 the Cervical Cancer Screening program was initiated in Tbilisi (capital of Georgia) and funded by Tbilisi Municipality and UNFPA. Screening is based on the conventional Pap test (Bethesda system 2001), target age group - 25-60 years, screening interval – three years. The cervical scrape is done by gynecologists and at the same time all women undergoes routine gynecological examination. The detailed digital case history is created for each woman. Screening is opportunistic; women's enrollment is arranged with extended media advertising campaign. In order to avoid loss of follow-up all women with abnormal Pap results and suspicions for High Grade Lesion are referred to colposcopy and biopsy (if necessary). During two years about 27 000 women were enrolled in Screening. In 88,7 % Pap tests were negative, and 11,3% - positive: ASCUS – 6 %; ASC-H – 0,7 %; LSIL – 3,2 %; HSIL – 1,2 %; AGC _ 0,2 %. The rate of different types of cytological abnormalities among positive Pap results were: ASCUS – 55,5 %; ASC-H – 6,9 %; LSIL – 28 %; HSIL – 9 %; AGUS – 0,6 %. colposcopy was done in 12 % of screened women. Among women with positive Pap test: • 38% did not reveal any abnormalities during colposcopic examination. These women were called for follow up cytology test after 6 or 12 months. • in 23% was diagnosed CIN1 by colposcopy/histology. Taking into consideration the risk factors of development of HGCL (especially smoking) also age, location of lesion, desire of fertility, 52% of women from this group were referred to cytology and colposcopy after 12 months, another 48% _ were advised to remove lesion via ablation or excision. • in 8% was diagnosed CIN2,3. All women were suggested LEEP or hysterectomy in the cases of conjunctive pathology of corpus uteri. In each case of treatment was offered follow up after 6 months with cytology/colposcopy. • in 31% colposcopy was unsatisfactory due to invisible SCJ, but transformation zone on the ectocervix was normal. In these cases women with Pap results – ASCUS, ASC-H and LSIL were recalled for cytology after 6 or 12 months. Especially important were cases with HSIL and unsatisfactory colposcopy (30% of women with HSIL diagnoses and 3% of all Pap positive women), because occult high-grade disease might be presented. All these women with HSIL were advised LEEP. Unfortunately, screening program had not covered treatment costs in 2008-2009, but from 2010 the treatment of CIN2,3 is founded by municipal budget which will improve the quality and results of cervical screening.
Conclusion: The high rate of revealed Cervical Lesions confirms the effectiveness of Cervical Cancer screening in Georgia, nevertheless the improvement of quality of program is essential. The development of digital data base creates the ground for steady change of opportunistic screening in organized one

MA-02-005

Cervical cancer screening in Poland

Antoni Basta
Jagiellonian University, Gynecology and Oncology, Poland

Objective: In Poland we have high incidence of cervical cancer (standardized notes -18,4) and standardized mortality rates is 7,8. So, the cervical cancer is the 3 rd most common cancer in polish women, whilst the 2rd most common in women under 44 year of life. 5-years Survival rate of Polish women treated because of cervical cancer is below 50%. In 60-ties of last century the morbidity and mortality of cervical cancer were similar in Poland and Finland. Finland introduced an active population-based cytological Pap screening. This screening decreased cervical cancer incidence rate by 60% and mortality rate by 70-80%.So prophylactics plays an important role in cervical cancer incidence and mortality reduction. Till 2006 years in Poland 3 million from 14 million women aged above 20 years of life were diagnosed with Pap smear. The result of such strategy was only small decease of mobility and mortality because in majority of cases Pap smear was performed in these same women
Method: Since 2006 the National Cervical Cancer Screening Programme in Poland was introduced based on conventional Pap smear triaged with colposcopy. This screening is based on secondary prophylaxis i.e. detection of precancers and cervical cancer lesions. For this purpose 16 regional and 1 central coordinating center was created. It is an active organized screening program with letter invitation of women aged 25-60 years.

The first phase of this screening concerning cytological smears is based on Bethesda System. The recall of negatives is every 3 years. For quality control all positive and 10% negative slides are referred for secondary evaluation by pathologist. The second phase is the colposcopic verification of women with positive cytological result and histological assessment of colposcopy guided cervical biopsy. In selected cases HPV infection diagnosis is performed. This model allows for decrease of false negative results rate Pap according the Bethesda classification.
Results: But screening program based an Pap smear have little influence on glandular cervical cancer incidence which is the highest in regions of lowest squamous epithelial cervical cancer incidence. As we know the trigger factor of squamous and glandular cervical cancer is high oncogenic HPV infection especially 16/18, which is the background for concept to replace Pap by HPV diagnosis. But the cost of HPV testing is about 5x as expensive as the cytological test. The second reason is that approximately 80% of HPV infection regress spontaneously. But prophylactic vaccination against HPV will result in decrease of squamous and glandular cervical cancer incidence probably. In Poland prophylactic vaccination with quadrivalent and bivalent vaccine has begun in 2006 and in some regions is covered by local government. The primary prophylaxis introduction i.e. HPV vaccination does not allow us to quit the cytological screening, presently. But in the future, the potential result of primary prophylaxis will result in primary in cervical cancer screening strategy modification. Also tertiary prophylaxis it is proper diagnosis and treatment which improves 5 years survival rate is updated by creation of new specialization i.e. gynecologic oncology and establishment of new centers of gynecology oncology.
Conclusion: This above data creates a realistic chance for cervical cancer morbidly and mortality rates decrease in Poland.

MA-02-006
Piloting HPV screening in EU: The Wolfsburg experiment
K. Ulrich Petry
Frauenklinik im Klinikum, Wolfsburg, Germany
A. Luyten, K. Theile, A. Reinecke-Lüthge

Objective: In eight large randomised controlled trial primary HPV screening was more efficient in reducing moratlity from and incidence of invasive cervical cancer and in detecting CIN 3 lesions compared with Pap smear screening. However, this benefit was only observed in age groups being 30-35 years or older. Furthermore it is unknown if primary HPV screening outside of studies will show a similar rise in efficiency and how such a concept is accepted by the general population.
Method: Design of the pilot project The leading regional health insurance, Deutsche BKK, all gynaecologists in private practice and the city hospital of Wolfsburg founded the project, which started 1-FEB-2006 and is supposed to run at least until 2011. All female members of Deutsche BKK who live in the region, are 30 years or older and did not undergo hysterectomy can be included. All are screened with HPV-testing (HC2) and Pap smears. For participants with negative test results the next screening round will start after 5 years instead of the annual screening standard in Germany. Women with positive HC2 and Pap smear were referred for colposcopy while women with one positive screening test were only referred when positive results persisted.
Results: Until April 2010, 18,770 women were recruited. 92.9% had negative screening result and 5.9% tested positive for HPV-HR. The referral rate for colposcopy was 3.1% after 4 years of follow-up. 140 CIN3+ lesions were detected overall (0.75%), 70 in women with positive Pap smears and positive HC2 test, one case in the double negative population while 69 cases were found in women with normal cytology but with positive HC2 tests. 85% of all patients with CIN3+ lesions had an earlier diagnosis compared with the German routine screening. Acceptance of the project was high, less than 1% of women who were offered participation declined. Adherence to patient pathways was high in the HC2+/Pap+ (87.1%) and in the HC2+/Pap- cohort (84.6%)
Conclusion: Primary HPV screening allows for a better and earlier detection of patients with CIN3 in structured programs outside of clinical trials. However the best triage concept for women who are HC2 positive but Pap negative still needs to be determined. The Wolfsburg concept with referral to colposcopy only for women with atypical Pap smears after 6 months or persistently positive HC2 results after 12 months lead to a delayed diagnosis in 5 of 18 women with invasive cervical cancers.

Friday, 28 May 2010, 13.45 – 16.00, Potsdam I/III

MA-03 Main Audience

Impact of HPV Vaccination
Chairs: M. Arbyn (Belgium), L. Gissmann (Germany), A. Kaufmann (Germany)

MA-03-001
HPV Vaccination-up-date
Andreas Kaufmann
Charité-Universitätsmedizin, Clinic for Gynecology, Germany

Prophylactic vaccines to the most common Human Papillomavirus (HPV) types inducing anogenital dysplasia and cancer have been developed and approved by the EMEA. Two vaccines are available, Gardasil (Sanofi-Pasteur MSD) and Cervarix (GSK) since 2006 and 2007, respectively. Although using the same principle of virus-like particles as antigen both vaccines are different concerning number of HPV types formulated and adjuvant systems used. After the pivotal phase II clinical trials large phase III trials were performed. These trials verified the safety and very high prophylactic efficacy of both vaccines. Continuously new studies are initiated in order to investigate the safety, immunogenicity, and efficacy in additional groups of persons like children, women above the age of 26, and men, or even in population-based phase IV studies. Recommendations for the use of HPV vaccines and the way of introduction differ widely in the European countries. Mostly the target age is for girls 12 to 14 years, followed by some catch-up period for older girls and young women. The success of the introduction, however, differs greatly. Only well organised vaccination programs guarantee high vaccination rates. Some advances have been achieved also with therapeutic vaccines. It turns out that therapeutic efficacy can be shown merely in the premalignant situation. Importantly, an immunocorrelate has now been demonstrated for successful vaccination. The current status will be presented and recent advances will be discussed.

MA-03-002
Recommendations/Guidelines across Europe
Peter Hillemanns
Germany

The tetravalent HPV vaccine received an EU marketing authorisation in September 2006 and was followed by the bivalent vaccine which has received a positive opinion on July 2007. Numerous European countries have issued recommendations and guidelines for the implementation of HPV vaccination in their respective countries. There exists a huge discrepancy in respect to the implementation of HPV vaccination among European countries which profoundly effects the coverage rate: in school-based programs a coverage between 75% and 90% can be achieved whereas only about 30% coverage is being seen otherwise. The following table gives an overview about the current situation in Europe.

MA-03-004
How will HPV vaccines change colposcopy?
Margaret Cruickshank
United Kingdom

Objective: Following the introduction of HPV vaccination, the focus of our attention is now on the most effective way to screen women in the immunised cohort. We accept that these women still need to be screened. The primary screening test and schedule may very well change but will colposcopy still play an important role? Colposcopy examination is essential to the identification and treatment of cervical intra-epithelial Neoplasia (CIN). As colposcopists, our recognition of the visual features at colposcopy determines our impression of cervical disease and consequently the site that we select for biopsy and treatment. One of the most important is 'acetowhitening'. The application of acetic acid gives clear visualisation of cervical morphology and helps us to identify metaplasia or abnormal epithelium. There are several factors that we consider in our assessment of the severity of any lesion: time to develop acetowhitening, intensity of acetowhite, mosaicism and punctuation, lesion margin and surface contour are all related to underlying severity of the pathology. Colposcopy is subjective and influenced by a number of factors including the referral cytology, age, hormonal status and planned management policy. Any screening test will have a different performance profile as a result of any change in disease prevalence. As the vaccinated cohort reaches the age for screening, the incidence of CIN will fall significantly and impact on the ability of colposcopist to identify CIN. Whilst this is predictable, evidence is also emerging that elimination of HPV 16 could exert an additional impact. Analysis of data from both the ASCUS (atypical squamous cells of undetermined significance)-LSIL (low-grade squamous intraepithelial lesion) Triage Study (ALTS) and the Trial of Borderline and other Low Grade abnormalities (TOMBOLA) have identified an important effect of high risk HPV on colposcopic impression. The ALTS findings show that infection with HPV-16 is associated with the most definite visual abnormalities and this is independent of underlying pathology. TOMBOLA suggests that colposcopy is more subjective in non-HPV16/18 lesions resulting in higher biopsy rates. This is not seen in high risk HPV positive lesions.
Method: In Scotland, women who have been vaccinated in the 'catch-up' vaccination programme targeted at girls aged 17-18 years in 2008 will be invited to participate in the national cervical screening programme this year. As part of the Scottish Cervical Cancer Prevention Programme (SCCPP), we are examining the effect of HPV genotypes and RNA expression on colposcopy findings in young women.
Results: Analysis of data from both the ASCUS (atypical squamous cells of undetermined significance)-LSIL (low-grade squamous intraepithelial lesion) Triage Study (ALTS) and the Trial of Borderline and other Low Grade abnormalities (TOMBOLA) have identified an important effect of high risk HPV on colposcopic impression. The ALTS findings show that infection with HPV-16 is associated with the most definite visual abnormalities and this is independent of underlying pathology. TOMBOLA suggests that colposcopy is more subjective in non-HPV16/18 lesions resulting in higher biopsy rates. This is not seen in high risk HPV positive lesions. Results from SCCPP will be presented.
Conclusion: As well as rethinking out approach to screening, we now need to think how we are going to identify the site of CIN to be able to treat it effectively.

MA-03-005

Characterization of T-helper cell responses induced by prophylactic HPV vaccines in a comparative longitudinal study

Hannah Emily Rosenthal
Charite Berlin, Germany
S.-K. Pacher, H. Perlitz, J. Stanke, T. Waterboer, M. Pawlita, A. Kaufmann, A. Schneider

Objective: Two prophylactic HPV vaccines have been developed and their immunogenicity and clinical efficacy was extensively investigated. The quadrivalent vaccine Gardasil contains virus-like particles (VLP) of HPV types 6, 11, 16, and 18 adjuvanted with aluminium salts. Cervarix contains VLP of types 16 and 18 together with the TLR 4 stimulating adjuvant AS04. Both vaccines showed comparable efficacy in phase II/III clinical trials in protection from infection with vaccine-type HPV and dysplasia. T helper cells are important for B cell differentiation, sustained memory, activation of recall reactions, and thus anamnestic responses. Only few reports on cellular immune responses to the prophylactic HPV vaccines are available to date.
Method: In 36 vaccinated individuals (19 Gardsil; 17 Cervarix), blood samples taken before, after each vaccination, and 6 months after the last vaccine dose were analysed by ex vivo flow cytometry. L1-specific T cell frequencies were identified by intracellular staining for CD4, CD154, IL-2, IL-4, and IFN-γ.
Results: T helper cell responses to the vaccine HPV types were readily detectable after the first vaccine dose. There was a trend for higher T cell frequencies after Cervarix for both HPV16 and HPV18 L1. Cross-reactive T cell responses to HPV31 L1 and HPV 45 L1 were induced by both vaccines again with higher frequencies for Cervarix. Unexpectedly, also HPV6 and HPV11 L1-reactive T cells were induced after Cervarix at comparable frequencies as in Gardasil vaccinees. Sequence homology of the L1 of HPV types is high and conserved MHC class II-restricted epitopes can be found that allow for T-helper cell cross-reactivity.
Conclusion: To date clinical efficacy of both HPV vaccines is comparable. T helper responses to high-risk HPV types are higher for Cervarix. Analysing T cell responses may help understand mechanisms of vaccine cross protection. Enhanced T-helper cell responses may support B cell differentiation, deposit of antibody producing plasma B cells, and in turn strong and sustained antibody responses. So far HPV 6 and 11 specific antibodies were not investigated in Cervarix recipients. Any difference in immunogenicity of the two vaccines is interesting for the evaluation of sustained immunity.

Friday, 28 May 2010, 16.30 – 18.00, Potsdam I/III

MA-04 Main Audience

EFC-Standards in Colposcopy

Chairs: J. Jordan (United Kingdom), M. Menton (Germany), C. Redman (United Kingdom)

MA-04-001

How to assess quality of trainees and trainers

Simon Leeson
United Kingdom

Objective: Quality assurance for colposcopy training involves the effective execution of all activities concerned with attaining quality in colposcopy. This provides objective evidence that the quality of training for trainees satisfies stated requirements as a level of guarantee. With effective quality assurance in place all colposcopists trained by any approved training course would be capable of managing lower genital tract precancer and cancer to standards of care defined by the EFC. Quality can be measured by assessing structure (trainers, trainees, clinic facilities and record systems); process (aspects of training performance); and outcome (exit assessment and details of completion of training). The EFC Education Committee aims to co-ordinate and support national training to provide Europe wide availability of training places and regular training courses. The Committee also aims to standardise training programme content and agree a format or equivalent alternative formats for an exit assessment.
Method: National training programme leads from all EFC member states were asked to provide details of their national training including details of training programmes, requirements for trainees, completion of training assessments and any assessment of continued practice in colposcopy.
Results: Provisional results are reported.
Conclusion: Quality assurance of training programmes requires close co-operation with member states and limited data is available at present. However it is facilitated with an agreed core curriculum of training to measure process. An on-line trainee database to record

training activity has been developed by the EFC is now active in the UK. This will facilitate quality appraisal. However there is long way to go. Trainee feedback, mandatory returns on trainee throughput and web based learning on the EFC website would support process and structure. The most difficult measure practically is obtaining outcome data by agreeing locations and the format or formats for an EFC co-ordinated exit assessment.

MA-04-002

Spanish experience in colposcopy accreditation. A way forward?

Javier Cortes Bordoy
Spain

1. Recognising our objectives Establishing mechanisms for quality control, self-appraisal and accreditation for gynaecologists who practice colposcopy in Spain and for the Colposcopy Units in which they carry out their work is a necessary and desirable objective, to be achieved in the short term. The present situation of the teaching of colposcopy for Residents in their Speciality Training Units is not good. In a survey carried out in 2007 (Aznar FM.: Lecture given during the XIX AEPCC Congress. Oviedo, 2007), 55% of Obstetrics & Gynaecology Residents in their 4th year admitted to not having an adequate knowledge of colposcopy. 2. Mechanisms chosen to reach these objectives Each country has its own specific educational, cultural and sanitary circumstances. Consequently, a programme which is very effective in a particular country may not be applicable to another. A programme's design and its implementation must be adapted to the specific characteristics of the population to which it is destined. In Spain, colposcopy is always carried out by the gynaecologist. The objective is always the same - quality control, accreditation - but the means can, and perhaps should, be different for each country. Besides, these programmes should be as simple as possible and of easy implementation, without ever compromising their quality. 3. Control by the European Federation of Colposcopy (EFC) Each national society would inform the EFC about their programmes and subject them to its approval. The EFC would encourage each member society to develop its own initiatives and integrate them in a common frame. THE AEPCC'S ACCREDITATION PROGRAMMES FOR COLPOSCOPISTS In 2006, the AEPCC began its Colposcopists' Accreditation programme. An Accreditaton Committee was created and a programme designed. This programme established two different ways by which the Accreditation could be obtained: through CV appraisal or via an exam. 20 of the appraised CVs achieved a sufficient score, and their owners have received their respective Accreditations. Until today, four Accreditation Exams have taken place, coinciding with the AEPCC's Annual Meetings in Granada 2006, Oviedo 2007, Madrid 2008 and Cadiz 2009. A total of 207 gynaecologists have passed the exam and have subsequently received their Accreditation for a period of 5 years, which represents 33.17 % of those who applied. FOR COLPOSCOPY UNITS This is a mid-term objective for the AEPCC. At present, an open discussion on this subject is taking place. THE AEPCC'S TEACHING ACTIVITY The AEPCC has an itinerant course on Lower Genital Tract Disease, organised in collaboration with the Spanish Society of Gynaecology and Obstetrics. It has become a tradition that the first day of the AEPCC's Annual Congresses is wholly dedicated to a highly interactive Colposcopy Course, with theoretical lectures and clinical case seminars. The AEPCC's webpage has a section for its members in which the Scientific Committee presided by Prof. Puig Tintoré publishes regularly updated information. The AEPCC has published a Colposcopy CD, available to all its members. In conclusion, the AEPCC considers it to be one of its main objectives to achieve high levels of quality in the practice of colposcopy in Spain, in colaboration with the EFC. To this effect, it offers to all its members the possibility to have on-going learning access to simple, consensuated and renewable self-appraisal and accreditation mechanisms, as a means to keep up the training effort and its results.

MA-04-003

What are the EFC-training standards in colposcopy and how is the status of training in Europe?

Mahmood Shafi
United Kingdom

Europe has wide variation in relation to Colposcopy and its practice. Training is becoming increasingly formalised under the EFC organisation. We would like to see all member countries adopting certain core principles in relation to training and then implement the programme to suit the specific needs of the member country. The BSCCP has made its web based training programme available to the EFC and anticipate that it will be increasingly used. We need member countries to share good practice so that we have high quality assurance for those training in colposcopy.

MA-04-005

Controversy: Is a common European colposcopy diploma useful? (Pro)

Joseph Jordan
BSCCP Office, Norton Court, United Kingdom

Although colposcopy was introduced in 1926 there is still disparity in colposcopic training and colposcopically directed management of CIN. The European Union has directed that every doctor has a right to be employed in any other European country. However, working in another country demands individual evaluation and qualifications. The European Guidelines for Quality Assurance in Cervical Cancer Screening (2008) states that colposcopy is essential in the management of CIN. The EFC was founded in 1999 with this in mind and has produced guidelines for both colposcopy training and the management of CIN. At the moment is no Pan European Certificate of Accreditation in Colposcopy. Young doctors would welcome such a certificate which would be given after they had completed a universally agreed planned programme of training. This requires a Certificate of Completion of Training which would be acceptable anywhere in Europe or indeed anywhere in the world. Women will welcome the opportunity for their cervical problems to be managed by a colposcopist who has been trained and accredited to an agreed high standard.

MA-04-006

Controversy: Is a common European colposcopy diploma useful? (Pro)

Jens Quaas
Germany

To understand, why I prefer an European Colposcopy Diploma one has to know, how screening, early detection and management of CIN, VIN and VAIN works in Germany. There are 15000 gynaecologists and more than 6500 of them have their own office. Full Screening, Colposcopy and the following procedures are only done in such offices and rarely in special units. Because of the underrepresented colposcopical education during the residency/specialist training and the wide spectrum of such private offices, Colposcopical skills and management experience are limited. The number of patients with abnormal screening results is not low. Proven CIN, but VIN and VAIN too, need to undergo a different and individual procedure. If a gynaecologist doesn't often deal with it, an acceptable outcome is not guaranteed. Therefore, he needs to know where to send these patients. The Colposcopy Diploma and the publication of qualified offices/units helps him to ensure a proven procedure in cases of abnormal screening results. The common gynaecologist, the informed patient and we colposcopists too, need to get an overview of where these problems are best dealt with. A Diploma and furthermore a certification of offices/units guarantees an optimal treatment. At least this is how it is in Germany! Who knows how the situation is in Europe?

It is possible that more differences and strategies create even more problems. For our European-wide mobile patient we also need a clear structure. Furthermore, one needs an overview of where the best units are located. The basis could be an European Diploma. How such a diploma could be done? Our German diploma could be an option. We are already sharing one with Austria. After attending a Basic (8 hour lessons) and an Advanced Coposcopy Course (2x8 hour lessons) one can take the Colposcopy Exam. This is structured in to 2 parts: A theoretical (Questionaire) and a practical (Colposcopic Features). The theoretical part consists of 2 sections, a national specific and an international common section. So we ensure that national interests and common colposcopy knowledge are considered.

Saturday, 29 May 2010, 09.30 – 11.00, Potsdam I/III

MA-05 Main Audience

Diseases of Vagina and Vulva

Chairs: A. Basta (Poland), M. Hampl (Germany), S. Dexeus (Spain)

MA-05-001

Epidemiology, incidence and primary prevention of vulvar intraepithelial neoplasie (VIN)

Elmar Joura
Austria

Objective: To give an overview on the epidemiology and the data of vaccination against human papillomavirus (HPV) causing vulvar neoplasia
Method: Review of the literature
Results: A significant increase in the incidence of VIN was observed in Europe, Pacific region and the US. This was followed by an increased rate of vulvar cancers in young women (up to 40%). These vulvar cancers are HPV related (in contrast to the classic vulvar cancer, ususally associated with lichen sclerosus in older women). Most of these invasive vulvar cancers are associated with HPV 16. No screening exists and the treatment is potentially mutilating. The quadrivalent HPV vaccine (Gardasil, Sanofi Pasteur MSD) has been demonstrated to prevent 100% of VIN related to HPV 6/11/16/18 through four years. No vulvar data exist on the bivalent HPV vaccine.
Conclusion: VIN is not a rare but now a preventable disease

MA-05-002

Vulvar cancer of the anterior fourchette: a new tumour entity in Europe

Monika Hampl
Universitäts-Frauenklinik, Düsseldorf, Germany
K. U. Petry, Studiengruppe Kolposkopie, M. Dürst, M. von Knebel Doeberitz

Objective: The incidence of vulvar cancer in young women has increased in Germany during the last decade. The mean age has dropped significantly (by about 8 years) and we observed an increase of small tumors located between clitoris and urethra. We initiated a multicenter study in Germany asking members of the Study Group for Colposcopy and gynecological centers specialized in the treatment of vulvar cancer to provide tumor samples from patients with invasive tumors (max. T2) strongly located between clitoris and urethra.
Method: We received 129 tumor samples from vulvar cancer of the anterior fourchette including clinical/histological data and treatment characteristics of all patients reported in a standard questionnaire. 53 vulvar cancer not located in the anterior furchette are used as controls. We will analyze these tumor samples and some control samples for the presence of HPV DNA and if positive type, herpes simplex DNA, p53/p16/Ki 67 expression and presence of immuninfiltrating cells by IHC.
Results: Preliminary results of 13 tumors show that two third of the tumors are p16 negative with a strong or moderate expression of p53. Of the p16 positive samples (n=5), only two are p53 negative. HPV DNA and Herpes simplex DNA results as well as the IHC studies are still pending
Conclusion: Our preliminary results suggest that this specific entity of vulvar cancer is HPV induced in about 30% of the cases whereas in the majority of the tumors p53 as a key tumor suppressor gene seams to play a role in tumorigenesis besides factors we are still working on.

MA-05-003

Treatment of VIN and Condylomata acuminata with Imiquimod

Andreas Clad
Germany

Objective: Imiquimod 5% cream has been approved for topical treatment of genital warts for almost 10 years while treatment of VIN with imiquimod is still "off-label". Published studies and our own data show very encouraging results both for treating genital warts and VIN. However, length of treatment and frequency of application of imiquimod have to be adjusted individually to achieve optimal treatment results.
Method: All patients with warts or VIN who presented at the outpatient clinic of the gynecology department of the university clinic in Freiburg had several follow-up visits during treatment with imiquimod. At the start and during follow-up visits colposcopic findings were documented with a digital camera. Treatment results were analysed using an ACCESS data bank.
Results: In a randomized prospective double-blind placebo controlled study (Seters et al., NEJM, 2008) 52 women with grade 2 or 3 vulvar intraepithelialneoplasia were treated either with imiquimod 5% cream or placebo twice weekly for 16 weeks. Lesion size was reduced by more than 25% at 20 weeks in 21 of the 26 (81%) patients treated with imiquimod and in none of those treated with placebo ($p<0.001$). Nine (35%) patients, all treated with imiquimod, had a complete remission at 20 weeks and remained free of disease at 12 months. In 3 of 49 patients (2 in the placebo, 1 in the imiquimod group) with follow-up for 12 months the lesion progressed to invasion (to a depth <1mm). HPV cleared from the lesion in 15 (58%) patients in the imiquimod group, as compared with 2 (8%) in the control group. We treated 34 patients with VIN with imiquimod and observed complete remission in 74% and partial remission in 16% after an average treatment period of 4.5 months and average application of 36 sachets (once a weekly at the start, after partial remission twice weekly). Complete remission occurred in 100% in patients with VIN smaller than 1cm² and in only 29% in VIN >5cm². Imiquimod treatment of condyloma has been published in several randomized prospective double-blind placebo controlled studies (16 weeks´ treament, 3 sachets weekly) with complete remission rates of 50 – 75%, partial remission rates of 70 - 85% and recurrence rates of 13 - 22%. We treated 111 patients with condyloma with imiquimod (some of them for more than 6 months): complete remission 77%, partial remission 16%, recurrence rate 12%. Duration of treatment appeared to be independent of age and number of warts, but varied considerably between different individuals.
Conclusion: According to Manon van Seters et. al. (NEJM, 2008) topical imiquimod is "the first-choice treatment for vulvar intraepithelial neoplasia". Our results definitely support this notion! Imiquimod is well tolerated if application frequency and application area are adjusted individually. Recurrence rates after treatment of VIN or warts with imiquimod are considerably smaller than after ablative therapy. However, the action of imiquimod has to be explained thoroughly to the patients in order to avoid side effects and to achieve optimal treatment results.

MA-05-004

HER-2/neu expression in Paget's disease of the vulva and new options in therapy with Herceptin and Imiquimod

Oliver Brummer
Asklepios Klinik Altona, Germany
A. Luyten, K. U. Petry

Objective: Paget's disease of the vulva is a rare lesion that accounts for < 1% of vulva neoplasms. A 12% prevalence of invasive Paget carcinoma and a 4% prevalence of associated adenocarcinomas are described. Furthermore a high recurrence rate of 32% after surgical therapy is observed. It was the aim of this study to search for therapeutic strategies with higher tolerability than re-excision, x-ray therapy and chemotherapy for recurrent disease. Trastuzumab (Herceptin) is a recombinant monoclonal antibody against HER-2/neu, approved by the U.S. FDA for the treatment of patients with metastatic breast carcinomas and Imiquimod an immune stimulator is approved for therapy of condylomata acuminata.
Method: Using HercepTest, we analyzed HER-2/neu overexpression in 7 non-invasive. 2 invasive and 1 vulva Paget's disease with underlying adenocarcinoma. In addition we investigated 5 mammary Paget's diseases. In a second analysis we examined more than 30 cases of genital Paget's disease retrospectively and the therapies in recurrent disease.
Results: Overexpression of HER-2/neu oncoprotein labelling exclusively the membranes of Paget cells could be demonstrated in 8 out of 10 cases. 2 of them were invasive, 1 non-invasive and 1 with underlying adenocarcinoma stained negative. Overexpression of HER-2/neu has been demonstrated in all 5 cases of mammary Paget's disease. In the group of treatment with Imiquimod in recurrent Paget's diseases total and partial remissions were noted.
Conclusion: Our study suggests a usefulness of HER-2/neu antibodies. Therefore the use of. Trastuzumab, when overexpressing HER-2/neu, or Imiquimod should be considered for the treatment of patients. with recurrent Paget's disease of the vulva.

MA-05-005

Vaginal intraepithelial neoplasia- clinical diagnosis and treatment

Ralph J. Lellé
Frauenklinik des Universitätsklinikums Münster, Germany

Objective: Vaginal intraepithelial neoplasia (VAIN) accounts for approximatly 1% of intraepithelial neoplasias of the lower genital tract. However, no exact data are available. Furthermore, little is known of the natural history of the disease. Most likely it is similar to that of cervical intraepithelial neoplasia (CIN) and may be considered to be a precursor of invasive disease. Patients with VAIN usually have a previous history of CIN, especially with hysterectomy having been performed for treatment of recurrent dysplasia of the cervix. However, patients with no history of cervical disease might develop VAIN many years after hysterectomy for a benign condition.
Method: In the vast majority of cases VAIN is asymptomatic and is usually diagnosed by an abnormal Pap test. Colposcopic appearance of high-grade VAIN is different from that of high-grade CIN and may present as Lugol negative epithelium only.
Results: Usually, patients with high-grade VAIN undergo some kind of treatment. However, no consensus exists on the most effective therapeutic modality and treatment failures occur frequently. Laser vaporization, upper colpectomy, 5-fluorouracil cream or imiquimod and even brachytherapy habe been proposed to treat VAIN.
Conclusion: Several clinical cases will be presented to illustrate the diagnostic and therapeutic challenges associated with VAIN.

MA-05-006

10 years review of VAIN (Vaginal Intraepithelial Neoplasia)

Mohammad Aziz
St. Marys Hospital, Obstetrics and Gynaecology, United Kingdom
M. Colquhoun, E. Turner, L. McMullen, D. Lyons

Objective: The aim of the study was to review all cases of VAIN at St Mary's hospital and to a) Assess if there was increase in diagnosis of VAIN, b) To examine all VAIN patients with regards to diagnosis and outcome, c) To analyze those patients with previous hysterectomy.
Method: Retrospective study done at the colposcopy department at St Mary's hospital for the period of 10 years, from 2000-2009 (inclusive). We obtained the histology results from all vaginal biopsies over the time period and identified all those patients with the diagnosis of VAIN. An ordered proforma was created and completed for each patient detailing reasons for referral, colposcopic findings, histological findings and subsequent management completed for each patient.
Results: Total number of patients attending colposcopy clinic within this 10 years were 12000 patients. Total number of vaginal biopsies was 959. Of these there were 62 patients with VAIN. This represents 0.51 % of patients attending the colposcopy clinic for that period. We noted a distinct increase in the incidence of VAIN over the 10 years period from 3 patients in 2002 to 12 patients in 2009. The vast majority (96%) of patients aged 30 years old or more. Vaginal biopsies results showed 48% with a low grade VAIN lesion and 52% with a high grade VAIN lesion. In those 62 patients with VAIN, 95% had history of CIN, 22% had history of VIN and 11% had history of AIN. 17% of patients had multicentre disease involving anal /perianal , vulva and /or cervical lesions. 20% of patients VAIN discovered incidentally during colposcopy examination for other reason (i.e. abnormal cervical cytology) Immunosuppression was evident in 32% of patients .the type of immune suppression range from HIV, renal transplant patients to patients on steroid therapy. In those patients with high grade VAIN, 64% of them had at some time a high grade CIN lesion or invasive cervical cancer. In those patients with multicentric disease 75% were immunosuppressed. 35% of patients were treated conservatively with observation and repeated colposcopy follow-up only. Different modalities of treatment used for the treatment of the rest of the patients, including: Diathermy ablation, Diathermy excision, Laser treatment, Vaginectomy, Hysterectomy with removal of vaginal cuff and Radiotherapy. There was 9 patients with previous hysterectomy. In 6 women they had hysterectomy for CIN lesions but interestingly ,there were 3 patients who had hysterectomy for benign gynecology cause with negative cervical histology on the hysterectomy specimen. In those with hysterectomy for benign cause VAIN appeared 1-3 years following the procedure. Majority of patients developed VAIN within one year following CIN, but some patients had developed VAIN after 5-17 years.
Conclusion: We found that the incidence of VAIN is increasing. Most of high grade lesions were in patients who are immunosuppressed. Of concern however is the time period for development of VAIN after CIN and in hysterectomised patients. There is one patient with VAIN 3 being followed up throughout her second pregnancy. Interestingly 20 % of VAIN lesions were discovered incidentally during colposcopy examination. Our findings also agree with published data which suggest VAIN can appear many years after CIN.

Saturday, 29 May 2010, 11.30–13.00, Potsdam I/III

MA-06 Main Audience

New biomarkers, new techniques

Chairs: C. Meijer (The Netherlands), M. von Knebel Doeberitz (Germany), H. Ikenberg (Germany)

MA-06-002

Primary Screening with p16 - PALMS study

Ruediger Ridder
mtm laboratories, Germany
J.-P. Bogers, H. Ikenberg, H. Griesser, C. Angeloni, C. Bergeron, R. Dachez, L. M. Puig-Tintore

Objective: The detection of p16 over-expression is an indicator of cell-cycle deregulation and thus for the presence of cervical dysplasia. Additional staining for the Ki-67 proliferation marker within the same cell may enhance specificity of the test and so improve further the diagnostic performance of cervical cytology. A prospective diagnostic study was conducted in five European countries to assess sensitivity and specificity of p16/Ki-67 dual-stained cervical cytology for the detection of high-grade CIN (HGCIN) in primary screening and in ASC-US or LSIL triage settings.
Method: 27,349 women attending routine cervical cancer screening visits were enrolled. Pap, HPV, and dual-stained cytology testing was performed, and all women with any positive test result (except for HPV test positivity in women aged <30 years as the only positive test) were referred to colposcopy/biopsy follow-up. Pathologist majority consensus diagnoses on biopsy served as gold standard. The diagnostic performance of dual-stained cytology was evaluated and compared to Pap and HPV testing.
Results: In screening, sensitivity of p16/Ki-67 dual-stained cytology for HGCIN was found significantly higher (90.1%) than Pap cytology (66.4%). Specificity was identical for both tests (95.3% vs. 95.4%, respectively). The sensitivity of HPV testing was 96.4%, but with a substantially lower specificity (90.2% over all ages) as compared to the cytology based tests. In women aged <30 years, specificity of dual-stained cytology was 92.3% compared to 81.4% for HPV testing. In ASC-US and LSIL triage dual-stained cytology showed high sensitivity, while reducing the number of false-positive results by 43% vs. HPV testing.
Conclusion: Dual-stained cytology testing was shown to combine both high sensitivity and high specificity for the detection of women with underlying HGCIN in primary screening and for the triage of Pap cytology results categorized as ASC-US or LSIL..

MA-06-003

Diagnostic profile of three different screening tests (HC2, APTIMA HPV mRNA, and CINtec p16 cytology test) in a high risk cohort for cervical disease

Miriam Reuschenbach
Germany
A. Clad, C. von Knebel Doeberitz, N. Wentzensen, J. Rahmsdorf, F. Schaffrath, H. Griesser, N. Freudenberg, M. von Knebel Doeberitz

Objective: Cervical cancer screening is hampered by the low sensitivity and reproducibility of Pap cytology. Detection of HPV DNA is considered as more sensitive and reliable. However, due to the very high prevalence of transient HPV infections, HPV DNA testing suffers from poor diagnostic specificity. Biomarkers that highlight the shift from self limited transient to potentially dangerous transforming HPV infections may improve the accuracy of cervical cancer screening. We evaluated HPV E6/E7 mRNA detection (APTIMA), p16INK4a-immunocytology (CINtec), and HPV DNA testing (HC2) to identify women with high grade cervical neoplasia in a disease enriched cross-sectional cohort.
Method: Liquid based cytology specimens were collected from 275 patients. All assays were performed from these vials. Detection rates of each test were evaluated against conventional H&E based histopathology alone and stratified by p16INK4a-immunohistochemistry (IHC).
Results: All assays yielded a high sensitivity for the detection of CIN3+ (96.4% (95%CI 90.4-98.8) for HC2, 95.5% (89.2-98.3) for APTIMA and CINtec) and CIN2+ (91.5% (85.8-95.1) for HC2, 88.4% (82.3-92.7) for APTIMA, 86.6% (80.2-91.2) for CINtec). The specificity to detect high grade dysplasia was highest for CINtec p16INK4a-cytology (60.6% (52.7-68.0) in CIN3+ and 74.8% (65.5-82.3) in CIN2+), followed by APTIMA (56.4% (48.4-64.0) in CIN3+ and 71.2% (61.7-79.2) in CIN2+) and HC2 (49.1% (41.3-56.9) in CIN3+ and 63.4% (53.7-72.1) in CIN2+). All tests had higher sensitivity using p16INK4a-IHC-positive CIN2+ lesions as endpoint.
Conclusion: Biomarkers that detect HPV induced dysplastic changes in the transforming stage are promising tools to overcome the current limitations of cervical cancer screening.

MA-06-004

Results of the Rhine-Saar-Study, a randomized trial comparing conventional cytology with thinlayer cytology and computer-assistance

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S. J. Klug, B. Jordan, W. Harlfinger, A. Malter, F. Brinkmann-Smetanay, J. König, K. J. Neis

Objective: Since 1971 there is a legal claim for an annual conventional cytologic smear in Germany. Although Germany does not have an organized cervical cancer screening program, the participation rate on a 3-year base equals the highest rates reached in other countries. However, the incidence of cervical cancer in Germany is still among the highest in Western Europe. A recent study (Siebers et al. JAMA 2009; 302: 1757) within the framework of an organized program did not show significantly increased sensitivity for cervical intraepithelial neoplasia (CIN) with ThinPrep thinlayer cytology (TP) as compared to conventional cytology (CC). Against this background the professional associations of gynaecologists (BVF) of Rhineland-Palatinate and Saarland in Germany conducted a large randomized trial to compare CC with TP. In addition all slides were investigated with the computer-assisted ThinPrep Imaging System (TIS).
Method: Between August 2007 and October 2008, 21.081 women attending routine screening at 20 office-based gynaecologists were recruited. Weekly randomization allocated them to either CC or TP/TIS. Only patients of public sickness funds within the framework of the legal cervical cancer prevention were included to avoid bias because privately insured patients (8% of the population) are already predominantly served with thinlayer cytology. The evaluation of smears was only performed by experienced cytotechnicians (>2.000 slides in each technique). All women with cytological abnormalities (>Pap III = ASC-H/LSIL/HSIL) were invited for expert colposcopy, including biopsy if indicated. The primary outcome was the detection of histologically confirmed CIN 2+.
Results: In total 20.607 women (97.8%) were included in the analysis. 45% of the participants received CC and 55% TP/TIS. The colposcopy rate reached 90% among women with Pap IVa+ (CIN 3+), while it was lower in women with minor abnormalities. The relative sensitivity for histologically confirmed CIN 2+ compared to CC was 2.74 (95% CI: 1.66-4.53) for TP and 3.17 (95% CI: 1.94-5.19) for TIS. Sensitivity analysis confirmed statistically significant increased relative sensitivity. Detailed results on detection rates, relative sensitivity, positive predictive values and relative positive predictive values will be presented.
Conclusion: This is to our knowledge the first randomized direct-to-vial study using computer-assisted thinlayer cytology under field conditions. Thinlayer cytology had a significantly higher relative sensitivity for histologically confirmed CIN 2+ than conventional cytology when applied under opportunistic conditions.

MA-06-005

Triaging of HPV-positive women with P16 / Ki-67 double stain within a primary HPV screening setting

Alexander Luyten
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S. Scherbring, A. Reinecke-Lüthge, D. Schmidt, R. Ridder, K. U. Petry

Objective: Background: Co-testing for Pap cytology and HPV has been proposed as an approach to increase the sensitivity for the detection of high-grade CIN (HGCIN) in women aged 30 years and older. To increase sensitivity over Pap cytology testing, HPV co-testing requires the follow-up of women tested negative for Pap abnormalities, but positive for HPV. As the amount of underlying HGCIN within the group of Pap negative, HPV positive results still is relatively low, we analyzed the potential of a new immuno-cytochemical dual staining approach that detects the co-localization of p16 and Ki-67 expression as an indicator of cell cycle deregulation, to efficiently triage Pap negative, HPV positive screening results.

Method: Out of a group of 7,976 women enrolled into a prospective cervical cancer screening study for Pap cytology and HPV co-testing in 2007/2008 in the Wolfsburg/Germany area, a total of 427 Pap negative, HPV positive cases were retrospectively analyzed for the presence of cells showing immuno-cytochemical co-expression of both p16 and Ki-67. Positive test results were correlated to the presence of HGCIN confirmed during colposcopy and histology follow-up.
Results: 109 out of 427 (25.5%) of Pap negative, HPV positive women tested positive for the p16/Ki-67 Dual stain. Sensitivity of baseline Dual stain testing for the detection of CIN2+ during follow-up (mean follow-up time period of >12 months) within the group of Pap negative, HPV positive women was 91.9% for CIN2+ (34/37 cases), and 96% for CIN3+ (27/28 cases). Negative p16/Ki-67 Dual stain test results at baseline had a negative predictive value of 99.1% for the development of HGCIN during the study follow-up period.
Conclusion: The detection of co-localization of p16/Ki-67 expression in cervical cells identifies women that may benefit from immediate colposcopy, whereas negative Dual stain test results may exclude HGCIN with a high NPV.

MA-06-006
Diagnostic efficacy of optical coherence tomography in the management of CIN
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Klinikum der Universität München, Germany
L. Turk, H. Stepp, K. Friese, J. Gallwas

Objective: Optical coherence tomography (OCT) is a noninvasive high resolution imaging technique that permits characterization of microarchitectural features up to 2mm in depth in real time. The purpose of this study was to evaluate the feasibility of OCT in the characterization of preinvasive and invasive cancer of the uterine cervix.
Method: We conducted a single-institution, institutional review board–approved, prospective study on the use of OCT in women with suspected CIN. The images were immediately evaluated independently by two investigators and later compared to the corresponding histology. Sensitivity and specificity of the new technique were calculated.
Results: We compared 189 images with corresponding histology in 106 women undergoing colposcopy for suspected CIN. With 130 (127) true positive, 22 (23) true negative, 34 (33) false positive and 3 (6) false negative results the sensitivity calculated for both investigators with the threshold at CIN1 was 98% and 95% respectively. The specificity was 39% and 41% respectively.
Conclusion: OCT ist a promising technique in the management of preinvasive and invasive cancer that needs further evaluation.

Saturday, 29 May 2010, 14.30–16.00, Potsdam I/III

MA-07 Main Audience

Management of CIN
Chairs: E. Paraskevaides (Greece), W. Prendiville (Ireland), S. Rogovskaya (Russia)

MA-07-002
Interim suggestions from the Nomenclature committee of the IFCPC
Jacob Bornstein
Western Galilee Hospital, Obstetrics & Gynecology, Israel

Objective: During the 2008 world congress in New-Zeland the IFCPC has founded a new Nomenclature Committee.
Method: a. To prepare an up-dated, user-friendly colposcopic nomenclature for colposcopists worldwide. b. To incorporate into the new nomenclature critiques that have been voiced since the 2002 proposal. c. To add terminology of different loop excision techniques. d. To consider adding vulvar and vaginal nomenclature. e. To examine the current nomenclature by an evidence-based medicine approach.
Results: The committee reevaluated the reliability of some of the following concepts of previous IFCPC colposcopy terminologies: differentiation of colposcopic changes into minor and major, the significance of keratosis. The committee discussed whether the following concepts should be introduced to the terminology: size of the lesion, the signs of inner border and ridge, location of the lesion in relation to the transformation zone, performing random biopsies, rapidity of white epithelial color appearance, Lugol's staining results. The committee considered proposing a colposcopy reporting form. The committee discussed whether the following risk assessment factors should be included in the IFCPC terminology: cause of referral, woman's age, the colposcopy being satisfactory or adequate, HPV 16 status, HPV vaccination status.
Conclusion: These considerations will be the basis for a discussion with the European Federation of Colposcopy

MA-07-004
Follow-up after treatment for CIN
Galina Minkina
Voyage Tour LLC, Corporate Travel, Russia

Objective: Treatment of CIN is generally successful, although the risk for development of cervical cancer remains higher than for women never having CIN. In multiple studies, rates of recurrence or persistence of CIN range from 5 to 25%. Persistence of CIN (residual lesion) is treatment failure which is usually found within the first year of surveillance. Therapy does not achieve cure in all cases due to the missed lesion extending into the cervical canal or laterally beyond the removed specimen. So, the highest treatment failure rates have large lesions and positive resection margins. Disease may appear years later after treatment and represent new lesion (true recurrence), probably as a result of autoinoculation with persistent oncogenic HPV in epithelium that was not treated, incorporation of HPV into the healing tissue or owing to a new HPV infection. Therefore, intensive follow-up within the first year after treatment is required for detection treatment failures and long-term follow-up is essential for detection new lesions. Until recently frequent follow-up with cytology and colposcopic evaluation of the cervix was the preferred strategy. Recent prospective and retrospective studies show the importance of HPV test after treatment for CIN 2+. A number of follow-up protocols have been recommended. They are based on cytology, colposcopy, HPV DNA testing and combinations of these options.
Method: In our prospective study we compared different options for post-treatment follow-up of CIN. 325 women have been tested with cytology, quantitative HPV test on the basis of real time PCR, and colposcopy examined at 6, 12 and 24 months after treatment for CIN 2+ by LEEP or cone.
Results: The best characteristics have been shown by HPV test. In detection of residual disease at 6 and 12 months follow-up both the sensitivity and the negative predictive value for HPV test were 100%. A combination of HPV testing and cytology was the equal sensitive but the least specific. On the basis of this analysis we consider HPV testing along at 6 months as an initial follow-up strategy. Negative HPV test identifies women which can return to routine screening. Positive HPV result, on the contrary, demands close follow-up with repeat colposcopy and endocervical sampling to detect the residual lesion.
Conclusion: Although only randomized controlled trials comparing HPV testing to cytology, with follow-up over a period of at least five years, can determine the optimal follow-up protocol, it is now clear, that the high sensitivity and negative predictive value should establish HPV testing as a standard in post-treatment evaluation.

MA-07-005
Size matters when excising the TZ
Evangelos Dimitriou
United Kingdom

Objective: The aim of this study is to address whether or not there might be individual physical variables of the extirpated LLETZ that might allow a prediction of adverse obstetric outcomes such as the depth &Volume of LLETZ as well as the duration between LLETZ & subsequent pregnancy.
Method: This is a retrospective cohort study that enrolled all women who had LLETZ treatment in the colposcopy service during the four year period between 1999 and 2002 and who subsequently delivered a baby in our hospital. Out of 1808 records of LLETZ treatment within the period 1999-2002, a total of 353 women was identified that fitted required criteria. We looked at the obstetric outcome, in relation to the size variables.
Results: 74.6% delivered at or after term, 10% had a pre-term delivery (<37 weeks) and there were 15.4% miscarriages (<24weeks). There was a more than 3-fold increase in the risk of PTL if the excision volume exceeds 6cm3 (RR=3.17, 95%CI 1.56-6.43). For excisions where the thickness was greater than 12mms there was a very much greater risk of PTL (RR=3.05, 95%CI 1.31-7.08). The LLETZ-to-Pregnancy time interval didn't appear to have any effect on PTL rates. Finally we found no association between grade of abnormality and risk of PTL.
Conclusion: This study shows that the depth and the total volume of the excised cervix do increase the risk of PTL. Excisions deeper than 1.2cm and larger than 6cm3 carry 3 times higher risk for PTL and related morbidity than smaller ones. This inspired the idea of a new classification for excisions and could be the base of appropriate counselling.

MA-07-007
Individualised Scoring Systems: potential applications in screening programmes
Petros Karakitsos
University General Hospital, ATTIKON, Greece

Objective: The investigation of the potential value of tree classifiers for the triage of HgSIL.
Method: The data set is composed of 562 histologically confirmed cases having a complete range of ThinPrep pap-test, reflex HPV DNA test, E6/E7 HPV mRNA test and P16 immunocytochemical examinations. These are composed of 469 histologically negative cases and 93 positive cases. The Cytological diagnosis was made according to the TBS2001. There was attempted classification into two groups: the first one concerning CIN-II and above histologically confirmed cases and the second CIN-I and below. For classification purposes, 50% of the cases have been randomly selected as training set, in order to construct the discriminant tree classification model and the remaining cases were used as a test set, used to validate the method.
Results: The application of tree classifiers on the test set gave a correct classification equal to 84.7% of the CIN-II and above cases and 97.9% of the CIN-I and below cases, producing an overall accuracy of 95.7%, this result outperforms the cytological diagnosis alone.
Conclusion: Based on our preliminary data, the application of tree classifiers, based on the standard cytological diagnosis and the expression of the studied biomarkers, produces improved classification results for CIN-II and above lesions. Due to the encouraging and promising results, in the future it is planned to investigate more statistical and artificial neural network techniques. Such experiments will be applied to an augmented patient data base to avoid data dimensionality issues. Via these experiments it is expected to have results with higher accuracy and greater stability.

Saturday, 29 May 2010, 16.30 – 18.00, Potsdam I/III

MA-08 Main Audience

Difficulties / Trouble shooting in Colposcopy
Chairs: J. Quaas (Germany), M. Sideri (Italy), V. Dvorak (Czech Republic)

MA-08-001
Risk assessement in the management of abnormal screening tests: is there a role for colposcopy?
Mario Sideri
European Institute of Oncology, Gynecology Division, Italy
S. Boveri, F. Sanvito, C. Casadio, E. Preti, D. Radice, M. T. Sandri, S. Igidbashian

Objective: in the recent past data from studies investigating highly sensitive molecular tests have challenged the ability of colposcopy to detect cervical pre-cancers. Colposcopy is a technique to identify the area to place a biopsy, and so colposcopy result equals the biopsy pathology report. It has been suggested that the entire cervical cancer screening process can be viewed as a risk stratification system where the result of different exams, cytology, molecular analysis etc., acts as risk stratifier which trigger intervention (closer follow up or treatment). In this way the patient is managed by level of risk and not on the basis of the histologic diagnosis of a colposcopic directed biopsy. We tested the hypothesis that colposcopic impression alone can act as risk stratifier in patients with abnormal screen results
Method: data from 556 patients submitted to LEEP or laserconization were analyzed. The pathology results of the excised specimen served as gold standard. Results of Pap smear, high risk (HR) HPV test, HPV genotyping and colposcopy at the time of treatment were recorded. Pap smear results were classified according to the 2001 Bethesda system; HR HPV test results as positive or negative; HPV genotyping as high risk 16 positive or high risk HPV non 16 positive; colposcopy results as negative, grade 1, grade 2 or suspicion of invasive cancer.
Results: When grade 2 colposcopy results were associated with a positive Pap smear result at an ASC-US threshold, the histology of the excised specimen was CIN2+ in 87% of the cases and when it was associated with any positive HR HPV test in 88% of the cases; conversely the finding of a grade 1 colposcopy result in the presence of an high grade intraepithelial lesion (HSIL) at cytology or in the presence of a positive HPV 16 test result predicted CIN2+ at histology in about 76% of the cases.
Conclusion: the results suggest that colposcopic pattern and grading without histology can be used as risk stratifier in a management algorithm based on risk stratification

MA-08-002
Long-term follow-up after mild to moderate dyskaryosis; risk stratification by human papillomavirus testing
Marielle Kocken
Erasmus Medisch Center, Obstetrics and Gynaecology, Netherlands
J. Louwers, A. Zaal, J. Berkhof, M. Nobbenhuis, P. Snijders, T. Helmerhorst, C. Meijer

Objective: Although testing for the presence of high-risk types of the human papillomavirus (hrHPV) is less specific than cytology in detecting high-grade Cervical Intraepithelial Neoplasia (CIN), it is more sensitive and has a higher negative predictive value. Despite extensive research on the short-term predictive value of the hrHPV test, little is known about its value in predicting the long-term risk of cervical abnormalities. To study the cumulative number of high-grade cervical lesions (CIN3+) developed in women up to 18 years after the first detection of an abnormal smear (PAP3a (mild to moderate dyskariosis)) and the value of additional hrHPV testing.
Method: Women (n=297) with an abnormal smear of mild to moderate dyskariosis who participated in a previous study (Nobbenhuis et al. Lancet 1999) were followed until June 2008 using the Dutch nationwide network and registry of histopathology and cytopathology (PALGA). All women were also invited to participate in active follow-up at the outpatient clinic of the VU University Medical Center, Amsterdam, the Netherlands for cytology and hrHPV testing, or to participate by self-sampled hrHPV testing. This active follow-up was performed between January and November 2009. If an abnormal cytological result or positive hrHPV test (GP5+/6+) was detected, a colposcopic examination with mandatory biopsy was performed.

The histological endpoint was CIN3+ (including CIN3 lesions, adenocarcinoma in situ and squamous or adenocarcinoma) in either biopsy or treatment specimen. Cumulative incidence was calculated with Kaplan-Meier analysis and additional value of hrHPV testing calculated with Log-rank test.
Results: Passive follow-up was available for all, and active follow-up for 126 (42.4%) of the women with a median follow-up of 158 months (range 3-231). At baseline 183 women (61.6%) were hrHPV positive and 114 (38.4%) hrHPV negative. In 79 (26.6%) women a CIN3+ lesion was detected during follow-up. If an hrHPV test was added to cytology at baseline, a negative hrHPV test resulted in a significant reduction of the risk to develop CIN 3+ lesions (26.6% without hrHPV testing to 2.6% with a negative hrHPV test, Table 1). In the hrHPV negative group three women developed a CIN 3+ lesion, none of these occurred within 24 months of follow-up (25, 55 and 62 months respectively). Table 1: Effect of additional hrHPV testing to mild to moderate dyskariosis in cytology at baseline hrHPV (t=0) __total (%) __CIN3+ (%) __P (log rank) _____ 297 (100) __ 79 (26.6) negative ____ 114 (38.4) __ 3 (2.6) __ <0.001 positive ____ 183 (61.6) __76 (41.5) __ 0.001
Conclusion: Over 25% of all women with mild to moderate dyskariosis develop a CIN3+ lesion during follow-up. In this group additional hrHPV testing should be performed, since hrHPV negative women have a significant lower risk to develop CIN 3+ lesions. In these women (cytological) testing after two years should be sufficient, while women who test hrHPV positive should be referred for colposcopy immediately, due to their high risk to develop CIN3+.

MA-08-003
The prevalence of CIN in women with postcoital bleeding over 10 years in a colposcopy clinic
Claire Newton
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D. Lyons, L. McMullen, E. Turner

Objective: To determine the prevalence of cervical intraepithelial neoplasia (CIN) in women with postcoital bleeding with normal, or abnormal cytology within 3 years.
Method: Retrospective study of 917 women aged between 19 and 64 with postcoital bleeding seen at St.Marys hospital colposcopy department between 1st January 2000, and 31st December 2009 inclusive.
Results: Of 386 patients with normal cytology at referral, 32 (8.3%) had CIN I, and 14 (3.6%) had CIN II/III. Interestingly only 6 (13.0%) were smokers. 2 patients (0.5%) had glandular abnormalities and 1 (0.3%) had invasive cervical cancer stage 1b1 despite normal cytology. Assuming cumulative smears are up to 93% sensitive, our results indicate a more than expected increase in CIN in patients presenting with PCB despite normal cytology (using Chi-squared test p<0.01). Of 92 patients with no referral cytology, 9 (9.8%) had CIN I, and 5 (5.4%) had CIN II or III, while 3 patients (3.3%) had glandular abnormalities. Of 40 patients with borderline cytology, 4 (10%) had CIN II/III. Significantly more patients with mild dyskariosis and postcoital bleeding had CIN II/III (34 out of 202 (16.8%) than mild dyskariosis alone in our unit (13%, using Chi-squared p<0.01). 1 (0.2%) patient had glandular abnormalities. Out of 79 patients with moderate dyskariosis, 46 (50.6%) had CIN II or III, and 2 (2.5%) had microinvasive cervical cancer, none had glandular abnormalities. Out of 70 patients with severe dyskariosis 53 (75.7%) had CIN II/ III. Of 3 patients with glandular abnormalities 2 had CIN II/III only, and 1 patient had high grade glandular disease.
Conclusion: Patients with postcoital bleeding have a statistically significant higher incidence of CIN. All patients should be referred to colposcopy with postcoital bleeding after excluding polyps and infection.

MA-08-004
The Conservative Management of High-Grade Smears
Esther Moss
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G. Owen, C. Redman

Objective: The conservative management of high-grade smears is controversial due to concerns over missed or progressive disease.
Method: All referrals for colpscopy due to moderate dyskaryosis between March 2004 and December 2006 were selected. Women found to have no cervical abnormality on colposcopic examination, despite adequate visualisation of the squamocolumnar junction, and who did not undergo a LLETZ biopsy at first presentation were investigated.
Results: Thirty-six women were identified, median age 27.5 years. The reason given for not treating at the first visit was colposcopy/cytology discrepancy in 25 cases, request for conservative management in 10 cases and return for treatment in 1 case. 22 women underwent a LLETZ biopsy at some point following the initial colposcopic examination, median time to LLETZ 4.3 months (range 3.1-21.7 months), of these 73% of specimens contained CIN 2/3. 14 women did not undergo a LLETZ and were discharged once their cytology had returned to normal. The median time for the return to normal cytology was 12.5 months (range 2.9-38.5 months). The median follow-up period following normal cytology was 44.9 months (range 10.3-66 months) and during this period the conservatively managed women had a median of 3 negative smears (range 1-5). Only one woman had an abnormal smear during the follow-up period, a borderline nuclear abnormality.
Conclusion: A proportion of cervical intraepithelial lesions will regress with time. This study shows that the conservative management of moderate dyskaryosis in the absence of colposcopic abnormalities appears to be acceptable management in a selected group of patients.

MA-08-005
Diagnosis and Management of Microinvasive Carcinoma of the Uterine Cervix
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There are three latency phases in the natural history of microinvasive cancer of the uterine cervix (MIC). The first is between the appearance of intraepithelial neoplasia and the first invasive breakthrough into the cervical stroma, the second phase is between this first breach of the basement membrane and the formation of recognizable buds. The third phase ends when the small buds in the stroma establish themselves as entities capable of further spread. The colposcopic appearance of MIC depends on its location and size of the field of CIN from which it arises. One third of early invasive foci originate from the ectocervical epithelium (1). Such foci of early stromal invasion do not have a pathognomic appearance at colposcopy, they have the appearance of the CIN from which it arises. Somewhat larger lesions appear as a small ulcer or produce a slight bump. These lesions are more amenable to colposcopic diagnosis. Foci arising from cervical glands are hidden from colposcopy until they establish a relationship to the surface of the ectocervix. Foci in the cervical canal are not accessible to colposcopy and epithelial abnormalities on the ectocervix provide no clue to their presence. Most colposcopic clues to the presence of early invasion are indirect: 1. The larger the surface area of a major colposcopic lesion, the higher the likelihood of early invasion. 2.Early invasion is more common when different major colposcopic abnormalities are combined. 3. Increased vascularity with focal collections of atypical vessels also suggests microinvasion. The vessels are often drawn out, have an irregular course, and are prone to bleed. The definitive diagnosis of MIC is usually based on examination of a specimen obtained at an excisional procedure. Punch biopsy is inadequate to diagnose MIC. Before deciding how to treat MIC it is important to know how the diagnosis was made. This raises the following questions:

1. What are the dimensions and histologic characteristics of the lesion? 2. Were the microinvasive lesion and its preinvasive components removed in their entirety? In cervical cancer, the extent of treatment increases with the extent of invasion and the size of the lesion. Women with larger lesions have a higher risk of lymph node metastases and recurrence than those with smaller lesions. Extensive experience at our institution indicates that MIC with a tumor volume of <350 mm3 is not associated with metastatic spread. MIC <350 mm3 can be considered localized disease and may be treated by local therapeutic measures if the excision of lesion was complete. If preinvasive disease is present at a margin of the excised specimen, and if the uterus is to be preserved, than the management is similar that to CIN. If preservation of fertility is not an aim, simple hysterectomy is adequate.
Not processing excisional specimens as step-serial sections may increase the risk of missing more advanced, invasive disease in a excisional specimen. This suggests that the histologic processing of excisional specimens might profit from standardization (2). On the basis of an adequately evaluated specimen, radical surgery for MIC is unnecessary. Combined conization and laparoscopic pelvic lymph-node dissection is an option for selected patients with FIGO stage Ia2 disease or FIGO Ia1 lesions with lymphvascular space involvement. Sentinel lymph node biopsy is under study to produce adequate staging in small lesions with risk factors. Although still performed at many institutions, there is no place for parametrial dissection, radical hysterectomy or radical trachelectomy. (1) Reich O, et al. Obstet Gynecol 2001;97:890; (2) Reich O et al. Int J Gynecol Pathol 2002;21:416

MA-08-006

Conservative management of stage IB1 cervical cancer by conization and pelvic lymphadenectomy

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Objective: To assess the safety and effectiveness of conservative therapy for stage IB1 cervical tumours in patients desiring to preserve fertility.
Method: From 1995 to April 2007 12 patients with cervical tumour ≤2 cm., aged ≤40 years with no uterine and lymphnode neoplastic involvement were evaluated. One woman was diagnosed by cervical biopsy. Eleven patients had previously received cervical conization in other hospitals and restaging was planned by means of cervical biopsy and pelvic lymphadenectomy. Repeated cervical conization was scheduled in case of risk factors present in the previous cone specimen or positive cervical biopsy.
Results: Twelve women accepted the conservative approach. Median age was 32.5 years and median tumour size was 9 mm. (range 8-20 mm.). Adenocarcinoma was present in 5 cases (42%) and undifferentiated neoplasia in 5 (42%). One patient with a 20 mm. squamous neoplasia underwent cold-knife conization and pelvic lymphadenectomy in our hospital. In all eleven cases referred after conization performed elsewhere, PAP smear and cervical biopsy resulted negative: all of them underwent pelvic lymphadenectomy, along with repeated cervical conization in four. Histological examination of these four conization specimens revealed mild dysplasia in two cases and no residual tumour in two. No pathologic lymphnode involvement was found in the whole series. After a median follow-up of 94 months one pelvic relapse was observed (treated by chemo-RT) and one patient underwent LEEP for CIN3. Twelve pregnancies occurred in 10 patients and 6 live babies have born (two preterm at 27 and 32 weeks), while one pregnancy is ongoing; furthermore two first-trimester miscarriages, one second-trimester fetal loss, an ectopic pregnancy and a termination of pregnancy (due to genetic anomaly) have been recorded. Three patients decided to undergo hysterectomy 3, 9 and 12 years after conservative therapy: in one microinvasive adenocarcinoma was found in the hysterectomy specimen.
Conclusion: Stage IB cervical carcinoma up to 2 cm. can be safely treated by conization and pelvic lymphadenectomy and the role of radical trachelectomy, widely used in these cases, should be reconsidered. Successful pregnancies are possible with acceptable obstetric morbidity. Removal of the uterus should be considered after offspring desire has been resolved.

PS-01-001

Lymphangiogenesis in early stage of squamous cell carcinoma of the uterine cervix.

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R. Jach, P. Basta, W. Kolawa, T. Banas, A. Basta, L. Szczudlik

Objective: The contribution of lymphatic system to the dissemination of the tumor has been generally well-known for many years. Owing to discovery of new and specific lymphatic vessel markers and growth factors in recent years it has been observed that during cancer development formation of new lymphatic vessels may be present and, by analogy to tumor angiogenesis, this process was named lymphangiogenesis. Moreover, it was found that the endothelial growth factors produced by neoplastic cells of several tumor types influence their growth and dissemination. The aim of the study was the assessment of the existence of lymphangiogenesis in early stage uterine cervix cancer, and if found, their influence on the disease prognosis.
Method: The study group consisted of 71 women with invasive squamous cell carcinoma of the uterine cervix, stage IA2-IIA according to FIGO classification. To assess the differences in expression of VEGF-A, VEGF-C, VEGF-D and lymphatic vessel density between the tumor an normal cervix the control group was created. It consisted of 31 women treated surgically for reasons other than cancer. The expression of VEGF-A, VEGF-C and VEGF-D in both groups was assessed immunohistochemically. Results of immunohistochemical reactions were classified by estimating the percentage of stained cells with no respect to intensity of staining. Prox-1 and LYVE-1 were used as markers of lymphatic vessels in study and control groups. The markers were detected immunohistochemically. Assessment was performed in 50 fields under large magnification. Number of Prox-1 positive and LYVE-1 positive groups of cells per square millimeter was assumed as lymphatic vessels density.
Results: Compared to the normal cervix intratumoral and peritumoral lymphatic vessels density (LVD)was significantly increased. Peritumoral LVD was significantly higher than the intratumoral one. Intra- and peritumoral LVD showed a positive correlation with stage, grade and volume of the tumor, depth of stromal invasion, barrel growth type of cancer and VEGF-C expression. Intratumoral lymphatic vessel density correlated additionally with the presence of necrosis, while peritumoral LVD correlated with macrometastases, mononuclear cells infiltration and expression of VEGF-D and -A. Intratumoral and peritumoral lymphatic vessel density correlated with each other as well. Patients with high peritumoral LVD had significantly shorter disease-free survival and overall survival than women with low peritumoral lymphatic vessel density. In multivariate analysis stage and peritumoral lymphatic vessel density were independently predictive of disease-free and overall survival in patients with early stage cervical cancer.
Conclusion: In cervical cancer, lymphangiogenesis is observed both within the tumor and peritumorally and is more intense in the latter location. Clinical stage and the degree of peritumoral lymphangiogenesis are independent prognostic factors of disease-free and overall survival in early stage cervical cancer.

PS-01-002

Micrometastasis in sentinel lymph nodes in early stage of squamous cell carcinoma of the uterine cervix.

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P. Basta, T. Banas, P. Mach, M. Pietrus, A. Basta

Objective: One ot the significant and interesting problems in oncology are the micrometastases in various tissues of the body, already present at the time of diagnosis, but not detected with the use of standard imaging techniques or histological methods. Lymph nodes are one of the places where micrometastases often occur. In the tumors of the breast, esophagus, head and neck or melanoma the presence of micrometastases in the lymph nodes has a significant prognostic value.
The more frequent use of the sentinel node biopsy has made more intensive research regarding this question possible. Limiting the detection to one, or to only a few lymph nodes has allowed for the clinical use of expensive and time-consuming immunohistochemical and molecular methods . The aim of this work was to ascertain the frequency of occurrence of micrometastases in the sentinel lymph nodes in early stage of squamous cell carcinoma of the uterine cervix , and their influence on the course of the disease.
Method: The study group consisted of 71 women with invasive squamous cell carcinoma of the uterine cervix, stage IA2-IIA according to FIGO classification. The patients were primarily treated by radical hysterectomy and radical pelvic lymphadenectomy. Sentinel node detection were performed in 22 patient by dye method only and in the remaining 49 women by double labeled method (blue day and gamma probe-guided method). Sentinel nodes taken from 46 women were divided into two parts: one part was examined by traditional histopathology and the other by immunohistochemistry. In 22 patients sentinel nodes were divided into three parts: for standard histology, immunohistochemistry and molecular examination respectively. Detection of micrometastases in the sentinel node was only conducted in cases where no metastases was found during the standard histopathological procedure. Immunohistochemical assays were applied in 51 patients while molecular methods were utilized in 21 women. Immunohistochemical reactions were performed routinely with the use of Dako Immunostainer (DAKO, Denmark). Primary antibody, CK monoclonal, MNF116 (DAKO) in solution 1:100 was used. Micrometastasis was defined as the cluster of tumor cells not exceeding 2 mm. Cytokeratin-19 was assumed as a marker of tumor cells in the molecular method. RT-PCR was performed in order to detect its presence in the sentinel nodes.
Results: Micrometastases in the sentinel nodes were detected immunohistochemically in 4 out of 51 women (7.84%), and molecularly in 7 out of 21 patients (33.33%). In cases of positive results differences in intensity of RT-PCR reaction in sentinel nodes removed from the same patient were observed. There was a positive correlation between the presence of micrometastases and the depth of invasion, grade of VEGF-C expression and peritumoral lymphatic vessels density. There were no differences in the groups of patients with and without micrometastases as far as the disease-free survival and overall survival were concerned.
Conclusion: In early stage of cervical cancer, lymph node-localized tumor cells, forming macro- or micrometastases, that are detected directly (standard histopathology and immunohistochemistry) or indirectly (molecular method), occur in more than 60% of patients. There is a positive correlation between micrometastases in the sentinel node and the depth of tumor invasion,

PS-01-003

P16 INK4A and Progression of Low-Grade Squamous Intraepithelial Lesions

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Objective: The aim of this study was to evaluate the role of P16 (INK4a) immunocytochemistry in women with low-grade squamous intraepithelial persistent lesions, who were treated by loop electrosurgical excision procedure (LEEP) according to the risk of progression of these lesions.
Method: The study included 81 women with histologically confirmed diagnosis of CIN 1, who were followed with cytology and colposcopy until the indication of conization for persistent lesions, in the Department of Gynaecological Oncology of the Women's and Children's University Hospital of the Canary Islands, between January 2000 and December 2008. Immunohistochemical analysis of p16INH4a was performed in the cervical biopsy samples and in the conization specimens.

Results: Among 81 cervical biopsy samples analyzed by immumocytochemistry, 60 (74.1%) were positive for p16 (INK4a). Progression was observed in 26 women (32.1%), 54 (67.7%) had a persistent lesions and one case regressed. Progression to CIN 2-3 was identified in 26 of 60 (43.3%) women with positive and none of 34 women with negative P16 (INK4a) immunocytochemistry (p=0.0023). P16 (INK4a) immunostaining yielded 100% sensitivity, 33.3% specificity, 57.1% positive predictive value, and 100% negative predictive value for predict progression.
Conclusion: We concluded that P16 (INK4a) negative cervical intraepithelial neoplasia grade 1 rarely progress and may benefit from a less intensive follow-up.

PS-01-004

Age as a risk factor in patients with ASCUS

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Objective: To evaluate the age as a risk factor in patients with ASCUS and the age influence in the progression to precancerous lesions.
Method: Review of patients with the diagnosis of ASCUS obtained by Pap smear, period October 2006-August 2009 in the gynecology outpatient public health department in the city of Hospitalet de LLobregat (Barcelona). Testing HR-HPV DNA in all ASCUS Pap smear (genotypes 16,18,31,33,35,39,45,51,52,56,58,59). Prospective study evaluating the ASCUS progression to cervical precancerous lesions in the following year of diagnosis. We introduced the results in a computer database for analyzing the age (35 years old and younger or older than 35) in 3 groups: ASCUS, ASCUS with HR-HPV, and ASCUS with HR-HPV that progress to precancerous lesions (LSIL, HSIL, and Carcinoma "in situ").
Results: A total of 34.334 Pap smears were collected during the study period. 681 of them were diagnosed with ASCUS. From those ASCUS patients, the 59.3% of patients were 35 years old and younger and the 40.7 % were older than 35. The HR-HPV prevalence in ASCUS Pap smears was 33.4% in patients aged 35 and younger and 20.9% in patients aged older than 35. In patients aged older than 35 years the 53.4 % of ASCUS with HR-HPV progressed to precancerous lesions while in patients aged 35 and younger the progression was of 28%.
Conclusion: In our cohort of ASCUS there were a higher percentage of patients aged 35 and younger. This group of age showed more prevalence of HR-HPV in ASCUS Pap smears. However, progression to precancerous lesions was higher in patients older than 35 in our cohort.

PS-01-005

Ligneous cervicitis (three cases report)

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Objective: To report three cases of ligneous cervicitis cataloged after the diagnosis of plasminogen deficiency
Method: Evaluation of cases with pseudomembranous vaginal lesions and other systemic manifestations
Results: First patient was studied for dysmenorrhea, dyspareunia and primary sterility. Exophytic excrescences appeared in recurrent cervix with normal smears. After an episode of severe conjunctivitis, was performed and analytical study showing moderate Plasminogen deficiency. She was diagnosed of ligneous conjunctivitis and ligneous cervicitis parallel to. The other two cases are two sisters diagnosed with ligneous conjunctivitis at early ages, and genital problems that made us discover the presence of ligneous cervicitis.
Conclusion: The presence of component type I heterozygous plasminogen deficiency is a major cause of a rare inflammatory condition that primarily affects the mucous membranes of various human body sites in which patients develop pseudomembranous lesions on mucosal surfaces. The most common clinical is ligneous conjunctivitis (80%). Other less common manifestations are ligneous gingivitis (34%), half otitis, bronchitis and ligneous pneumonia, involvement of intestinal mucosa or the female genital tract (ligneous vaginitis) (8%). May be associated with infertility. The diagnosis requires both clinical and laboratory findings. Membranous lesions must be well documented pathologically. The laboratory analysis confirmed by measuring the activity of plasminogen. This is an unusual disorder that should be taken into account in the differential diagnosis of cervical lesions as it can lead to a false diagnosis and subsequent overtreatment.

PS-01-006

Expression of vascular endothelial growth factors VEGF- C and D, VEGFR-3, and comparison of lymphatic vessels density labeled with D2-40 antibodies as a prognostic factors in vulvar intraepithelial neoplasia and vulvar cancer

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Objective: The aim of the study was to establish the correlation between expression of VEGF-C, VEGF-D, VEGFR-3 and microvessel density as morphological prognostic factors for VIN and vulvar cancer. Vulvar cancer is uncommon and affects approximately 26 800 women worldwide, accounting for nearly 3% of all gynecologic cancers in 2002. Vulvar cancer is more common among older women and approximately 66% of patients are diagnosed at ages 70 and older. VIN lesions proceed the invasive vulvar cancer and their model of natural history resembles CIN. Lymphangiogenesis in VIN and vulvar cancer is not yet well researched. Currently, many molecular and immunohistochemical attributes, including factors associated with angio- and lymphangiogenesis have been researched in order to define their prognostic significance.
Method: The material consisted of tissue material and clinical data from patients diagnosed with: vulvar intraepithelial neoplasia VIN-10 and invasive vulvar cancer- 10. VEGF-C, VEGF-D and VEGFR-3 were analyzed using immunohistochemical staining. Microvessels were stained with LV(D2-40) antibodies and calculated intratumorally with count technique.
Results: No statistical difference was observed regarding VEGF-C, D and VEGFR-3 expression between VIN and invasive cancer, while weak expression of VEGF-C was observed in two cases and VEGF- D and VEGFR-3 expression in all cases. The strongest VEGF-D and VEGFR-3 expression was observed in vulvar cancer. The most dense lymphatic vessels pattern was observed in VIN.
Conclusion: The results showed that the switch to the lymphangiogenesis phenotype occurs prior to the stage of invasion and suggest an important role of VEGF-C, VEGF-D, VEGFR-3 and LV(D2-40) in vulvar carcinogenesis.

PS-01-007

The Columnar Epithelium Hypothesis of Cervical Carcinogenesis

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HPV is the essential etiologic agent for intraepithelial and malignant squamous as well as glandular disease of the cervix. The science community agrees that HPV infection is initiated when a trauma exposes the reserve cells of the cervical metaplastic squamous epithelium of the transformation zone to infectious virus particles. It is now hypothesized that the major pathway of cervical carcinogenesis does not start with HPV infection of the reserve cells of the metaplastic squamous epithelium after microtraumata but with the HPV infection of a distinct number of subcolumnar reserve cells of the columnar epithelium with and without microtraumata.

PS-01-008

HPV DNA presence in pelvic lymph nodes in cervical cancer

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Objective: This study intends to present a systematic overview of data that has been published so far about methods used for tissue sampling, DNA testing, prevalence of HPV DNA in pelvic lymph nodes (LN) and its prognostic significance.
Method: HPV DNA status of LN in women with cervical cancer is being explored as a potential marker of „occult" metastases. Although the presence of HPV DNA in LN usually correlates with their metastatic involvement, there is always a subgroup of HPV-positive but histologically negative LN.
Results: The significance of HPV in negative LN remains uncertain, although several studies have concluded that HPV is a risk factor of recurrence.
Conclusion: Small group size and short follow-up are the main limitations for drawing any conclusion concerning prognostic significance of the presence of HPV DNA in LN.

PS-01-009

The first results of Cervical Cancer Screening in Georgia

Tamar Alibegashvili
GSCPC, Georgia
R. Gvamichava

Objective: To analyse the first results of pilot Cervical Cancer Screening Program in Georgia
Method: The retrospective analyses of examination of 27000 women participated in Screening Program in 2008-2009
Results: In 2008 the Cervical Cancer Screening program was initiated in Tbilisi (capital of Georgia) and funded by Tbilisi Municipality and UNFPA. Screening is based on the conventional Pap test (Bethesda system 2001), target age group - 25-60 years, screening interval – three years. The cervical scrape is done by gynecologists and at the same time all women undergoes routine gynecological examination. The detailed digital case history is created for each woman. Screening is opportunistic; women's enrollment is arranged with extended media advertising campaign. In order to avoid loss of follow-up all women with abnormal Pap results and suspicions for High Grade Lesion are referred to colposcopy and biopsy (if necessary). During two years about 27 000 women were enrolled in Screening. In 88,7 % Pap tests were negative, and 11,3% - positive: ASCUS – 6 %; ASC-H – 0,7 %; LSIL – 3,2 %; HSIL – 1,2 %; AGC _ 0,2 %. The rate of different types of cytological abnormalities among positive Pap results were: ASCUS – 55,5 %; ASC-H – 6,9 %; LSIL – 28 %; HSIL – 9 %; AGUS – 0,6 %. colposcopy was done in 12 % of screened women. Among women with positive Pap test: • 38% did not reveal any abnormalities during colposcopic examination. These women were called for follow up cytology test after 6 or 12 months. • in 23% was diagnosed CIN1 by colposcopy/ histology. Taking into consideration the risk factors of development of HGCL (especially smoking) also age, location of lesion, desire of fertility, 52% of women from this group were referred to cytology and colposcopy after 12 months, another 48% _ were advised to remove lesion via ablation or excision. • in 8% was diagnosed CIN2,3. All women were suggested LEEP or hysterectomy in the cases of conjunctive pathology of corpus uteri. In each case of treatment was offered follow up after 6 months with cytology/colposcopy. • in 31% colposcopy was unsatisfactory due to invisible SCJ, but transformation zone on the ectocervix was normal. In these cases women with Pap results – ASCUS, ASC-H and LSIL were recalled for cytology after 6 or 12 months. Especially important were cases with HSIL and unsatisfactory colposcopy (30% of women with HSIL diagnoses and 3% of all Pap positive women), because occult high-grade disease might be presented. All these women with HSIL were advised LEEP. Unfortunately, screening program had not covered treatment costs in 2008-2009, but from 2010 the treatment of CIN2,3 is founded by municipal budget which will improve the quality and results of cervical screening.
Conclusion: The high rate of revealed Cervical Lesions confirms the effectiveness of Cervical Cancer screening in Georgia, nevertheless the improvement of quality of program is essential. The development of digital data base creates the ground for steady change of opportunistic screening in organized one

PS-01-011

Testing for human papillomavirus by self-obtained cervicovaginal lavage samples in women 20 to 30 years of age

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Objective: To assess suitability and acceptance of the usage of self-sampling devices for an HPV prevalence study, HPV-genotyping results from gynaecologist-sampled endocervical brush were compared with self-obtained cervicovaginal lavage.
Method: Two groups of women presenting at gynaecologist offices for routine screening were recruited: An HPV high-prevalence group (hp-group) including women with recent history of dysplasia and a low prevalence group (lp-group). Self sampling kits were shipped to the women one week before their doctor's appointment together with a questionnaire. The self-obtained and the gynaecologist-obtained samples were analysed for HPV by general primer GP5+/GP6+-based PCR and genotyped by luminex-based multiplexed genotyping. Statistical analyses were conducted by EpiData 3.1 and STATA 10.0.
Results: Of a total of 229 self sampling kits, 165 (72%) were reobtained. 45% of women in the lp-group and 73% in the hp-group were tested HPV positive. Prevalence of high-risk HPV strains in the lp-group and the hp-group was 34% and 52%, respectively. A good concordance of both sampling methods (82%, $\gamma = 0.62$) was demonstrated with no difference between lp- or hp-groups. Using the combination of both tests as gold standard, sensitivity of both methods did not differ within the lp-group (both 0.84) and hp-group (both 0.9). On a running scale between 1 (adeaquate) and 10 (displeasing), women rated user-friendliness of the self-sampling test in the lp-group or hr-group as 1.7 and 1.9, and sensation as 2.8 and 2.5, respectively.
Conclusion: The self-sampling method yielded a similar sensitivity to detect high-risk HPV strains when compared to gynaecologist-sampled endocervical brush method. Self-sampling was highly accepted and reported as easy-to-use. The method fulfilled our criteria to be further used for an HPV prevalence study in Germany in 2010.

PS-01-012

Colposcopy in women after previous "cold knife" conisation

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Objective: To find whether colposcopy is reliable in diagnosing cervical intraepithelial neoplasia in patients who have undergone a previous cold knife conization.
Method: A prospective study comprising women admitted at our clinic in the period 2007-2009.
Histological diagnosis of the grade of cervical intraepithelial neoplasia was available for 311 in the treatment- naive group and 61 in the group treated with cold knife conization.
Results: Kappa coefficients comparing the colposcopic impression (negative, low-grade, high-grade, or invasion) with histological diagnosis disclosed that there was no difference between the treatment-naive group, weighted kappa 0.44, and the previously treated group, weighted kappa 0.45. The sensitivity, specificity, positive predictive value, and negative predictive value of colposcopy for any cervical disease in the treatment-naive women were 93.8%, 57.9%, 95.7%, and 35.1%, respectively, compared with 88.5%, 68.7%, 88.4%, and 36.4% in previously treated women.

Conclusion: Previous cold knife conization of the cervix seems not to impair the ability of colposcopy in differentiation of the normal cervix from all grades of cervical dysplasia in women where the squamocolumnar junction is visible.

PS-01-013

ASCUS Pap Smears in Pregnancy

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Objective: With pregnancy, both cervical glands and stroma undergo physiologic changes, therefore the association between the cytologic diagnosis and histologic findings is significantly different in pregnant and non-pregnant women. The analysis was performed to determine the correlation among atypical squamous cells of undetermined significance (ASCUS) Pap smears in pregnant and nonpregnant women, colposcopy and histology.
Method: 50 pregnant and non-pregnant patients having ASCUS PAP smear in the period of 1 year were analysed. Inclusion criteria were: colposcopic exam within 6 months of the ASCUS Pap smear and ages between 16 and 45. The association between colposcopic and histologic data was subsequently reviewed.
Results: Our results showed that 50 women were diagnosed with ASCUS Pap smears. 41 of them were included.Of those, 20 were pregnant and 21 were nonpregnant. 11 (52.3%) of the nonpregnant patients had histologic findings of cervical intraepithelial neoplasia (CIN) compared with 6 of the 15 (40%)obstetric patients who had biopsies within the first 6 months postpartum. CIN 1 was detected in 5 of the 15 (33.3%) biopsies of the postpartum patients and 10 of the 26 (38.46%) gynecologic patients. CIN 2,3 was found in 1 of the 15 (6.6%) postpartum patients versus 2 of the 26 (7.6%) gynecologic patients.
Conclusion: A cytologic diagnosis of ASCUS in pregnancy is associated with a significantly lower rate of neoplasia than those in nonpregnant women. Therefore, in both pregnant and nonpregnant women with ASCUS Pap smear colposcopy and close follow-up are acceptable methods for management.

PS-01-014

Human Papillomavirus (HPV) DNA testing in women younger than 35 years in times of economical crisis. Does it make sense?

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Objective: Our goal was to compare the capacity of the two techniques commonly used for detection of high risk HPV to accurately predict patients with high risk cervical intraepithelial neoplasm (CIN 2 or greater) in daily clinical practice. Emphasis was put on a group of women younger then 35
Method: The study was carried out in our laboratory, which is a regional reference center for national cervical cancer screening initiative from January of 1998 to December of 2008. The study observed a total of 1538 patients referred to our unit for evaluation from primary healthcare centers, hospital wards, private practices, emergency room, patients receiving transplants and a marginal community groups (drug addicts, prostitutes and inmates). Cervical HPV DNA sampling was carried out as a first step in an exam using endocervical Dacron brush. Specimens were deposited in a commercial medium (Digene) and delivered the very day to our microbiology unit. Cervical cytology (Wied), colposcopy and Lugol guided biopsy were performed by any of three of our investigators, members of national colposcopy and cervical pathology society. Punch cervical biopsy was performed only in patients that met the clinical criteria of our staff on a colposcopic exam.
We excluded patients that had previous treatment for cervical lesions, had no valid HPV DNA result or patients that did not have a punch cervical biopsy or whose biopsy results were ambiguous or misleading. We also excluded patients that had pathological findings in vulva or vagina. HPV DNA specimens were evaluated by our hospital microbiology unit by Hybrid Capture technique between January 1998 and December 2003. From January 2004 until December 2008 an abbreviated polymerase chain reaction technique specific for HPV screening (PCR LIPA) was used. Biopsy specimens were evaluated by a specialized gynecological pathologist. The patient with CIN 2 or higher were defined as cases. We calculated sensitivity, specificity and negative predictive value for each one of the technique used to identify cases. The cohort was split in two age groups based on their age, younger and older than 35.
Results: A total of 648 patients were studied. There were 338 patients younger than 35 and 310 patients older than 35. There were 61 cases of CIN 3, 1 of adenocarcinoma and no cases of cervical carcinoma in a group of women under 35. The prevalence of biopsy results of CIN 2 or higher for women younger than 35 in our study is 27,8%, significantly higher then in the reference studies presented by Baseman (1) and Kulasingam (2).
The performance of Hybrid Capture and PCR LIPA
Case (biopsy ≥ CIN 2)
Screening technique
Positivity threshold
Sensitivity (%)
Specificity (95% IC)
Prevalence of + result
NPV Hybrid capture (278 patients)
Younger than 35
HPV DNA
Hybrid Capture HPV + HR
67,9(54,8-78,6) 75,9(65,9-83,6)

39,2 78,6
Older than 35
HPV DNA
Hybrid Capture HPV + HR
70,8(56,8-81,8) 79,3(69,6-86,5)

35,6 83,1
PCR LIPA (370 patients)
Younger than 35
HPV DNA
PCR LIPA HPV + HR
56,9(45,4-67,7) 49,6(40,9-58,3)

36,9 66,3
Older than 35
HPV DNA
PCR LIPA HPV + HR
80,0(71,4-86,5) 52,9(41,3-64,1)

60,0 63,8
Conclusion: We had a very small proportion of cervical cancer in a group of women younger than 35 (only one case of adenocarcinoma). Both tests perform poorly in women younger than 35, being PCR practically useless in this age group, so their use does not seem an economically rational option.

PS-01-015

The performance of high risk human papillomavirus (HPV) genotype detection techniques in a real life settings. Why Hybrid Capture and not PCR?

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Objective: Our goal was to compare the capacity of the two techniques commonly used for detection of high risk HPV to accurately predict patients with high risk cervical intraepithelial neoplasm (CIN 2 or greater) in daily clinical practice. It is uncommon to dispose of these data outside of large clinical studies
Method: The study was carried out in our laboratory, which is a regional reference center for national cervical cancer screening initiative from January of 1998 to December of 2008. The study observed a total of 1538 patients referred to our unit for evaluation from primary healthcare centers, hospital wards, private practices, emergency room, patients receiving transplants and a marginal community groups (drug addicts, prostitutes and inmates). Cervical HPV DNA sampling was carried out as a first step in an exam using endocervical Dacron brush. Specimens were deposited in a commercial medium (Digene) and delivered the very day to our microbiology unit. Cervical cytology (Wied), colposcopy and Lugol guided biopsy were performed by any of three of our investigators, members of national colposcopy and cervical pathology society. Punch cervical biopsy was performed only in patients that met the clinical criteria of our staff on a colposcopic exam. We excluded patients that had previous treatment for cervical lesions, had no valid HPV DNA result or patients that did not have a punch cervical biopsy or whose biopsy results were ambiguous or misleading. We also excluded patients that had pathological findings in vulva or vagina. HPV DNA specimens were evaluated by our hospital microbiology unit by Hybrid Capture technique between January 1998 and December 2003. From January 2004 until December 2008 an abbreviated polymerase chain reaction technique specific for HPV screening (PCR LIPA) was used. Biopsy specimens were evaluated by a specialized gynecological pathologist. The patient with CIN 2 or higher were defined as cases. We calculated sensitivity, specificity and negative predictive value for each one of the technique used to identify cases
Results: A total of 648 patients were studied. The prevalence of biopsy results of CIN 2 or higher in our study is 43, 4%, significantly higher then in the reference studies presented by Baseman (1) and Kulasingam (2).
The performance of Hybrid Capture and PCR LIPA
Case (biopsy ≥ CIN 2)
Screening technique Positivity threshold
Sensitivity (%) Specificity (95% IC) Prevalence of + result NPV
Hybrid capture (278 patients)
HPV DNA
Hybrid Capture VPH + HR
69,2(59,8-77,3) 77,6(70,8-83,1)
37,4 80,8

PCR LIPA (370 patients)
HPV DNA
PCR LIPA VPH + HR
70,6(63,5-76,8) 50,8(43,8-57,7)

47,8 65,3
Conclusion: Our study shows somewhat different real life performance of commonly used high risk HPV DNA tests for cervical cancer screening when compared to the clinical reference studies. The higher sensitivity and lower specificity and negative predictive value could be in part due to a significantly higher proportion of patients defined as cases (CIN 2 or higher) in our study. Hybrid Capture seems to be clearly more useful for population screening due to its higher specificity and negative predictive value.
References: 1. Baseman J, Kulasingam S, Harris T, Hughes J, Kiviat N, Mao C, Koutsky L. Evaluation of primary cervical cancer screening with an oncogenic human papillomavirus DNA test and cervical cytologic findings among women who attended family planning clinics in the United States. Am J Obstet Gynecol 2008; 199:26.e1-26.e8. 2. Kulasingam SL, Hughes JP, Kiviat NB, et al. Evaluation of human papillomavirus testing in primary screening for cervical abnormalities: comparison of sensitivity, specificity, and frequency of referral. JAMA 2002; 288:1749-57.

PS-01-016

Data from RACOMIP - Randomised Controlled Trial to Study Methods to Increase Participation in Cervical Cancer Screening Program

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Objective: Several studies including a recent audit of the Swedish screening program (Andrae 2008) have found that the foremost risk factor for cervical cancer in the context of a screeningprogram is non-participation. Women who do participate are well protected from cervical cancer. In western Sweden coverage is 81% and increasing due to systematic improvements with the aim of increasing participation The aim of the study is explore two suggested promising interventions to increase participation in a large scale randomised trial and study the effectiveness within the framework of a population based well-run screening program in which smears are routinely taken by midwives at antenatal care units.
Method: Selection was done by random among women aged 29 - 63 in West Sweden who did not have a pap smear registered within the two recent screening rounds. Women who were excluded from invitation due to total hysterectomy and women who could be identified as have immigrated into the region under the period were excluded before randomisation. July 1 2008 there was 52362 women who fulfilled the first criteria (before exclusions) identified through the Register for Prevention of Cervical Cancer in West Sweden. 8800 women were randomly selected and included in the study. 4000 women were sent a letter informing them a midwife will contact them by phone, to be offered an appointment to take a smear. After sorting out those who declined, midwifes tried to get in contact with the women and help and encourage them to participate. There was set a maximum limit of 10 attempts to call and 30 minutes spent on each woman. 800 women were randomised to the self-test HPV-arm. They were sent a letter offering a commercially available self test (QvinTip, Aprovix, Uppsala, Sweden). Thos who did not reply received a reminder. Women with positive tests were referred to a gynecologist for colposcopy and smear taking. 4000 women constitute a control group. Primary analyses are made as Intention to treat
Results: Base line Results: Telephone reminder: 752 women (19%) rejected the invitation for a call. Of the remaining no telephone number could be found for 661 women (17%). Personal telephone contact was accomplished with 2108 women (53%). The mean time used by the midwifes was 7 min per woman included. HPV-self testing: 210 (26%) of the women ordered a HPV- self test, and 120 (15%) women has returned a test. 8 of those (7%) were positive for high risk HPV.
Conclusion: Telephone reminder appears to be a feasible way to reach and encourage non-participation women to participate in a screening program. Self-testing for HPV can marginally increase participation in a well-run cervical screening program.

PS-01-017

The examination of anal smears in a selected female population, using molecular markers

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Objective: The association between HPV and cervical cancer is well established and many studies have previously emphasized on the prevention of invasive cervical cancer. The anal epithelium is also a common site of HPV transmission and infection. Few studies focused on the relation between HPV and anal infection as anal cancer is much less frequent. The aim of this study is firstly to provide epidemiological data on anal HPV infection and it's relation with cervical HPV infection. Secondly to estimate the sensitivity and specificity of three methods of anal smears examination, as screening tools in a high risk population.

Method: The study population has been classified into the following subgroups: 1. Women with cervical cancer due for radical hysterectomy 2. Women with CINII/III due for treatment 3. Women with genital warts 4. Women with negative Pap and HPV DNA tests as negative controls. Using a specific brush the anal smear is collected and transferred to a Thin-Prep Medium. At the same time cervical smear is collected too. The evaluation of the anal smear is accomplished using three tests: 1. Flow cytometry (flow- fish) of E6,E7 genes (Inviron Oncotest) 2. PCR for the identification of HPV genotypes (Genomica, HPV oligonucleotide based detection system) 3. Morphological cytology Proctoscopy is selectively applied for diagnosis only to women who are referred because of a positive test. Furthermore, it is important to note that one or more environmental, lifestyle, host-genetical co-factors might influence the appearance of anal HPV infection. For this reason a detailed sexual history is taken from the studied population.
Results: At the moment a total of 46 cases (cervical cancer, CINII/III, warts, negative controls) have been tested by flow cytometry and PCR. From the nine cases of cervical cancer eight were cervical HPV DNA positive, three were anal HPV DNA positive, two were cervical mRNA positive, while there were no anal mRNA positive cases. From the twelve cases of CINII/III nine were cervical HPV DNA positive, six were anal HPV DNA positive, four were cervical mRNA positive and one anal mRNA positive. Finally from the nineteen cases of genital warts seventeen were cervical HPV DNA positive, sixteen were anal HPV DNA positive, nine were cervical mRNA positive and five were anal mRNA positive. The negative controls have no HPV DNA or mRNA positivity either in the cervical nor anal smear. There is also high cross-correlation, partial or complete, between HPV types of cervical and anal smears. Anal smears were significantly more likely to be inadequate than cervical ones (McNemar's test, $p<0.05$). The statistical analysis of the 46 samples using the Spearman index ($r = 0.05$), showed no correlation between flow cytometry values of the cervix and anal smears. Moreover, relative risks were calculated for anal HPV infection. High risk groups for anal HPV infection are females with pre-existing cervical HPV infection (RR=17,3), and females with more than 3 life-time sexual partners (RR=2). Reported anal intercourse and the use of condom appeared to have little or no effect on anal HPV infection.
Conclusion: Women with pre-existing cervical HPV infection are more prone to be infected with anal HPV too. Whether this leads to clinical lesions is to be established in the course of the study. Examination of anal smears with PCR and flow cytometry is feasible. It seems it is more difficult to obtain an adequate smear from the anus than from the cervix and therefore more vigorous brushing is required.

PS-01-018

Significance of humanpapilloma virus E6/E7 mRNA testing and cigarette smoking in risk assessment for high grade cervical disease.

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Objective: Infection with high risk humanpapilloma virus (HPV) combined with cigarette smoking are associated with an increased risk of developing cervical cancer with HPV DNA present in up to 80% of women with LSIL of the cervix. The colposcopic management of women with low grade abnormalities remains controversial. A significant proportion of these abnormalities will regress spontaneously but some will not and will require treatment. While cytology is an effective tool for cervical screening, HPV testing has the potential to refine screening by defining which women require focused clinical attention. This study will evaluate the utility of testing for HPV mRNA E6/E7 transforming gene expression and urinary cotinine levels in women presenting at colposcopy with persistent low grade abnormalities.
Method: Subjects comprise of women presenting to the colposcopy clinic with low grade smears (LSIL and ASCUS) at the National Maternity Hospital, Dublin for their first time. Prior to colposcopic procedure women were requested to give a urine sample, a cervical smear specimen was taken for HPV testing and biopsy taken for histological evaluation. HPV DNA testing was performed using the Hybrid Capture II (Qiagen, UK) and HPV E6/E7 mRNA testing was performed using the PreTect™ HPV-Proofer (NorChip AS, Norway). Urine cotinine analysis was performed on 10ml urine samples using Immulite 2000 Nicotine Metabolite assay (Siemens, UK).
Results: 545 patient samples have been collected from women referred to colposcopy with a mean age of 31 years (range 18-63years). To date HPV testing has been performed on 232. Histology confirmation shows 53% (122/231) are CIN 1+, 27% (62/321) CIN 2+ and 47% (109/231) were normal. The overall prevalence rate of HR HPV DNA was 65% (149/231) compared with 35% (82/231) E6/E7 mRNA positive. Of HPV positive women 65% were 30yrs or younger. HPV DNA was significantly more often positive in histological confirmed normal cases 57% (62/109) compared to 29% mRNA positive. At first visit 58% of HPV DNA positive women and 65% of HPV mRNA positive women were CIN 1+. Of the 231 women recruited, to date 62 have been treated by LLETZ. HPV prevalence rates in treated cases are 67% and 34% for HPV DNA and mRNA respectively. The Positive Predictive Value for detection of CIN 2+ for HPV DNA was 79% and for HPV mRNA 87%. Preliminary urinary cotinine analysis also suggests that higher levels are detected in women with high grade disease.
Conclusion: This suggests that incorporating HPV testing into management of women presenting with low grade abnormalities could be useful in triage for persistent LSIL.

PS-01-019

Primary experience of implementation of Cervarix vaccine in Moldova.

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Objective: According to Moldova`s Cancer Register data there is tendency of cervical cancer morbidity rate growth from 13,6 to 17,9 %000 from 1999 to 2007. As well as considerably predominance of the advanced form of cervical cancer (3d and 4th stages) about 60% of all the cases of cervical cancer are the alarming facts in Republic of Moldova during last years. Despite the existence of the cervical cancer screening program, such a predominance shows inefficiency of the existent Screening program. Thus the implementing of Cervarix vaccine in Moldova is the important point in Human papillomavirus (HPV) prevention which is the CC risk factor. This main objective of this work is to evaluate the efficacy of the project of implementation of Cervarix vaccine in Moldova and to define activities for its improvement.
Method: Cervarix vaccine; 105 women were vaccinated with Cervarix at 3 private medical centers (Immuno plus) in Chisinau (Moldova) since 2008
Results: Analyze of the HPV vaccination project with using Cervarix showed that there were not serious adverse effects and 30 % of all vaccinated women mentioned just about slight painfulness in the injection place. At the same time this project meets several obstacles and disparities: insufficient awareness of medical staff and population; age group of vaccinated women (14-58 years old) mismatches the WHO recommendations (9-26 years old); charged vaccination sufficiently reduces access of low incomes women.
Conclusion: Generally, the project of Cervarix implementation has to be evaluated as an important issue in CC prevention in Moldova. Simultaneously this project should be improved by: - target group selection followed to WHO recommendations; - raising population and medical providers awareness on CC screening and HPV vaccination; - reinforcing CC screening program and introduction HPV vaccination in the National cervical cancer prevention program.

PS-01-020

The knowledge and attitude of a black ethnic minority population living in the United Kingdom to Human Papilloma virus (HPV) vaccine.

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Objective: The aim of this study was to assess the knowledge and attitude of a black ethnic minority group (Nigerian women) in Leeds to the HPV vaccine and use for prevention of cervical cancer.
Method: This is a questionnaire based survey of a group of black ethnic minority women in Leeds attending a focus group health awareness programme on cervical cancer in April 2009.
Results: Fifty women attended this meeting and forty-four questionnaires were returned completed. The age range was 18 - 50 years. All but two responders have been sexually active. 31% of women had heard of the vaccine for the prevention of HPV infection and cervical cancer. Majority of responders want HPV vaccine offered to all women. 43% of responders agreed it should be administered to girls who had never had sexual intercourse. 64% of women would agree for their daughters to receive the HPV vaccine, however only 57% of the responding women believe their partners would support the decision for their daughters to be vaccinated.
Conclusion: There is a poor knowledge of the relationship between HPV and cervical cancer. However, the attitude of women towards the vaccine uptake is encouraging. We do not exactly know what the attitude of their spouses will be but given the patriarchal cultural tradition, the successful uptake of the vaccine in young girls will improved if the fathers are targeted for health education and awareness programmes. Local community groups may be helpful in disseminating health information in a culturally appropriate manner.

PS-01-022

Are colposcopic scoring systems useful and can they improve colposcopic accuracy?

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Objective: Colposcopic accuracy is less reliable than once presumed. The Reid colposcopic index (RCI) is the most well known scoring system designed to assist in the prediction of histological diagnosis. A scoring system developed by Strander et al has included lesion size in addition to the four variables found in the RCI. The aim of our study was to validate this new scoring system, further to this a pilot study has been designed to investigate the performance of the Swede score when patient information is absent.
Method: A four month, prospective, observational study was carried out at the Royal Free Hospital, London, U.K. A total of 200 women who attended for diagnostic colposcopy or inpatient treatment for cervical intraepithelial neoplasia (CIN) were included. Both trained and trainee colposcopists participated. Swede scores were calculated during colposcopy, in addition the RCI was applied to women undergoing treatment. Scores were compared to the final histological diagnosis.
Results: Swede scores of eight or more had a specificity of 95% (95% CI 0.89-0.98) for high-grade lesions and lower scores showed good negative predictive value. Both the RCI with the Swede score performed well when aiming to predict for high grade disease in the treatment group. The trainees had a significantly greater negative predictive value when scoring three or less on the Swede score (fisher exact test, two tailed p value = 0.01).
Conclusion: At higher scores the Swede score system appears predictive of high grade disease. The Swede score was considered more user-friendly compared to the RCI. The pilot study has been designed to test the predictive value of the scoring system when colposcopists are 'masked' to patient information. If results show good predictive values, the Swede score may become beneficial in settings where cytological screening is absent.

PS-01-023

Clinical outcome of incomplete histological excisional margins following Large loop excision of transformation zone (LLETZ) for treatment of women with High Grade Cervical Intraepithelial Neoplasia (CIN)

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Objective: To establish if treatment is complete following a large loop excision of transformation zone (LLETZ) procedure for abnormal cervical cytology/ histology. Moderate and severe dyskaryosis on cervical smears require a rapid referral for colposcopic assessment. LLETZ is a form of treatment that can be reported as having incomplete histological excision margins. The objective was to evaluate the treatment offered and clinical outcome using cytology, colposcopy and histology in high grade disease.
Method: A retrospective case study of 178 women who had a LLETZ procedure for high grade CIN detected on cervical biopsy between May 2007 and May 2009. The histology report of the LLETZ sample was reviewed for its comments on histological margins. The patients were brought back to colposcopy clinic for a follow up smear and colposcopy. Results of the cytology of the follow up smears over an 18 month period were also reviewed as well as colposcopic findings for correlation.
Results: 75 cases had incomplete histological margins with a median patient age group of 27years (23-53). CIN grade 2/3 were confirmed in 93.3% (n=70) and Cervical glandular intraepithelial neoplasia(CGIN) in 4% (n=3). Microinvasive carcinoma was detected in 2.6% (n=2) and these 2 women were referred to a tertiary cancer centre for hysterectomy. Incomplete endocervical margins were detected in 85%(n=63), Incomplete ectocervical margins were detected in 4% (n=3), difficult to interpret margins due to thermal artefact occurred in 5.3%(n=4). The two squamous cell carcinomas had a hysterectomy procedure (2.66%) and two Cervical glandular intraepithelial neoplasia women had normal cytology on follow up (2.66%) while one woman opted for a hysterectomy (1.3%). Follow up cytology on all other women were normal in 89.3% (n=67), Borderline in 5.3% (n=4), Unsatisfactory in 4%(n=3) and Mildly dyskaryotic in 1.3%(n=1).Colposcopy revealed mild acetowhite changes in 1.3% of cases. Further cytology and histology showed normality. Recurrent disease subsequently occurred in 1.3% of cases at 24months with positive cytology and histology showing low grade CIN . This recurrence was in the initial incomplete endocervical histological margin group.
Conclusion: Our study shows - Incomplete histological margins following a LLETZ procedure for high grade CIN does not mean incomplete treatment. Reference: National Health Service Cervical Screening Programme (NHSCSP) Publication Vol 20: April 2004. ISBN1 84 4630145.

PS-01-024

Application of a colposcopic scoringsystem (Swedescore) in pregnant women diagnosed with atypical cytology

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Objective: In order to reduce the need for biopsies in pregnant women we evaluated the use of the Swedescore colposcopic scoring system, in pregnant women with cervical dysplasia (1).
Method: The study comprised 261 pregnant women (mean age 29,5 years) investigated with suspicion of cervical neoplasia owing to either/or atypical cervical cytology taken just before or in early pregnancy, recurrent non obstetrical bleeding and suspicious appearance of the cervix. The colposcopies were carried out by two expert colposcopists. The observations were scored to 0,1 or 2 points in five variables (grade of aceto-whiteness, margins and surface, vessel pattern, size of the lesion, response to iodine staining). Colposcopically directed punch biopsies or LEEP biopsies were taken from all lesions.

Almost all of the specimens were blindly revised by an expert on cervical pathology. The outcome of the histological examination was compared with the colposcopic score. Sensitivity and specificity were calculated for each sum of predictors and with high grade lesion (HGL),CIN2+, as end point. The importance of each of five different predictors to detect CIN2+ were analyzed by multiple logistic regression.
Results: The specimens consisted of normal tissue in 19,5%, low grade lesions, LGL (L-SIL) in 26,1%, HGL in 52,9% and cancer in 1,5%. All CIN2 and all CIN3 had a score of 5 or more and all cancers had a total score of 8 and more. The sensitivity for CIN2+ was 100% with at total score less than 5 but the specificity for CIN 2+ with a total score of 8 or more was lower than in non pregnant women (70% vs 90%(1)). With CIN3+ as end point the specificity did not significantly increase. For detection of CIN2+ lesions among pregnant women margins and surface, vessel pattern and lesion size proved to be of more significance than aceto-whiteness and iodine staining.
Conclusion: The colposcopic scoring system (Swedescore) performed almost as good in pregnant women as in a previous study in non–pregnant, menstruating women (Strander et al. 2005 (1)). Thus, the Swedescore seems to be a useful tool in reducing the need for biopsies in pregnant women with atypical cytology. The significance of lesion size in pregnant women was higher than in non-pregnant women and, therefore, alterations of lesion size during pregnancy might be an important prognostic factor for progression or regression of the lesion post partum. References: 1. Strander et al, Acta Obstet Gynecol Scand 2005: 84; 1013-1017

PS-01-025

Does the use of Iodine reduce the incidence of infection after cervical biopsies?

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Objective: Schiller's Test is been widely used in colposcopy. In the test Lugol's iodine is applied to the cervix. Normal cervical tissue stains brown due to its high glycogen content, while abnormal dyskaryotic tissue does not take up the stain. Additionally, Lugol's iodine solution can be used as an antiseptic and disinfectant pre- and post-operatively. One of the great advantages of iodine as an antiseptic agent is the wide scope of antimicrobial activity and the ability to kill most pathogens including spores. At present most clinicians only use Lugol's iodine as part of schillers test and not routinely to minimise post operative infection. The main morbidities of large loop excision of the transformation zone (LLETZ) and other cervical treatments are infection and bleeding. Secondary haemorrhage is often due to infection. The aim of this retrospective observational study is to assess whether the regular use of Iodine before and after cervical biopsy procedures is associated with reduced rates of post operative infection.
Method: Data was collected via compuscope (software that stores details of each colposcopic consultation). 630 patients underwent cervical treatment during the period of July 2007 to June 2009. Of these patients, 110 had LLETZ, 339 had a single cervical biopsy, 157 had multiple biopsies and 24 women had cervical polypectomy. All patients had pre and post treatment with iodine. Each woman was interviewed at their 6-month follow up appointment by the same clinician using a structured questionnaire. Questions included whether the patient had any offensive vaginal discharge which required a visit to their GP or hospital and whether they were given any antibiotics.
Results: The mean age of women attending the clinic was 36 years old (ranged 21 to 76). Twenty six percent of patients had high grade disease including twelve cases of glandular abnormalities; the rest had low grade disease or had been referred for other reasons. Of the 630 patients, only one patient (0.2%) reported that she visited her general practitioner with PV discharge/bleeding and was given antibiotics. None of the patients were admitted to the hospital or reported secondary haemorrhage.
Conclusion: Infections after cervical biopsies are uncommon but can be very distressing for the women, especially since it is recognised that colposcopy clinics are associated with high patient anxiety levels. In this study, the incidence of post operative infection after cervical biopsies procedures using Lugol's iodine was 0.2%. This is much lower than the cited infection and secondary haemorrhage rates reported after cervical treatments. The use of Lugol's iodine pre and post procedures may provide a simple and inexpensive measure to prevent secondary infection in colposcopy clinic. There is a need for a large prospective randomised controlled study to confirm this finding.

PS-01-026

Value and feasibility of cone biopsy for pregnant patients with suspicion on HSIL and/or microinvasive cervical cancer – a retrospective analysis.

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Objective: The aim of this study was the evaluation of the efficacy and outcome of patients who underwent cone biopsy during pregnancy regarding preoperative cytological and histological results compared with postoperative histological results as well as complications during surgery, following pregnancy and delivery.
Method: We performed a file review and found 26 patients who underwent cone biopsy during pregnancy at our institution between 2003 and 2009 .All patients initially consulted our outpatient department because of abnormal cytological screening results. Here a Pap smear, HPV-testing (HC2 and nested multiplex PCR) and a colposcopic examination including biopsies was performed. Suspect findings during these examinations for HSIL and/or suspicion on invasiveness led to further surgical evaluation by cone biopsy. Four patients underwent laser conization and 22 LLETZ. The data collection contains histological results, size of pathological specimen, intraoperative complications, the affection of the margins, pre- and peripartal complications. Additionally a questionnaire was created to get further information about the mode of delivery, postpartum cytological results and procedures.
Results: The median of the week of gestation in which the conization was performes was 12 weeks with a range of 11 weeks. Three patients showed an invasive cancer, two with a microinvasion and one with a pT1b1 tumor. In 21 patients a CIN3 lesion and one CIN2 lesion were found in the cone biopsy. In one patient we could not evaluate the histological result. In HPV-typing we found HPV16 in 13 patients, in one patient HPV18. Four patients showed HPV 31, 52, 39+51 and 35. In 8 patients HPV-DNA could not be detected. No intraoperative complications were observed. One patient presented a missed abortion evaluated by postoperative ultrasound. In 15 patients we found positive microscopic resection margins (58%), 9 patients showed complete resection with no microscopic residual tumor. In two patients surgical margins could not be evaluated. Colposcopic impression matched with the histological result of the biopsy in 10 patients and with the histological results after the conization in 11 patients, respectively. The histological results of the biopsy and of the conization correlated in 10 patients (38,5%). Here 8 cases showed more low-graded lesions in the colposcopically-assisted biopsy than in the histological examination of the cone. All three cases of invasive cancer presented as no more than Pap IV and CIN3 in preoperative cytology and colposcopically assisted biopsy, respectively.
Conclusion: LLETZ and laser conization are feasible in early pregnancy. Careful colposcopic examination should select patients with suspicion on HSIL and/or microinvasive cervical cancer for whom these procedures should be discussed.

PS-01-027

The associations of HPV infection with clinical data and cervical pathology

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Objective: (i) describe the prevalence of HPV infection among women indicated to colposcopy, (ii) assess the associations between the HPV infection and patients´ clinical data, and (iii) find the risk factors for cytologic-histologic changes in cervix.
Method: The protocols of colposcopy of 927 women (mean age 33.8±10.27 years) were analyzed retrospectively. All participants were indicated to colposcopy by their gynecologists and the protocols were included to the study consequently.
Results: (i) Twenty three HPV genotypes were tested in 76.8% of participants. The prevalence of HPV infection was 80,9%. Among those, 73% were carrying high risk HPV, 3,5% low risk and 4,4% were suffering from HPV infection of uncnown risk level. The most prevalent genotype of HPV was 16 (33,9%), followed by type 33 (10,1%) and type 31 (7,6%) (proportion test, p<0.05). Types 51 (5,4%), 53 (4,8%), 58 (4,8%) and 66 (5,1%) were presented equally, but significantly less frequent than type 31 (p<0.05). Type 18 (3,9%) was also less frequent than previous group and followed by types 6, 45, lvx160, 61, and types 81, 62, 11, 83, 39, 56, 82. The most unusual types were 54, 35 and 60. (ii) Linear regression analysis adjusted by marital status revealed that women who carried HPV with high or unknown risk were significantly younger [regression coeficients (r) 4.3, p=0,018 and 2.8 years, p=0,002, respectively] than patients who were tested HPV negative. The associations between HPV infection and clinical data were assessed by logistic regression models adjusted by age, marital status, number of abortions or births, and number of sexual partners during patients´ lifetime. The risk of high risk HPV infection increased with every abortion gone thrue [adjusted odds ratio (aOR)=1.19, p=0.038] and was higher in singel women compared to the marryed ones (aOR= 2.03, p=0.018). The risk was decreased, when a patient was older (aOR=0.96, p=0.001 for a single year) or was giving birth compared to nulliparous women (aOR=0.59, p=0.039). The HPV negativity showed associations opposite to the high risk HPV infection. The risk of low risk HPV infection was not significantly influenced by age, marital status, number of abortion or birts. (iii) High risk HPV infection was most significant risk factor for HSIL, followed by ASCUS and LSIL (aORs 3.39, p=0.001, 2.49, p=0.003 and 2.47, p=0.005, respectively). Similary, HPV type 16 was associated with increased risk of HSIL and ASC-H (aORs 3.26, p=0.002 and 3.12, p=0.016, respectively). The infection of high risk HPV was also a strong risk factor for histological changes at cervix in following order: CIN II (aOR=7.99, p<0.0001), CIN III and carcinoma in situ (aOR=6.72, p=0.003), CIN I (aOR=4.21, p<0.001), and cervicitis (aOR=2.24, p=0.022). HPV infection with low or unknown risk level were not significant risk factors for cervical pathology. In addition, age adjusted analysis showed increased risk for cervical pathology (CIN III aOR=6.4, p=0.019; CIN I aOR=3.62, p=0.007; cervicitis aOR=3.47, p=0.007) among couples who used hormonal contraception compared to the codome users.
Conclusion: The prevalence of HPV genotypes in Estonian women is similar to Europien and Asian women. Younger single women, who experiance unsafe sexual intercourses and plan their family throu abortions is the risk population for high risk HPV infection. High risk HPV is a significant risk factor for cervical pathology while low risk HPV infection is not.

PS-01-028

Does post-coital bleeding warrant a referral to a colposcopy clinic?

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Objective: A 2001 study published in the British Journal of Obstetrics and Gynaecology found that although post-coital bleeding is often not the result of a serious abnormality, it should continue to be considered as an indication of cervical cancer or cervical intraepithelial neoplasia, therefore requiring prompt referral to a colposcopy clinic1. Some of the women featured in the study who were found to have invasive cancer had normal smears or normal colposcopy findings. However, the British Society for Colposcopy and Cervical Pathology (BSCCP) published guidelines in 2004, recommending that women presenting with post-coital bleeding should be referred for gynaecological examination with onward referral for colposcopy only if cancer is suspected. Although the majority of cases of post-coital bleeding are not due to malignancy, is a referral to colposcopy and subsequent biopsy indicated from the outset? Does negative cervical cytology or normal colposcopy findings exclude serious pathology?
Method: A retrospective analysis of all cases referred with post-coital bleeding to colposcopy clinic at Liverpool Women's Hospital and Aintree Centre for Women's Health between 1st January 2008 and 31st December 2008. Information was identified using Compuscope Report Writer, a routinely used computerised medical recording system.
Results: There were 362 patients seen in colposcopy clinic following referral with post-coital bleeding. 34.8% had a smear taken during the appointment. 8.7% showed mild dyskaryosis and 0.8% showed moderate dyskaryosis. 21% of those who had a normal smear result then went on to have a biopsy taken which showed inflammation (52.4%), koilocytosis (28.6%), metaplasia (19.0%) and CIN 1 (14.2%). Cervical opinion at the first presentation showed low grade CIN in 12.4% and high grade CIN in 2.2%. 33.3% of those who had a normal colposcopic opinion received a biopsy which showed CIN 1 (10.4%), CIN 1 & 2 (5.2%), inflammation (49.3%), koilocytosis (28.6%) and metaplasia (10.4%).
Conclusion: The data showed a large number of patients with normal colposcopic opinions and normal cytological smear patterns who had abnormalities found on biopsy only. Treatment for the post coital bleeding with cryocautery or cold coagulation may have been inadequate treatment for some patients. Therefore, post-coital bleeding does warrant a referral to a colposcopy clinic and a smear and biopsy is indicated despite normal appearances at colposcopy.

PS-01-029

Topography of abnormal colposcopic findings. Is the involvement of external cervical os a marker of high-grade cervical intraepithelial neoplasia?

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Objective: To assess the correlation between topography of abnormal colposcopic findings (ACF) and grade of CIN.
Method: We studied a series of 383 patients by colposcopy. 358 of them were referred by an abnormal cytology (30 ASC-US, 152 LSIL, 162 HSIL, 14 cancer) and 25 due to abnormal colposcopy with negative cytology. During colposcopy digitalized images were obtained. We classified ACF as central if the lesion contacted with the cervical orifice or it introduced into the endocervix, and as peripheral if there was a more or less broad band of normal epithelium between the cervical os and the ACF. Directed biopsy and/or endocervical curettage, if the transformation zone was not fully visible, was performed in all patients in whom an ACF was observed, independently of its degree (minor or major changes).
Biopsy was classified as negative, CIN 1, CIN 2/3 and cancer. For the statistical analysis odds ratios (OR), 95% confidence intervals (CI), and p values were calculated using the chi square test.
Results: (see table). Colposcopic location of the ACF was peripheral in 64.9% of patients with negative or LSIL histological diagnosis; conversely location of ACF was central in 70.8% of patients with HSIL or cancer. These differences were highly significant.

Conclusion: Topographic classification of the ACF into or outside the transformation zone is often difficult to establish due to the subjective recognition of its external border. The identification of the external cervical os and its involvement by the ACF is an objective criterion easily identifiable at colposcopy that significantly correlates with a high-grade CIN or cancer. Peripheral location of ACF correlates more often with low-grade lesions.

PS-01-030

Assessment of the Dynamic Spectral Imaging System performance in three different concentrations of acetic acid solution

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Objective: To investigate the effect of the concentration of acetic acid in the diagnostic signal associated with the acetowhitening (AW) effect and to assess the performance of the DySIS colposcope in three different concentrations of acetic acid solution.
Method: Colposcopy suffers from low sensitivity, high biopsy sampling error rate and high inter- and intra-observer disagreement in identifying cervical lesions. The Dynamic Spectral Imaging System (DySIS) is a novel colposcope, indented to improve the diagnostic performance in detecting, in vivo, cervical neoplasia. It measures the dynamic characteristics of the AW effect and calculates quantitative parameters, expressing the degree and duration of the effect for every image pixel. The spatial distribution of the calculated parameters composes a color-coded map, which is superimposed onto the tissue image for guiding biopsy sampling and treatment. Both colposcopic and color-coded images are stored in an integrated database, facilitating review and patient's follow-up. The advanced system's optics and imaging electronics provide glare-free and real-time mega-pixel digital microscopic imaging. We have, for the first time, investigated the effect of the concentration of acetic acid in the diagnostic performance of DySIS. Colposcopic practices worldwide are employing different concentrations (3%, 5% most commonly), based solely on empirical-qualitative criteria. Quantitative assessment of the AW effect in different concentrations would comprise an objective validation of the most appropriate concentration, providing better results. For the purpose of this study we have enrolled 57 women with abnormal cytology. Three cases have been excluded due to technical or device misuse reasons, resulting in 54 cases eligible for the analysis. Each subject has been examined with DySIS in three successive examinations, performed within the same day and using one of the 3%, 4% and 5% concentrations in each examination, totaling 162 colposcopic examinations. Preliminary tests have been conducted to define the proper time interval between successive examinations. This interval should be longer than that time required for the tissue to restore its original color, after the application of acetic acid solution. Quite impressively this time has been measured to be 45 min, which is much longer than commonly thought. Biopsy samples were taken from tissue areas corresponding to the most atypical sites of the DySIS color-coded map. All biopsies or loop excisions were submitted for histological assessment, which has been used as the "golden standard".
Results: The performance DySIS in detecting and mapping, in vivo, cervical neoplasia has been found to be: a) sensitivity for 3%, 86% (95% CI 69% to 94%); for 4%, 79% (95% CI 61% to 90%); for 5%, 82% (95% CI 63% to 92%) and b) specificity for 3%, 81% (95% CI 62% to 91.5%); for 4%, 77% (95% CI 58% to 89%); and for 5%, 77% (95% CI 58% to 89%). DySIS demonstrates very good performance in all concentrations, while the 3% shows the best performance (sensitivity 86%, specificity 81%). Moreover, it has been observed that features, such as mosaic pattern and atypical vessels, are better highlighted when the 5% concentration is used.
Conclusion: We have for the first time assessed quantitatively the effect of the acetic acid solution in the diagnostic information associated with the AW test.
We have also assessed the performance of DySIS technology in three different concentrations of the acetic acid solution. DySIS has demonstrated an impressive reproducibility, indicating that it can be operated with different concentrations with similar and high performance. The fact that DySIS has exceeded the typical colposcopic sensitivity in detecting high grade lesions by about 70%, suggests strongly that it can also substantially improve colposcopic performance in detecting and grading, in vivo, cervical neoplasia.

PS-01-032

Clinical features of vaginal intraepithelial neoplasia

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Objective: To study the clinical characteristics of Vaginal Intraepithelial Neoplasia (VAIN) in our population.
Method: Retrospective observational study of patients monitored in our clinic with a diagnosis of VAIN in the period 1997-2007. We study their personal history, clinical features, treatment and recurrence rate.
Results: 36 cases of VAIN were diagnosed. The mean age was 42.5 (22-79). Two groups are distinguished between presence and absence of HIV infection. The 22 cases of non-infected patients had an average age of 51 (27-74), 18 cases of them were more than 50 years old. The 14 HIV-infected had a mean age of 35.7 and were all under 50 years old. 18 of the non-infected compared to 4 of the HIV-infected had a prior hysterectomy due to simultaneous CIN in most cases (OR = 11.25, 1.85-80.02). Both groups were associated with previous or simultaneous cervical lesion but with vulvar lesion only 1 non-infected, compared to 9 of those infected (OR = 37.80; 3.30-1014.4). The most frequent forms of presentation were a raised acetowhite spot with micropapillary surface (30% of HIV-negative patients and 65% of HIV-positive), a negative iodine area and an acetowhite area with thick rough surface. Other less common forms were the presence of an acetowhite smooth area, a dotted negative iodine (condylomatous colpitis), an abnormal vascularisation or non colposcopic image. The treatments used were CO2 laser vaporization of the lesions, associated or not with surgical excision (55% of HIV-negative and 70% of HIV-positive) and surgical excision of the lesion as a single treatment (40% of the HIV-negative and 14% of HIV-positive, with no significant difference). Brachytherapy was used in 4 cases of multiple recurrences (3 HIV-negative over 50 years old and 1 HIV-positive without sexual intercourse). Recurrence occurred in 8 HIV-negative aged 50 or more (44%) and 7 HIV-positive (50%). All the cases showed persistence of HPV infection.
Conclusion: 1- VAIN is a disease of immunosuppressed patients, either by HIV infection or age > 50 years. 2- The HIV-negative group is characterized by older age, in which the lesion occurs mostly in the vaginal vault as a recurrence after hysterectomy for CIN. 3- The HIV-positive group, aged around 35 years, with CD4 + <500, in which VAIN is part of a multicentric disease. 4- The relapses are very frequent in both groups due to HPV persistence despite treatment.

PS-01-033

Treatment of vulvar intraepithelial neoplasia VIN with Iscador

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Objective: To evaluate Iscador M for the treatment of VIN. Alternatives to surgery are needed for the treatment of vulvar intraepithelial neoplasia (VIN).
Method: 24 patients with grade 2 or 3 VIN were randomly assigned to receive either Iscador M or placebo, applied twice weekly for 12 weeks. The primary outcome was a improvement of quality of life and reduction of more than 25% in lesion size at 16 weeks. Secondary outcomes were histologic regression and changes in immune cells in the epidermis and dermis of the vulva and relief of symptoms.

Reduction in lesion size was classified as complete, strong partial response (76 to 99% reduction), weak partial response (26 to 75% reduction), or no response (< or =25% reduction). The follow-up period was 6 months.
Results: Lesion size was reduced by more than 25% at 20 weeks in 9 of the 12 patients (75%) treated with Iscador M and in none of those treated with placebo (P<0.001). 11 subjects (91,7%) reported improvement in QOL in 16 week (according to quality-of-life scale of the EORTC (QLQ-C30)). Histologic regression was significantly greater in the Iscador M group (P<0.001). The number of immune epidermal cells increased significantly as compared with placebo. Iscador M reduced pruritus and pain at 16 weeks (P=0.008 and P=0.004) The lesion progressed to invasion (to a depth of <1 mm) in 1 of 24 patients (4,2%) followed for 6 months in the placebo group.
Conclusion: Iscador M is effective in the treatment of VIN in selected cases.

PS-01-034
Izoprinozin in the treatment of the patients with vulvodynia
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Objective: Izoprinozin in the treatment of the patients with vulvodynia
Method: To evaluate the effectiveness of Izoprinozin in the treatment of vulvodynia caused by infectious and inflammation processes. The dominant reasons for the vulvodynia development have been vulvovaginitis and vulvitis as a result of herpes simplex virus, human papilloma virus and recurrent mycotic infection.
Results: We had 50 patients aged 16-73 with vulvodynia observed. All the patients were examined to find out the presence of specific and non-specific infections (bacteriology, bacterioscopy, PCR) and cytological follow-up was carried out. 75% of the patients showed mixed infection (HSV, HPV, Ñandida albicans, etc.). The course of vulvitis and vulvovaginitis in all patients was chronic coinciding with the decrease of the local or systemic immunity. In 15% of the patients there was a relapse of HSV infection of more than 3 years. 65% of the patients were diagnosed with pointed condyloma, 10% suffered from recurrent candidosis. Non-specific microflora was discovered in all patients, 26% of patients were diagnosed with bacterial vaginosis. The patients have been divided into 2 groups depending on the treatment: the 1st group included 40 patients having combined treatment (etiotropic antibacterial or antivirus therapy and Izoprinozin), the 2nd group included 10 patients with etiotropic treatment only. Izoprinozin was taken as a dosage of 50 mg/kg a day during 10 days once a month; in total – there were three courses of therapy. The effectiveness of combined treatment using Izoprinozin was accurately higher and comprised 87,5%, while in mono-therapy – 50% (p<0,01) with the low frequency of relapses. Adding immunotherapy to etiotropic treatment provides fuller elimination of causative agents which increases its effectiveness and decreases the frequency of relapses.
Conclusion: Therefore, applying antivirus and immunomodulatory medicine Izoprinozin in the complex treatment of the patients with vulvodynia caused by chronic vulvovaginitis accompanied by vulvodynia can be considered as an effective and advanced method of treatment.

PS-01-035
Laser vaporisation in bartholin cyst
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Objective: Bartholin´s abcess and cyst account for 2% of all gynaecological visits per annum. Affects women in reproductive age.Definitive methods for treatment of Bartholin cyst and abcess include placement of a word catheter, marsupialization, application of silver nitrate, surgical excision and laser vaporisation.
The laser vaporization has been used for creating a new drainage pathway and for complete destruction of the cyst. This procedure is rapid with low complications. The patients heal with no obvious scar formation, no persistent drainage and no impairment of sexual life. Healing is complete in 4 week's
Method: A retrospective study of the last 5 years.We reviewed our experience with laser treatment in Barholin Cyst. We verified age, parity, race, symptoms after procedure (hematoma, equimosys, fever, pain),number of agudizations, other treatments tried before and recurrence.
Results: We obtained 140 patients that were submitted to laser vaporization.The mean age was 32 years. The majority were multiparous. Our failure rate is similar to the rate described in literature.
Conclusion: We conclude that laser vaporization is a safe, easy to perform and with low recurrence method.

PS-01-036
Prognostic role of the number of metastatic lymph nodes for loco-regional control in vulvar cancer
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Objective: Groin metastases are the most important prognostic factor for recurrence and survival in vulvar cancer. Adjuvant radiotherapy is currently recommended for ≥2 affected lymph nodes by the American National Cancer Institute (NCI) guidelines and ≥3 metastatic nodes by the guidelines of the German Arbeitsgemeinschaft Gynäkologische Onkologie (AGO). Both standards are based on small and heterogeneous patient cohorts. We therefore reanalyzed the impact of the number of affected nodes for loco-regional control in primary vulvar cancer in a large and homogenous patient cohort.
Method: One-hundred and fifty-seven consecutive patients with primary squamous cell cancer of the vulva treated at our center were analyzed. All patients underwent primary surgery by triple incision resulting in complete tumor resection.
Results: Median age was 61 years; 44% had FIGO stage I, 20% stage II, 28% stage III and 8% stage IV disease. 49 patients (31%) had lymph-node metastasis; 21 patients had 1, 13 had 2 and 15 had ≥2 metastatic lymph nodes. Median follow-up was 23 months; 22 patients (14%) developed disease recurrence (77% vulva, 18% groins and 5% both locations). Patients without nodal involvement had a significantly longer disease-free survival than the other groups (p<0.001). However, in case of lymph-node metastasis the number of metastatic lymph nodes did not result in a significant difference in disease-free survival (after 2 years, the proportion of patients without disease recurrence was 88% in node negative patients and 59%, 69% and 27% in patients with one, 2 and >2 affected nodes, respectively). 31% of the patients received adjuvant radiotherapy. There was no significant difference regarding the number of patients receiving adjuvant radiotherapy between the different nodal positive subgroups.
Conclusion: Lymph node metastases remain the most important prognostic factor in patients with vulvar cancer. In our cohort, the detrimental effect of nodal involvement appeared to be independent from the number of metastatic nodes. Therefore, it might be justified to consider adjuvant radiotherapy of the groins even in patients with only one metastatic node.

PS-01-037
3D Power Doppler study of blood flow characteristics in cervical cancer and precancerous lesions
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Objective: This study aims to identify the blood flow characteristics in patients with cervical cancer and precancerous lesions. 3D Power Doppler is very sensitive in detecting small amounts of blood flow

and low velocity blood flows and is used for the qualitative and quantitative study of blood flow and blood flow patterns in various organs.
Method: In our department we have started examining patients with cervical cancer who are treated either surgically or with radiochemotherapy in the Gynecologic Oncology Department of the Hospital and patients with low and high grade squamous intraepithelial lesions using 3D Power Doppler who attend the outpatient colposcopy department. We also examine healthy women with no history of cervical or uterine pathology and have a negative Pap smear within the last 12 months. We use a transvaginal probe of 7,5 MHz of Voluson 730 Pro Ultrasound machine (General Electric) and the images are processed using the 4D View program (9.0 Version, GE Healthcare). So far we have examined over 80 patients with cervical cancer and 60 patients with cervical precancer and 50 healthy women who constitute the control group.
Results: Normal cervix shows minimal blood flow but as the pathology increases in severity the blood flow becomes more prominent with disturbed vessel architecture, altered density of vessels in the cervix and increased overall blood flow. The first results show a significant quantitative difference in the blood flow parameters among these 3 groups: VI and VFI (Vascularity Index and Vascularity-Flow Index) are significantly higher in patients with cervical cancer than patients with cervical precancer (VI P<0.005, VFI P<0,01) and controls (VI and VFI P<0,0001). Furthermore, these indices are also significantly higher in patients with cervical precancer compared to normal controls (VI and VFI P<0,0001). The patterns of the vascular network are also different in these pathologic conditions compared to the normal controls. We have identified at least five different vascularization patterns in cervical cancers which are: central vessels pattern, peripheral vessels pattern, diffuse vessels pattern, scattered vessels pattern and regional vessels pattern.
Conclusion: These preliminary results implicate that 3D Power Doppler could become a useful tool for the study of blood flow parameters of cervical cancer and precancerous lesions. Cervical precancerous lesions and cervical cancer show significant differences in their blood flow characteristics and blood vessel architecture which could aid diagnosis and characterization of these lesions non-invasively. The clinical correlation of these differences in blood flow variables and blood vessel architecture remains to be determined.

PS-01-038
Obstetric Results after Diathermy Loop Conization
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Objective: To evaluate the possible consequences of performing diathermy loop excision procedures in the cervix, on subsequent pregnancies.
Method: We analyzed the results of conization procedures carried out between January 1998 and December 2006. There were 709 cases to be considered for this study. We evaluated the age, number of previous pregnancies, number of post-conization pregnancies, type of delivery, size of the cone, pregnancy complications such as premature rupture of membranes before 37 and before 34 weeks of gestation and threatened Preterm Delivery.
Results: The 709 cases of conization included 123 (22%) women who became pregnant post-conization, 438 (62%) women who did not become pregnant and 116 (16%) women whose post-conization data could not be found. The age range was 19 to 39 years with an average of 29 years. Regarding previous pregnancies, 36% of women who became pregnant post-conization and 10% of those who did not become pregnant were nulliparous. 10 of the women who became pregnant (8.2%) had more than one post-conization pregnancy. 60% of women who became pregnant reached term delivery without fetus-mother related complications, including: 53 spontaneous deliveries, 16 cesarean sections and 5 forceps deliveries.
Complications occurred in 47 cases (38%) noticeably including 7 cases (5.69%) of late abortions, 10 cases (8%) of Premature Rupture of the Membranes before 34 weeks of gestation and 6 newborn babies weighing less than 2000 grams (4.8%). We found no differences in the depth of cones between women with term delivery and those with Premature Rupture of Membranes.
Conclusion: We conclude that, although conization is relatively easy to carry out, it is associated to increased risk of preterm delivery in subsequent pregnancies. Thus, application of this procedure requires rigorous evaluation.

PS-01-039
Analysis of amplification of the chromosome 3q26 in liquid cytology specimens with an automated assay: A potential marker for risk stratification in LSIL and HPV-positive smears
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Objective: Progression markers for women with HPV-positivity without cytological abnormalities and women with LSIL are clearly needed. Earlier studies found an increasing frequency of gene amplifications on the long arm of chromosome 3 (where the TERC gene is located) with advancing grade of CIN. The aim of this study was to screen well characterized liquid cytology specimens with an automated assay to assess the potential of this marker for risk stratification.
Method: Slides were prepared from 128 routine Thinprep specimens (stored at room temperature for up to three years), selected to cover the main cytologic groups. 126 of them with the following cytological diagnoses were suitable for 3q analysis: 28 WNL, 35 ASC-US, 59 LSIL (all CIN 1) and 14 HSIL (all CIN 3). All cases had been HPV-tested (Digene-HC2), a number of them further analyzed for HPV16/18/45 and/or p16. Slides were hybridized with a single-copy probe for the chromosome 3q26 region and a probe for the centromeric alpha-repeat sequence of chromosome 7, using standard FISH methods. Subsequently, each entire slide was analyzed using an automated fluorescence microscopy system. Cases were rated as FISH-positive if at least 2 nuclei with >4 3q signals were identified.
Results: All cases except 14 WNL were HPV-HR-positive. Among the WNL cases only two (7.1%) were FISH+. Both were HPV-HR+ and review revealed single high-grade atypical cells. While only 6 of 49 LSIL (8.2%) and 8 of 35 ASC-US (22.3%) were FISH+ all 14 HSIL showed 3q gain. 13 of them were histologically confirmed (3 CIN 2, 10 CIN 3). Detailed results will be presented.
Conclusion: Automated analysis of 3q gain showed a clear association with increasing severity of CIN and a potential for a locator function in HPV-positive smears without apparent cytologic abnormality. A prospective study seems reasonable.

PS-01-040
Expression of VEGF, VEGF-C and VEGFR-2 in CIN and cervical cancer
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Objective: The quantitation of VEGF and its correlation with disease-free and overall survival rates are still unclear in cervical carcinoma. In this study we evaluated the correlation between VEGF-C and VEGFR-2 and clinicopathologic parameters in CIN and cervical cancer.
Method: The study assessed the expression of VEGF, VEGF-C and their receptor VEGFR-2 in 35 normal cervical tissues, 35 - CIN1, 35 - CIN2 (25 non-pregnant, 15 pregnant women), 35 - CIN3 and 30-CaCx. VEGF, VEGF-C and VEGFR-2 was analyzed using RT-PCR, RQ-PCR, immunohistochemical staining and Western blot. Sperman's rank correlation and chi-square test were used.Statistically significant values were set at the level of p value </= 0.05.

Results: The expression of VEGF, VEGF-C and VEGFR-2 in normal cervical epithelium was not detected. In CIN and CaCx, both forms of VEGF and its receptor were clearly observed, indicating a correlation between the increasing intensity of their expression and the stage of carcinoma progression.
Conclusion: The results showed for the first time that the switch to the lymphangiogenesis phenotype occurs prior to the stage of invasion probably between CIN2/3 and suggest an important role of VEGF in cervical progression.

PS-01-041
mRNA HR-HPV test in HIV -positive women
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Objective: Human Papilloma Virus (HPV) infection is one of the most common STD amongst HIV positive women. Genital warts and cervical dysplasia are more common, more persistent and of greater progression potency compared to seronegative women. The objective of this paper was to examine the role of NucliSENS EasyQ for the detection of E6/E7 mRNA expression in HIV positive women.
Method: We examined 30 HIV positive women attended the Colposcopy Unit Clinic of Gynecologic Oncology of Jagiellonian University in Krakow. All women were screened with gynecological examination, cytology, colposcopy and HPV tests: HC-2, and NucliSENS EasyQ.
Results: Histological confirmed LSIL was found in 32% of HIV positive women while HSIL in 10%. Positive Pap test was more frequent among women with HIV viral load between 500 and 8.000 copies/ml, and lower CD4/CD8 ratio. Using HC-2 test HR-HPV genotype has been detected in 42% of women (9% mixed LR, HR HPV infection). A positive mRNA test dealt with 54% of HIV positive patients.
Conclusion: HIV positive subjects are at higher risk for HR-HPV infection than seronegative ones. This risk is related to a higher HIV viral load and low CD4/CD8 ratio. In HIV positive women NucliSENS EasyQ is a useful method for triage of positive Pap test and identification of subjects in greater risk of cervical disease progression.

PS-01-042
Quantification of cyclin-dependent kinase inhibitor 2A gene expression (p16ink4a and p14ARF) contributes to cytological findings and is co-elevated by age.
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Objective: Cervical cancer screening is based on cytology and HPV testing. Molecular methods and biomarkers are investigated for triaging and as progression markers. Expression of high-risk HPV oncogenes generally results in a strong overexpression of cellular proteins p16INK4a and p14ARF. These proteins are derived of the differentially spliced CDKN2A transcript. Quantification of these transcripts may contribute to detection of patients with high grade cervical lesions or cervical cancer.
Method: 102 pap smears from different patients were collected. Our study cohort comprised 54 normal HPV negative cervical smears, 48 cervical smears referred to as HSIL, and 7 cervical cancer cell lines (HeLa, CaSki, SiHa, MS751, C33a, and recently established lines Marq, and Goe). We analyzed p16ink4a and p14 ARF mRNA expression in cervical scrapes in correlation to cytological findings using real-time PCR. Pap smears were taken and stored in RNAlater®. RNA was extracted and analyzed for p16ink4a and p14 ARF expression of transcripts relative to γ-Actin as a reference standard in exfoliated cervical cells.
Results: Subjects with HSIL diagnosis showed significantly increased p16ink4a and p14 ARF expression compared to cytological normal and high-risk HPV free cervical smears. Importantly, a significant enhancement of base line expression of p16ink4a and p14 ARF also occurred as a consequence of ageing as seen in healthy women of different age.
Conclusion: Conclusion: The level of p16ink4a and p14 ARF expression correlates to severity of the cytological diagnosis and may be further investigated as biomarker for triaging of cytological results under consideration of age.

PS-01-043
Dynamic Spectral Imaging Colposcopy
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Objective: Dynamic spectral imaging (DSI) offers in-vivo quantification and mapping of cervical acetowhitening at colposcopy. The DSI colposcope (DySIS™, Dynamic Spectral Imaging System, Forth Photonics, Livingston, UK) calculates and displays a colour-coded map, which is superimposed onto the cervical image to assist colposcopic evaluation and guide biopsy sampling. The objectives of the study were: 1) Validation of DSI colposcopy in discriminating high-grade from low-grade lesions and non-neoplastic tissue. 2) Selection of the most atypical site for biopsy sampling.
Method: The study population consisted of women 18 years and over, with an intact cervix, referred for colposcopy, mainly because of abnormal cytology. The study was designed as an open, prospective, comparative clinical trial; in total, 275 women were included in three Dutch hospitals. All examinations were performed or supervised by expert colposcopists. After the application of acetic acid (3%) there was a three-minute image acquisition time required for the mapping. During this period, the DSI colposcope was used as a regular video-colposcope, allowing locating and grading of the lesion(s) based on conventional morphologic criteria by the colposcopist. After recording the colposcopic assessment, a colour-coded map was displayed, representing localisation and severity of lesion(s) based on acetowhitening. The most atypical sites, as predicted by either colour-coded map or colposcopist, were sampled. Furthermore, a 'random' sample was always collected from the transformation zone (TZ), on the opposite side of the other biopsies. If no abnormalities were visualised, one 'random' sample was collected from the TZ at 12 o'clock. All histology slides were reviewed by an independent specialised gynaecological pathologist and classified in two groups: No neoplasia or low-grade cervical lesions (Cervical Intraepithelial Neoplasia (CIN) grades 0 and 1) versus high-grade cervical lesions (CIN2, CIN3 and carcinoma). In case of disagreement with the initial assessment, a third expert reviewer graded the lesion and the final diagnosis was reached by the majority rule. The data were analysed using 2x2 tables and 95% confidence intervals (SPSS software package version 15.0, Chicago, IL, USA), with a two-sided p-value of ≤ 0.05 considered significant.
Results: Of the 275 recruited women, 33 (12.0%) were eliminated. The main reasons for elimination were unsaved digital data (n=9, 27.3%) and no colour-coded map (n=9, 27.3%). Furthermore, in 59 (21.5%) cases the study criteria were not strictly met.
Main reasons were incomplete visualisation of the TZ during the mapping procedure (n=18, 30.5%) and lack of histology from potential high-grade locations as indicated by the colour-coded map (n=15, 25.4%). This resulted in 183 'according to protocol' (ATP) cases eligible for full evaluation. The mean age of the women in the ATP cohort was 36.6 years (range: 18.7-62.6 year). Eighty-six women (47.0%) had a high-grade lesion, including two cervical adenocarcinomas. The overall sensitivity of conventional colposcopic examination for the detection of high-grade lesions was 55% (95%CI 44-65) and the positive predictive value (ppv) was 76% (95%CI 65-86). The colour-coded map had a sensitivity to detect high-grade CIN of 79% (95%CI 70-88) and a ppv of 76% (95%CI 67-84). If the colour-coded map is used as an adjunctive test during the colposcopic examination, the combined sensitivity reaches 88% (95%CI 82-95) and the ppv 72% (95%CI 63-80).

Conclusion: The results indicate that DSI colposcopy has a statistically significant higher sensitivity to detect and grade high-grade lesions than using the DSI colposcope as conventional colposcopy. If the colour-coded map is combined with conventional colposcopic examination, the sensitivity increases further while the ppv remains similar. This signifies dynamic spectral imaging as a valuable asset to the colposcopic examination.

PS-01-044

Volume assessment of the uterine cervix in women prior to LLETZ conization with three-dimensional ultrasound: Comparison of two methods

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Objective: To evaluate the volume of uterine cervix in women with cervical intraepithelial neoplasia prior to conisation with the use of the sophisticated three dimensional ultrasound VOCAL technique and the simple geometric formula for a cylinder.
Method: 3D volume datasets of the uterine cervix from 81 women were obtained prospectively within a 1-year period. Volume measurements were performed using Virtual Organ Computer aided AnaLysis (VOCALTM), which is considered the gold standard technique, and the geometric formula for a cylinder by combining the three diameters of the cervix, as it is considered to be of regular cylindrical shape. Reliability between methods was evaluated using intraclass correlation coefficient (ICC) and Bland-Altman plots were produced to examine intermethod agreement. Time needed to perform measurements was compared with Student's t-test.
Results: There was good agreement between VOCAL and the geometric formula for a cylinder (mean, -0.78%; 95% limits of agreement, -17.59 to 16.03%). Measurements performed with the formula for a cylinder were slightly greater than VOCAL by a mean (±standard error of mean) of 0.78% (±0.95%). A high degree of reliability was observed between the two methods (ICC, 0.970; 95%CI, 0.954-0.981). Cervical volume estimation with the geometric formula for a cylinder was faster to obtain.
Conclusion: This method comparison study shows that the geometric formula for a cylinder has good agreement with VOCAL and can determine the volume of the cervix in a faster way. Though cervical volumetry has not yet been introduced into clinical practice, there are certain fields of interest where cervical volume can be used such as cervical volume estimation prior to conisation. In the absence of sophisticated 3D-ultrasound technology, cervical volume can be calculated even by inexperienced sonographers with standard 2D-ultrasound machines in routine Ultrasound Department Hospital settings with the simple formula for a cylinder in an equally reliable, accurate and simple manner.

PS-01-045

The use of 3q 26 region gain detection for identifying women at higher risk to progress from LGSIL to HGSIL of the uterine cervix

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Objective: Pap smear test has dramatically reduced cervical cancer mortality by identifying premalignant lesions. However, it can not differentiate which LGSIL lesions are more likely to progress to HGSIL. The most consistent genetic aberration independently associated with progressive potential of LGSIL is gain of chromosome arm 3q. The 3q26 region contains the human telomerase RNA gene which is up-regulated during carcinogenesis. **Objective:** To asses whether LGSIL patients expressing 3q26 region gain are more likely to progress to HGSIL in comparison with patients without this genetic aberration
Method: Cervical cytological specimens of 40 women with LGSIL, obtained from 12/07 till 6/08, were examined using an automated FISH assay for the detection of 3q26 region gain. After a mean follow up of 18 months all women were reevaluated with Pap smear, colposcopy and biopsies and results were correlated with baseline FISH results
Results: Overall 9 (22.5%) patients were FISH positive for 3q26 region gain at initial cytological evaluation and 31 (77.5%) were FISH negative. Three out of nine positive patients (33.3%) and none out of 31 negative (0%) progressed to HGSIL during follow up. LGSIL remained constant in 4 positive (44.4%) and 10 negative (32.2%) patients. Overall, in 7 positive patients (77.7%) and 11 negative (35.4%) the initial LGSIL remained constant or progressed to HGSIL.
Conclusion: Detection of 3q26 region gain using FISH technology may help in identifying women at higher risk to progress from LGSIL to HGSIL, but further prospective studies with larger patient number are needed.

PS-01-046

The Accuracy of Colposcopic Biopsy in CIN Diagnostics

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Objective: Early detection of the cervical neoplasia (CIN) is of high importance in prevention of cancer. Recent large-scaled studies have shown that severity of the CIN diagnosed by punch biopsy (PB) is frequently inaccurate. It is particularly important for Russia because the ablation is method of treatment of the first priority. The recurrence rate ranges from 15 to 40%. To estimate the sensitivity of PB in diagnosis of the cervical neoplasia as compared to the histological data of subsequent LEEP.
Method: 76 patients (mean age 27±4.7) have been observed and treated in the Centre of Ob\\Gyn and Perinatology named after V.I.Kulakov, Moscow. On the basis of PB all patients were diagnosed with high grade squamous intraepithelial lesions (HSIL or CIN 2-3). All cases required diagnostic and curative loop electroexcisional procedure (LEEP) or surgical conization which have been performed within 3 months.
Results: Histological findings of PB have shown CIN III and CIN II in 54 and 22 patients respectively. In 4 out of 54 women (7.4%) with the diagnosis of CIN III, subsequent histological analysis of post-excisional cone had detected invasive carcinoma. In 2 out of 22 women (9.1%) with CIN II according to PB, CIN III has been found and in 1 (4.5%) patient invasive carcinoma was diagnosed . The higher grade of CIN basically correlated with unsatisfactory colposcopy. Thus the severity of neoplastic process based on PB has been underestimated in 7 out of 76 (9.2%) women.
Conclusion: It has been shown that perfect agreement between PB and LEEP histological results was only in 90.8% cases. Colposcopic PB is not a trouble-shooting test which could provide an adequate estimation of severity grade of the CIN on all the extent of cervical lesion. A wider introduction of LEEP method into practice in Russia as diagnostic and curative tool would increase the efficiency of diagnostics and treatment of neoplasia and would decrease the recurrent rate due to inadequate ablation treatment.

PS-01-047

Photodynamic therapy of cervical intraepithelial neoplasia using hexylaminolevulinate

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Objective: Cancer of the human cervix is the second most common female cancer with about 500.000 cases per year and develops through precancerous lesions called cervical intraepithelial neoplasia (CIN).

Established ablative treatment methods like conisation procedures may cause substantial complications in following pregnancies including premature delivery and the birth of low-weight babies. Photodynamic therapy (PDT) of CIN using modern esters of 5-aminolevulinic acid (5-ALA) like hexylaminolevulinate (HAL) or methylaminolevulinate (MAL) represents a promising alternative.
Method: After local application of a photosensitizing agent, dysplastic cells become susceptible for light of a defined wave length, which is delivered to the cervix using a PDT laser and a special cylindrical light catheter. This procedure is easily supported by the patients and can be performed on an outpatient basis.
Results: Our studies report response rates of about 65 - 70 % six months after PDT using hexylaminolevulinate as the photosensitizer. Furthermore, histological and immunohistological data show no suspicion of sustained damage to the cervical tissue like scarring or inflammation which could lead to cervical insuffiency.
Conclusion: PDT seems to be a non-invasive, repeatable procedure for CIN and cervical HPV infection with minimal side effects and preservation of cervical function which can be easily performed on outpatient basis.

PS-01-048

Determination of the diagnostic accuracy of testing for high-risk human papillomavirus types 16, 18 and 45 in precancerous cervical lesions

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Objective: We tried to determine the positive predictive value of HR-HPV testing for precancerous lesions of the cervix uteri. Therefore, we focused on the diagnostic accuracy of testing for one or more of the HPV types 16, 18 and 45 for all HR-HPV positive women.
Method: Between 2007 and 2008 a group of 477 women with a history of known cervical lesions and/or HPV infections (eligibility criterion: HR-HPVDNA positive test result with HC2T) and a group of 109 women who were examined as part of their routine cervical cancer screening were recruited. Baseline HR-HPV-Status was measured at enrollment (Hybrid Capture® 2 Testand HR-HPV 16/18/45 Probe Set Test(PST). Results were converted to the nearest equivalent in the Bethesda system. Study subjects were followed up semiannually for a period of 11/2 years. Developement of a CIN2-3 lesion was used as a surrogate endpoint.
Results: To date data for 43.5% of the risk group and for the complete control group were available. 77 CIN2-3 were HR-HPVDNA+. 85.7% of them were PST+. 8.2% (60/68) of the histologically confirmed CIN 3 lesions and six out of nine (66.6%) CIN 2 lesions were positive PST+. All histologically confirmed squamous cell carcinomas (n=4) were PST+. Three (50%) out of six detected CIN 1 lesions were PST+. Nonetheless, histology confirmed no malignancy in three cases. Two of them were PST+. Within the next few month study results will be updated.
Conclusion: Cervical cancer screening at the age of 20 years remains important as seventeen of the 68 histologically verified CIN 3 lesions arose in women who were younger than 30 years. Detection of HR-HPV types 16, 18 and 45 in conjunction with cytology could help to identify women with an underlying cervical lesion who have an elevated risk of developing severe cervical lesions.

PS-01-049

High sensitivity and high specificity for CIN2+ of p16/Ki-67 dual stained cytology in the triage of ASC-US and LSIL: Results from the EEMAPS Study

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Objective: HPV testing is frequently used for the triage of Pap cytology results categorized as ASC-US. The specificity of HPV testing, however, is negatively influenced by the HPV prevalence, which makes HPV testing less effective in the ASC-US triage of younger age groups, and which prevents it from being efficiently used in LSIL Pap cytology results. We investigated the diagnostic performance of a new dual staining approach, which is based on the simultaneous immuno-cytochemical detection of the p16 and Ki-67 biomarkers in cervical cytology specimens in a large cohort of retrospectively collected cases of ASC-US or LSIL Pap cytology results. Sensitivity and specificity of this dual-stained cytology test for detection of underlying high-grade CIN (HGCIN) was compared to HPV testing.
Method: Left-over materials from a previous pan-European retrospective cytology study were used to prepare additional ThinPrep slides for p16/Ki-67 dual immuno-staining. A total of 362 ASC-US and 415 LSIL cases with corresponding, QC-reviewed biopsy results and HPV test results were available for analysis (EEMAPS Study). The presence of one or more dual-stained cervical epithelial cell(s) defined a positive test result, independent from morphology interpretation.
Results: Positive dual-stained cytology results provided a sensitivity for underlying HGCIN of 92.2% (71/77) for ASC-US, and 94.2% (129/137) for LSIL cases, comparable to HPV testing results. In contrast, specificity was found at 80.6% (ASC-US) and 68.0% (LSIL), significantly higher than the specificity rates observed for HPV testing (36.3% in ASC-US; 19.1% in LSIL cases, respectively).
Conclusion: Dual-stained cytology for p16/Ki-67 in this study with more than 200 biopsy confirmed HGCIN cases showed high sensitivity and high specificity levels for initial Pap cytology results categorized as ASC-US or LSIL. In addition to the potential for improving current ASC-US triage algorithms, this new test may for the first time provide a triage option for LSIL cytology.

PS-01-050

Routine Use of the Thinprep Imaging System in a German High Volume Laboratory Improves Screening Quality and Productivity

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Objective: Computerassistance is one option to avoid screening errors in cytology. Several studies showed a significant increase in sensitivity for HSIL with the computer-assisted ThinPrep Imaging System (TIS) compared to conventional cytology (CC) and even manually read ThinPrep thinlayer cytology (TP). Here we report the performance of the TIS compared with CC under routine conditions.
Method: Cytomol, a private lab, started with TP in 2000. Meanwhile an experience with 185.000 cases has been achieved. After a learning phase since 1.1.2007 all thinlayer specimens have been processed by the TIS. In Germany thinlayer cytology is reserved to privately insured and self-paying patients while public healthcare only reimburses CC. To avoid bias due to control cases after abnormal CC by self-paying patients we limited the analysis to privately insured patients. This group is well screened and has a low prevalence of cervical abnormalities.
Results: From 2007 to 2009 118.412 slides have been analysed among them 84.071 by the TIS. Except of some bloody and very cell rich probes 97.25% of the smears were accepted for analysis by the system. The TIS had a rate of Pap III D (=TBS: CIN 1+2) of 2.25% compared to 0.48% for CC (34.341). This was an increase of 369%. >Pap IVa (=TBS: >CIN 3) was found in 0.15% with the TIS and in 0.07% with CC (+114%). The rate of Pap IIK findings (ASC-US equivalent) was 1.5% in TIS and 0.62% in CC. The increase of 145% is much lower than the rise in Pap III D cases. This indicates that the higher sensitivity of the TIS was achieved without a loss in specificity. While with CC 8.5 slides/h were screened, this number rose to 13.4 for manually read TPs and to 21.9 with the TIS.
Conclusion: The TIS provided improved screening quality and higher productivity.

PS-01-051

The role of colposcopy and cytology in early diagnosis of recurrence of CIN and cervical cancer after surgical treatment.

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Objective: The role of colposcopy and cytology in diagnosis of precancerous and cancerous lesions within the cervix is widely accepted. In Poland, in many centers the colposcopy is treated as less useful method than cytology in diagnosis of residual and recurrence lesions after conservative surgical treatment of CIN and early invasive cancer. In the majority of cases only speculum inspection, palpation and cytological assessment is used in the follow-up after radical hysterectomy due to cervical cancer. The colposcopy and cytology is used in few referential centers in cases of recurrence unfortunately. The aim of the work is the evaluation of colposocpy and cytology in diagnosis of residual lesions and recurrences after conservative surgery of CIN and early invasive cervical cancer as well as central (i.e. in vaginal stump) recurrence after radical surgery of invasive cervical cancer.
Method: Material and methods: the clinical material consisted of 622 women: 403 CIN cases (186 treated with LEEP, 217 conisated), 54 FIGO stage IA (48 Ca IA1, 6 Ca IA2) who underwent also conisation, 149 cases of CaIB, in which radical hysterectomy was performed, and 87 CaIB and Ca IIA in whom radical hysterectomy with adjuvant radiotherapy was offered). In all cases in 3,6,12,24,36,48 and 60 months after completion of treatment the follow up consisted of cytology, colposcopy was done.
Results: The value of colposcopy and cytology in diagnosis of residual disease was based on concordance of cytology and colposcopy with histology evaluation of biopsy specimen. The concordance of colposcopy after LEEP in cases of CIN was 84,7% and was slightly higher than concordance of cytologic evaluation compared with histology which dealt with 80,4% of cases. The concordance of colposcopy with histology of residual lesions and recurrences in CIN cases treated with cone biopsy was 78,9% and was slightly lower then the concordance of cytology with histology which was 84,5%. The cytologic-colposcopic observation of cases after CaIA1 and CaIA2 cases treated with conisation revealed that the concordance of cytology and histology was 85,1% while colposcopy and histology 81,2%. The concordance of control cytology and colposcopy with histology of vaginal stump biopsy specimen after radical hysterectomy was respectively 50% and 75%, and after radical hysterectomy with adjuvant radiotherapy the Pap smear was in 37,5% of cases concordant with histology result, and in 62,5% false positive.
Conclusion: The comparative analysis of cytology and colposcopy revealed that: approximately 70% of recurrences and residual diseases are diagnosed in first year of follow-up. the residual lesions are diagnosed mostly in the first 3 months after surgery. in cases of CIN treated with LEEP colposcopy is slightly superior compared to cytology contrary to cases of CIN treated with conisation. systematic cytologic- colposcopic follow-up may diagnose recurrences in vaginal stump after radical hysterectomy in majority of cases. the majority of false positive cytologic- colposcopic cases after brachytherapy following radical surgery does not enable the detection of true recurrences. The positive cytologic result of vaginal recurrences obliges for more precise colposcopic evaluation the entire vaginal walls and punch biopsy of most suspected tissue.

PS-01-052

Comparison of two management strategies for patient with Atipical Squamous Cells of Undetermined Significance (ASCUS)

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Objective: To find the patient with CIN1-3 using colposcopy and directed biopsi among the patient with ASCUS. To find the patient with CIN1-3 using repeated thin layer citopatology among the patient with ASCUS.
To detect the sensitivity of each methods and to compare them. To detect the prevalence of CIN1-3 in patient with ASCUS.
Method: We determined the sensitivity for detecting cervical intraepitelial neoplasia(CIN3) and cancer using colposcopy and directed biopsy or repeated thin layer cytopathology. We take 102 women with ASCUS among 1034 women that came across at the Women Center,in th Maternity of Tirana during November2008-November 2009.
Results: This study report a group of 102 women,without taking in consideracion the age,or the other factors of risk for cervical cancer. The percentage of ASCUS was 9.7%.In total was performed 69 colposcopy and 33 cases performed repeated Pap smear in 3-6 mouth interval. The colposcopy and biopsy rivealed 4.3% of patient with CIN3 so the prevalence of colposcopy result 4.3%.From the repeated PAP tests result 3% with CIN3 and the prevalence 3%.The sensitivity of these methods result 90% for colposcopy and 65% for repeated PAP tests.P* 0.001,based on Hi2 test is 13.5.
Conclusion: The result based on statisticial analysis denote a highly sensitivity of colposcopy and biopsy for detecting CIN3 and Carcinoma in compare with repeated PAP tests in interval 3-6 mounths.

PS-01-053

Cervical Intraepithelial Neoplasia Treated with Diathermy Loop Excision in Older-Than-50 Women

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Objective: To assess the evolution of patients older than 50 years, with cervical intraepithelial neoplasia, who had been treated with diathermy loop excision at our Gynecology Oncology Unit.
Method: A total of 979 conization procedures were carried out at the Pathology Unit of the inferior genital tract of the Canaries University Hospital Maternity Ward, between January 2000 and December 2006. Patients' average age was 38.5 years. We included only patients older-than-50 years in our analysis. Patients underwent a control procedure, which consisted of colposcopy, cytology and virus determination, six months after conization.
Results: We selected 108 patients (11% of total conizations) aged 56.9 years on average (range 50-73); in 88.8% of them (96/108) the surgical indication corresponded to high-grade lesions and in 11.1% (12/108) corresponded to persistence of low-grade lesions. Examination of the specimens yielded: 12.9% (14/108) micro-invasive or invasive cancer; 55.5% high-grade lesions (60/108); 26.8% (29/108) low-grade lesions and in 4.6% (5/108) normal outcome. Analysis of the status of margins revealed: clear margins in 75.9% (82/108) of patients, involvement of both margins in 8.3% (9/108) of patients, involvement of the exocervical margin in 6.4% (7/108) and involvement of the endocervical margin in 9.2% (10/108). In 11.1% of cases (12/108) persistence/relapse were diagnosed during follow-up.
Conclusion: Statistical analysis of the status of margins and number of relapses revealed that involvement of both margins was significantly most frequent among women older than 50 years ($p < 0.05$). No differences were found in the occurrence of relapse.

PS-01-054

Study of High-Grade Lesions in Patients Younger Than 25 Years at the Canaries University Hospital Maternity Ward

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Objective: To assess the evolution of high-grade lesions in patients younger than 25 years as well as their epidemiological characteristics.
Method: Retrospective descriptive study on patients younger than 25 years, referred upon HSIL cytology and/or CIN 2+ biopsy, during the period 1998-2009.

The studied variables were: age, parity, age at first intercourse, number of sexual partners, use of hormonal contraceptive methods and smoking habits. The initial examination consisted in repeating the cytology, performing colposcopy and performing exo-endocervical biopsy when necessary.
Results: A total of 103 patients younger than 25 years were referred upon diagnosis of high-grade lesions (82.5% HSIL cytology and 17.5% CIN 2+ biopsy), with an average of 8 patients/year. The age range was 15 to 24 years with an average of 21.4 years. Epidemiological data revealed an average age at first intercourse of 15 years and an average number of sexual partners of 4. The obstetric history revealed that 49.5% of patients were nulliparous, 26% were primiparous and 20% were multiparous. Oral hormonal contraceptives were the most frequently used contraceptive method (58%), followed by condoms (15%). 22% of patients used no contraception at all. Analysis of data corresponding to the initial control cytology carried out at our Unit yielded: 19% HSIL, 37% LSIL, 19% ASCUS, 17% negative cytology results and 8% not-found. Colposcopy findings revealed that 33% presented major changes, 47% patients presented minor changes, 14% presented normal outcomes, and 6% were patients to whom colposcopy was not performed or whose data could not be found. Only 37% of the biopsies presented CIN 2+ lesions. 34% (35 patients) underwent diathermy loop conization. Analysis of these results showed 69% CIN 2+, 29% CIN 1, 2% not found (one case). No case of microinvasive or infiltrating carcinoma was detected. For the remaining 66% (68 patients) – including 10 patients referred upon CIN 2+ biopsy – high-grade histological lesions were not found during the initial evaluation except for two patients. From these patients, 53% have been discharged, 28% have been lost to follow-up, in spite of being re-appointed, and 19% continue with follow-up.
Conclusion: On the one hand, we observed that, in surgically treated patients, 29% CIN I was detected in the conization piece in spite of having previous histological outcomes of high-grade lesion. On the other hand, in non-surgically treated patients, almost no histological verification of CIN 2+ could be made. These findings support the postulated low inter-examiner reproducibility of high-grade lesion histological outcomes, their quick disappearance and the possible overestimation of high-grade findings in teenage patients. On the basis of these results, we conclude that conservative management of high-grade lesions should be preferred for patients of this age group (younger than 25 years), in order to spare them from surgical treatments and their associated consequences.

PS-01-055
Squamous intraepithelial lesion and pregnancy
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Objective: To study the evolution of Squamous Intraepithelial Lesion (SIL) during pregnancy and persistence factors.
Method: Retrospective study of patients controlled at our Cervical Pathology Consultation during the years 2000-2009 for SIL during their pregnancy. We compare the initial study results during pregnancy with those carried out 3 months after delivery.
During pregnancy we proposed not to treat unless the patient refused or if invasion was suspected after colpo-histological study. We defined regression of the lesion, the combination of normal cytology and HPV infection clearance in the control performed 3 months after delivery. The statistical analysis was performed using EPI. Info 3.5.1.
Results: In the period 2000-2009 we monitored 100 cases of SIL during pregnancy, 48 high-grade SIL (HSIL) and 52 low grade SIL (LSIL) with an average age of 29.5 (19-40). The determination of HPV by Hybrid Capture II (HC II) was positive for high risk types in 75 cases of the 83 tested. HPV was typed in 45 cases of which 60% were HPV 16 and 90% (16, 18, 31, 33, 51). We carried out 2 conizations during pregnancy: a patient who was pregnant immediately after a conization for cervical intraepithelial neoplasia (CIN) 3 in which recurrence was detected at the first control and one patient with cytology of carcinoma and biopsy of CIN 3 at 15 weeks pregnancy. We know the evolution of 80 patients who came to the postpartum control. The lesion regressed in 25 cases (32%), persisted in 51 (65%) and progressed in 3 (2 cases to microinvasive carcinoma). The first case of microinvasive carcinoma appeared in a patient previously diagnosed of CIN 3 who did not turn up for conization, and the second in a 35 week pregnant patient with bleeding and no prior Pap, who was diagnosed of HSIL and a great cervical condyloma. We found association between the persistence of SIL after delivery and: the degree of lesion, RR = 2.77, CI 95% (1.4 <RR <4.08) for HSIL compared to LSIL, the age RR = 1.91 CI 95% (1.02 <RR <3.56) for patients aged above 30 compared to those under 26. Among HSIL, age over 30 was associated with higher risk of persistence, RR = 11.00 CI 95% (1.38 <RR <87.64) compared to age under 26, whereas no significant differences were found between LSIL patients regarding the age, and HPV infection type 16, with a RR (of persistence) = 1.61 95% CI (1.02 <RR <2.53) compared to infection by other high-risk HPV types. No association was found between the kind of delivery and persistence of the lesion.
Conclusion: 1. - During pregnancy we detected regression of 47% LSIL and 17% HSIL lesions. 2. - Among HSIL, there was a greater percentage of regression (57% vs. 11%) in younger women (<26), which was not observed in LSIL cases. 3. - HPV infection type 16 was associated almost invariably (19 of 21 cases) to persistence or progression of the lesion during pregnancy.

PS-01-056
High-grade CIN in pregnancy
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Objective: To present the management and the outcome of the high grade intraepithelial cervical neoplasia (HSIL) in pregnant women.
Method: A retrospective study based on the medical reports of 33 patients with diagnosis of high-grade squamous intraepithelial lesions (HSIL) in the 5 year period. Besides HPV DNA genotyping, colposcopy and cervical biopsy were used in the diagnostics and were repeated every 8 weeks during pregnancy and after delivery. Regression and progression of lesions were evaluated.
Results: Among 33 patients, 9 were excluded of the sample because the diagnosis of high-grade squamous intraepithelial lesions (HSIL) was not confirmed by the biopsy. 5 patients were submitted to treatment (cold knife conization) during pregnancy, and 2 of them presented preterm delivery at the 26th and 33rd gestational week. 19 patients were followed-up by colposcopy and biopsy among which regression occured in 4 cases. 15 patients were submitted to cold knife conisation in the period around 12 weeks postpartum. In 13% of the cases, there was lesion regression in the cone specimen.
Conclusion: Pregnant women with HSIL should be submitted to colposcopy and biopsy to exclude the invasive lesion. The expectant procedure for intraepithelial lesions in pregnancy is quite reasonable due to the possibility of regression in the postpartum period.

PS-01-057
Atypical Glandular Cells (AGC) on smear - A 10year review of diagnosis and outcomes in women with specific reference to age.
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Objective: To fully examine the referral smear, the investigations, management and the final histology and outcome of these women. Background - The incidence of (AGC) on all smears is 0.05-0.01%. which is associated with a high prevalence of invasive adenocarcinoma (40-43%) and pre-invasive disease (20-28%). NHSCSP guidelines suggest all reports attempt a site of origin and a rigorous investigative and management protocol be employed.

Method: Retrospective analysis of all women with atypical glandular cells (AGC)on smear with specific reference to two age groups, <35yrs and >36 yrs over a 10 year period from 2000-2009.
Results: The total number of women referred with AGC was 129. Total number of notes available was 121.Sites of origin were cervical n=71(55%), endometrial n=29 (22.4%) and Unspecified n=29 (22.4%). Malignancy was detected in 42/121(34.7%), premalignancy in 45/121(37.2%) and benign disease in 34/121(28.1%). Cervical disease was found in 88/121 (72.7 %) and extracervical was detected in 33/121(27.3%). Women under 35yrs all had cervical disease (n=46), Adenocarcinoma was detected in 3/46 (6.5%), Squamous cell carcinoma in 3/46 women (6.5%), premalignant disease in 38/46 (82.7%) and benign disease in 2/46 women (4.3%). There was no extracervical pathology in this age group over the 10-year period. Women over 36yrs, cervical disease (n=42) and extracervical disease (n=33) were detected representing 54.5% and 45.5% respectively. Cervical cancer was detected in 12/42 (28.5%), premalignant cervical disease in 28/42 (66.7%) while benign cervical disease occurred in 2/42 (4.8%). The vast majority of extracervical cancer was endometrial 19/33 (57.5%). Other sites included Vaginal (6%), pancreatic (3%), Vaginal (3%), ovarian (3%) and malignant melanoma (3%).
Conclusion: In conclusion - the colposcopist should insist that a report of AGC's is always supplemented by an attempt at a site of origin.In women over 36yrs of age, ultrasound + endometrial sampling +/- hysteroscopy should be part of the routine investigative protocol as well as colposcopy for treatment of these women. References: 1. NV Pisal et al. How significant is a cervical smear showing glandular dyskaryosis. Eur Gynaecol Reprod Biol 2003 Jun 10;108(2):209-12. 2. T Van Dinh et al. Management of atypical glandular cells of undetermined significance pap smears: a reappraisal. J Low Genit Tract Dis. 2003 Jan;7(1):11-5.

PS-01-058

Diathermic Asa Versus Laser Cone

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Objective: To compare the techniques used in clinics in conizations in Consultorios Dexeus.
Method: Retrospective study of a serie of 1332 conizations performed in outpatient settings. The data are drawn from the database of the department.
Results: We performed a total of 1332 conizations, 610 cone-laser (45.79%) and 722 loops diathermy (54.20%). The average age of patients was 35 years (18 - 69). The main indication is the high-grade dysplasia HSIL 895 (67.19%). All conizations were performed in outpatient settings. The surgical pieces have an average diameter of 19.83 mm, with laser 20.38 mm + / - 5.16 and 19.36 mm loop + / - 5.71 (p <0.001). The height of the conizations has an average of 14 mm, where laser 16.44 mm + / - 5 and for loops 11.96 mm + / - 6.8 (p <0.0001). The only intraoperative complication was moderate bleeding with a total of 34 patients (2.6%).
Have been described 27 (2.0%) cases with postoperative complications, with moderate bleeding 25 (1.87%) the primary, the rest are cervical canal stenosis (0.15%). The vertices are free of disease in 1265 cases (95%) with no differences between conization by loop or laser. The side margins are free in most parts 1225 (92%).
Conclusion: In the treatment of cervical dysplasia have used interchangeably as both the loop diathermy conization laser. This is a surgery with minimal complications that can be done in consultation without income or general anesthesia. Because we believe these results have to be abolished conizations cold knife or just stick to very exclusive cases

PS-01-059

Estimation of cervical regeneration and obstetric outcomes after conservative excisional treatment of cin preliminary results from a prospective study

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Objective: Recent evidence demonstrated that excisional treatment for CIN is related to an increased risk of prematurity. Women with deep (>1cm) or repeat cones are in particular risk. It has been speculated that these adverse effects are actually related to the proportion of the cervical volume or the endocervical canal that is being excised rather than the depth itself. The aim of this study is to determine how the percentage of the cervical volume (and/or endocervical canal) excised affects healing and cervical regeneration after treatment and to assess whether there is a cut-off above which cervical function and regeneration is affected. Furthermore, this study aims to assess the correlation of the proportion of excision to the risk of prematurity in future pregnancies.
Method: Design: Prospective observational study Inclusion criteria: Women planned to undergo excisional treatment for CIN that have not completed their family. Exclusion criteria: Women with a history of previous treatment. Intervention: The cervical volume (and dimensions) is calculated with an MRI volumetric estimation technique prior to treatment. The volume (and dimensions) of the cone specimen is assessed prior to fixation with the use of a volumetric tube and a ruler. A repeat MRI estimation of the volume is performed at 6 months in order to assess the cervical regeneration and correlate it to the proportion of excision. Those women that subsequently become pregnant have serial cervical length assessment with transvaginal ultrasound every 2 months. The obstetric outcomes are assessed and correlated to the proportion of excision. Outcomes: Cervical regeneration as documented by the MRI volumetry technique and obstetric outcomes in future pregnancy. These include maternal outcomes, [preterm delivery (<37 weeks), caesarian section rates, precipitous labour (<2h), and preterm spontaneous rupture of membranes (pPROM)] and fetal outcomes (low birth weight (<2500g), perinatal mortality and neonatal intensive care unit (NICU) admission).
Results: So far, a total of 48 women have been recruited and treated with LLETZ and 29 have completed the six months follow-up. One treated woman has been retreated. Four, are currently pregnant. The age varied between 22-46 years old and 33(68.75%) were nulliparous. The majority (n=43, 89.5%) were treated for a high-grade lesion. Referral cytology was compatible with ASCUS in n=4 (8.33%), LgSIL in n=5 (10.4%), HgSIL in n=37 (77%) and AIS in n=2 (4.1%). Colposcopy, revealed LgSIL in n=8 (16.66%) and HgSIL in n=40 (83.33%). The pathology report, revealed LgSIL in 5 (10.5%) and HgSIL in 43 (89.5%) of the patients. The total cervical volume (MRI) prior to treatment varied significantly between individuals from 11-35.8cm3(median 24cm3) the volume of the excised cone between 0.6-6.4cm3 (median 2cm3) and the percentage of excision between 3.65-38.46%. The preliminary data for the 29 women that completed the six months follow-up identified complete cervical healing with no defect when the proportion of the excision was less that 10%, partial and incomplete healing if it exceeded 20%, while it ranged from partial to complete healing for those that ranged between 10 and 20%. The outcomes in pregnancy will be correlated to the proportion of excision and the completeness of the regeneration.
Conclusion: There appears to be a remarkable variation amongst the volumes of cervices, cone specimens and percentages of excision. Furthermore, this preliminary data reveals that there is possibly a cut off in the proportion of the volume excised, above which healing and regeneration is adversely affected. This cut off might also signify women at increased risk of prematurity and might prove to be helpful in predicting those that need further surveillance and/or management in future pregnancy.

PS-01-060

Aggressiveness of the Human Papillomavirus in a young immunocompetent woman: A case report

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Objective: Introduction: incidence of vulvar intraepitelial neoplasia (VIN) has been doubled in recent decades. Immunosuppression is a risk factor for the development of VIN and invasive carcinoma relapses after treatment. It is estimated that 90% of anal cancers are associated with High Rish-HPV
Method: Case report: Patient of 29 years old with no relevant medical history, nulligravida. Diagnosed of condylomas, VIN III and CIN III in February 2003 with affection for the vaginal margin and endocervical lesion free. During the 18 following months checkings are made and reveal persistent VIN III and CIN III.Conization is performed and reports affection of the surgical limit. HPV 16 and 33 are positive. Some controls can not be performed because of the patient's intense pain. In December 2004 the patient wants a simple vulvectomy and it is performed with removal of the clitoral hood, with pathological report: in situ vulvar carcinoma with extension into clitoroideo hood and perianal condyloma. Over the next year she has perianal lesions treated with Aldara and Inmunoferon and a year later presented HPV 16 +, 71 + and 66 +. 6 months later, she presented CIN III cytology suspicious. In 2007 he performed new wide local excision of perineal injury, and in successive controls is objectified persistence of HPV. At the end of 2008 13 serotypes of HPV are positive. The patient, aged 35, really affected psychologically by the course of her illness, wants simple total hysterectomy and it is performed without incident. Also a excision of an anal lesion is made which resulted to be a in situ anal carcinoma.
Results: Discussion: Most HPV infections are spountaneously resolve due to the host immune response. The cases of persistence are a high risk group for malignant transformation. Different factors have been described as associated with viral category, genetic, and environmental sexual behavior. The persistence of HPV and surgical margins affected are the greatest predictors of disease recurrence after treatment.
Conclusion: There are some cases where it is unknown what causes and determinates the persistence of HPV after successive treatments in an immunocompetent patient. The ubiquity of HPV in the genital tract causes that the disease can simultaneously affect the cervix, vulva, vagina and anus.

PS-01-061

Immunomodulation and cervical intraepithelial neoplasia management

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Objective: The aim of this work was: a/the evaluation of the Iscador QuS and Intron A (interferon alpha 2b) role in the management of CIN1 and CIN2, b/ the assesment of Iscador QuS and Intron A on the selected immunological system parameters in women with CIN1 i CIN2 .
Method: Clinical material were the 156 patients with CIN and HPV who have been diagnosed and treated in our clinic for 36 months. Methods: Patients were randomized to the Iscador QuS or Intron A or the control group based on cytology, colpscopy and histologic evaluation of colposopically guided biopsy specimen. The presence of HPV was detected using molecular method- Hybrid Capture I and II. The state of immunologic system was control with cytofluorometry evaluation of limphocytes CD3+, CD4+(Th), CD8 (Ts), CD4/CD8, CD19 (lymphocytes B), CD56+/CD3-(NK cells).
Results: The multivariate analysis of CIN1 and CIN2 remission in relation to lymphocyte percentage and mode of treatment (log rank) in Iscador QuS arm revealed the highest regression index for CD4/CD8 – 2,49, CD8-0,0068, CD56+/CD3- - 0,064, CD4-0,017 i CD3-0,007. In the Intron A arm the results were: CD4/CD8-9,050, CD56+/CD3- - 0,167, CD8-0,166, CD3-0,143, Intron A treatement- 0,118 i CD19- 0,037. P< 0,05
Conclusion: 1/ The pharmacological immunomodulation, especially with Interpheron alpha increases the percentage of CIN1 and CIN2 remission, by the efferent arm of cellular immune reaction. 2/ The evaluation of CD3+ lymphocytes and the ratio CD3+/CD3- before treatment of CIN has the potential predictive value of CIN outcome.

PS-01-062

Plausibility of early invasive cervical cancer detection in pregnancy

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Objective: Cervical intraepithelial neoplasia (CIN) and cervical cancer are relatively rare complication of pregnancy, although cervical carcinoma is the most common malignancy associated with pregnancy. The most important diagnostic issue is to detect invasive process and to single out early invasive cancer.
Method: We analyzed 128 pregnant women with cytological epithelial cell abnormalities. Material was divided into two groups. Group A – 69 women, Group B – 59 women. Colposcopy was performed in all women. In Group A women suspected for early invasive cancer underwent punch biopsy, while in Group B wedge cervical biopsy was performed. Colposcopy and biopsy diagnosis was verified by histology of surgical specimen. Surgery extension ranged from conisation to radical hysterectomy. Interval between biopsy and surgery ranged from 2 weeks to 12 months. Majority of all surgeries were performed after delivery and puerperium.
Results: In Group A punch biopsy revealed 2 cases suspected for invasion and 5 cases with confirmed invasion. In final diagnosis 2 cases were confirmed as cervical cancer stage IA1 according to FIGO classification, the latter 5 cases were verified as stages IA1 - 1 case, IA2 – 2 cases, IB – 1 case, and stage II – 1 case. Furthermore 4 CIN3 cases diagnosed by punch biopsy were verified by surgery as early invasive cancer stage IA1. In Group B wedge biopsy confirmed 2 cases of early invasive cancer stage IA1, and 4 cases of stage IB. One additional case of cancer stage IA1 was added after performing surgery (CIN3 in biopsy result). In one case of IA1 cancer no invasion was found in following conisation material – we assume that the whole invasion spot was removed in wedge biopsy. Altogether within 128 pregnant women referred for colposcopy we found 16 cases with invasive cancer of which in 10 patients early invasive cancer was found. In 5 cases early invasion was detected in histological specimen obtained from surgery performed after delivery and puerperium. No invasive cancer over stage IA was missed on colposcopy/biopsy stage of diagnosis.
Conclusion: Diagnosis of an early invasive cancer in colposcopy followed by a biopsy is the greatest challenge for a colposcopist and is even harder in pregnancy. In our material statistical analysis showed no significant difference between punch biopsy and wedge biopsy group, although it seems that performing wedge biopsy allows better accuracy of histological result. What seems to be of greatest value is the possibility to omit necessity of conisation during pregnancy in women with suspected early invasive cancer, when using wedge biopsy.

PS-01-063

Ablative treatment of CIN is associated with more severe recurrences than conisation

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Objective: Epidemiology of Recurrences after Treatment of a Cin
Method: From 1987 to 2008, the diagnosis of 3158 pre invasive or early invasive cervical lesions was made in our colposcopy clinic after histological control of patients with abnormal Pap smear.

100 of these patients (3.2 %) had already been treated for high grade (54) or low grade (46) lesion from one to 20 years before. All interval Pap smears were normal after the first treatment. This situation suggests a true recurrence of the lesion after an effective treatment. The previous treatment had been performed in our hospital (66) or elsewhere (34). The grade of recurrence was LGSIL (30), HGSIL (59), ACIS (2), micro invasion (4), or early invasion (5). The mean delay before recurrence was 6, 4 years. There was no correlation between the grade of the previous lesion and the severity of the recurrence and with the delay before recurrence. The previous treatment was conization (32) or ablative treatment (68): LASER vaporization (59), electro coagulation (4), cryotherapy (4) and one vaginal application of 5FU. There was a positive correlation between severity of recurrence and ablative treatment.
Results: Most HG/invasive recurrences occur after ablative treatments mainly after LASER vaporization for low grade SIL.
Conclusion: It is suggested that after a destructive treatment perhaps incomplete, the lesion has been hidden in the canal because of the healing process with more less cervical stenosis. Because of difficulties for diagnosis, the recurrent lesion was discovered later at an advanced stage. The greatest care must be taken to perform LASER vaporization on low grade lesions close to the canal. There is a risk of difficulties for further controls. Long term follow up by endocervical cytology is mandatory after any treatment even for low grade SIL.

PS-01-064

A Review of the Management of Women Referred to Colposcopy Aged 25 years and under.

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Objective: The NHS Cervical Screening Policy in Northern Ireland offers cervical screening to women age between 20 and 64 years. This is in contrast to England and Wales were, since 2004, women are not screened until the age of 25 years. Evidence has shown that screening is of little or no benefit in this age group. Treatment following screening can lead to an increased risk of preterm labour and associated perinatal morbidity. Following Jade Goody's diagnosis with cervical cancer and subsequent death in 2009 at the age of 27 years of age there was a call for the age of screening to be reduced to 20 years again. In May 2009 the independent Advisory Committee on Cervical Screening reviewed the current guidelines and unanimously agreed that no changes were required. The objectives of our audit were to assess how many of our patients referred to colposcopy were 25 years and under over a 3 month period and what their management and outcomes were.
Method: All new patients referred to colposcopy aged 25 years and under between July and September 2009 were included in this retrospective study. A proforma was designed and included patient demographics, cytology, colpscopy and pathology findings, symptoms of abnormal bleeding and if the patients smoked. Guidelines were obtained from NHSCSP Publication No 20 Colposcopy and Programme Management.
Results: A total of 40 patients were identified and they were 19 % of the total number of new patients seen during that time frame. Age ranged from 19 to 25 years. The majority of patients were nulliparous (57%) and smokers (67%). Those who had children ranged from Para 1 (12 patients) to Para 3 (1 patient). Contraception was used in 80% and included OCP (50%), Depoprovera (10%), Mirena coil (2.5%) and condoms (in only 17.5%). Referral Smears Number of Patients Borderline 6 CIN 1 12 CIN 2 12 CIN 3 4 Unclassifiable (0) 6 Biopsies were performed in 34 out of 40 patients. Four were deferred as the patients were pregnant. Two patients had a LLETZ performed at initial visit for high grade disease. Biopsy Results Number of Patients No CIN 2 Koilocytosis 6 CIN 1 6 CIN 1 and 2 2 CIN 2 8 CIN 2 and 3 2 CIN 3 7 CIN 0 1 Patients with no CIN or koilocytosis had no further treatment.
Those with CIN 1 only were managed conservatively with cytological and colposcopic follow up as per guidelines. Six patients who had CIN 1 and/or CIN 2 had cold coagulation after histological diagnosis as per guidelines. The remaining fourteen with CIN 2, 3 and unclassifiable (CIN 0) had excisional treatment in the form of a LLETZ. Ten of these patients had confirmed high grade lesions on histology (7 with CIN 4) and 3 had CIN 1. Of the twenty patients who had high grade disease on histology twelve of these patients were smokers and five had symptoms of abnormal bleeding or discharge
Conclusion: Women in Northern Ireland are still screened from the age of 20 years and comprise 19 % of our new referrals to colposcopy which is a considerable percentage of our workload. Half of all patients referred had histological diagnosis on biopsy of high grade disease and 35% underwent excisional treatment in the form of a LLETZ. These patients can be difficult to manage as one has to balance the risk of high grade disease developing into invasive disease and the risks associated with excisional treatment and future fertility. With half our referred patients having high grade disease is it better to keep screening 20 year olds and not increase to 25years?

PS-01-065

Is a colposcopically-directed punch biopsy a reliable diagnostic test in low-grade cervical intraepithelial neoplasia? A prospective study

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Objective: Colposcopy has a sensitivity of only 50% for high grade CIN and the validity of colposcopy-directed punch biopsy (CDPB) has been questioned. As a preliminary to performing a RCT evaluating the cost-effectiveness of using CDPB in the management of women referred with low grade smears, a prospective trial evaluating the accuracy of CDPB in patients with suspected low-grade CIN was performed.
Method: Entry criteria were patients with low-grade cytological and colposcopic findings and in whom the decision to perform a LLETZ biopsy had been taken. A single CDPB was taken immediately before the LLETZ. The trial was powered in order to detect a level of Kappa (ɣ) of 0.4 (ie fair to moderate agreement), with a two-sided significance level of 5% and a power of 90%.
Results: 63 paired CDPB/LLETZ specimens were analysed. Histologically inadequate specimens were excluded. 35% (n=22) of the cohort had high-grade CIN (CIN2/3) which was detected by punch biopsy in 9 cases. There were no false positive CDPB results.
Conclusion: The accuracy of CDPB in this context has never been performed. The amount of high-grade CIN detected despite there being only low grade findings accords with previous studies and exemplifies the lack of sensitivity of colposcopic assessment based on cytology and colposcopic findings alone. These data indicate that even a single CDPB will improve sensitivity without an increase in false positives thereby improving detection of high-grade CIN and suggests that this strategy would be cost-effective.

PS-01-066

Conisation depth and cone volume with LLETZ method for cervical intraepithelial neoplasia

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Objective: To assess LLETZ conisation performed for cervical pathology and to review existing data about future obstetric adverse effects in female patients.
Method: A retrospective observational study in the Colposcopy Unit of a University Hospital setting. Three hundred sixty one (n=361) cases of LLETZ cervical conisation were reviewed and intraepithelial lesion type, cone volume, conisation depth and excision margins were recorded.

Literature review was performed with the use of PubMed Medline, Embase and Cochrane databases.
Results: Mean age of women was 36.7 years with 181 (50.5%) cases of LGSIL, 166 (45.7%) HGSIL and 14 (3.8%) stage IA1 cervical carcinoma. Mean cone volume was 2.2ml, with 6.9% of cones >4cm3. Mean conisation depth was 10.9mm, with 30.2% of cones >10mm. In the general cohort, 25% of women had incomplete removal of lesion. Cones measuring ≥10.0mm in length had a significantly higher percentage of excision free margins than those with smaller length (P=0.01). Such correlation was not significant for cone volume (P>0.05). On review of literature, cone volume>4cm3 leads to a significant risk of preterm delivery (31.7% versus 3.2%), as well as conisation depth>10mm (pooled relative risk=2.6; 95%CI, 1.3-5.3).
Conclusion: Existing evidence suggests a possible adverse obstetric outcome in women treated with LLETZ method, when cone volume and conisation depth exceed certain limits. However, more conservative approachs in terms of a smaller cone would lead to a higher percentage of incomplete removal of lesion. Conisation should therefore be performed by experienced colposcopists who can achieve the best balance between maximum eradication rates of intraepithelial lesions and minimum disruption of cervical anatomy and function which may lead to future adverse effects.

PS-01-067

Volume and length restoration of the uterine cervix after LLETZ conisation for intraepithelial cervical neoplasia

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Objective: Investigation of volume/length restoration of the uterine cervix at 6 months following LLETZ conisation for intraepithelial cervical neoplasia.
Method: Three-dimensional ultrasound images of the uterine cervix from 78 women prior to conisation were obtained prospectively within a 1-year period. To date, 45 women have presented for ultrasound follow-up at 6 months post-conisation. Cervical volume and length prior to conisation and 6 months later was assessed with VOCALTM ultrasound technique (manual mode-9° rotation angle) and was correlated with the volume/length of the cervical cone excised and initial volume/length of cervix.
Results: The volume of the cervix at 6 months post-conisation (n=45) correlated significantly (P<0.001) with the cone volume (cm3) and the percentage of initial cervical volume excised (P<0.001). The length of the cervix at 6 months correlated significantly (P<0.001) with the cone height/conisation depth (mm) and the percentage of initial cervical length excised (P<0.001). There seems to be a cut-off point suggesting that when >15% of the initial cervical volume (mean cone volume>3.1cm3) is excised, then cervical volume at 6 months post-conisation falls below 85% the initial cervical volume; when >45% of the initial cervical length is excised (mean conisation depth>15 mm), then the restored length falls below 80% the initial cervical length.
Conclusion: Restoration of the cervix following LLETZ conisation at 6 months may be a function of the cone dimensions (volume/height) and initial dimensions of the cervix. It may be important therefore to sonographically determine the volume/length of cervix prior to conisation so as to be more conservative in terms of the amount of tissue removed with conisation, especially when the patient has initially a relatively small-sized cervix; in all cases, conisation should achieve the best balance between maximum eradication rates of intraepithelial lesion and minimum disruption of the process of cervical restoration.

PS-01-068

Role Of Human Papillomavirus Load Testing In Follow-Up After Hsil Treatment

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Objective: : HPV testing with or without cytology is offered as an alternative option in follow-up after CIN 2 -3 treatment (HSIL). As the HPV test demonstrates higher sensitivity than the cytology, HPV test could raise diagnostic efficacy in postreatment follow-up. The role of viral load in prediction of success of treatment requires further studying. To evaluate the role of HPV test and viral load in predicting of residual diseases or recurrence after HSIL treatment with LEEP.
Method: 140 patients with CIN 2- 3 were followed up in 3, 6, 12 and 24 months after LEEP with Pap smears and quantitative HPV test on the basis of real time PCR (AmpliSens HPV-screen-FRT). Viral load value evaluates in HPV DNA logs for 200000 cellular genomes, DNA HPV concentration more than 3 lg was considered to be clinically significant. HPV test was per-formed directly from the liquid-based cytology sample.
Results: : Before treatment, the presence of oncogenic HPV types was detected in 100% of patients with HSIL and the average amount of viral load was 5,02 lg. In 6 months after excision, the negative HPV test was registered in 80% of patients. Among HPV-positive patients 8 % had a low viral load and a negative Pap test. The concentration of the virus DNA among 12% of patients remained high (around 5,3 lg), and Pap test results in this group expressed cytological changes. In 6-12 months of posttreatment follow-up in 5% of cases among patients with persistent HPV - infection and high viral load residual lesion or recurence of CIN 2 -3 was diagnosed
Conclusion: Persistence of HPV DNA with high viral load after HSIL treatment can be considered as early predictor for failure of therapy.

PS-01-070

Outcome of patients with atypical glandular cells (AGC) diagnosed during pregnancy

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Objective: The incidence of cervical adenocarcinoma is increasing in all developed world. Diagnosis of glandular premalignant and malignant lesions is much common in women after 30 years of age. Due to trend of increasing age of pregnancy, higher number of cytological smears are interpreted as AGC in early pregnancy. While conservative management of squamous precancer lesions in pregnancy is considered safe, the optimal management of AGC is not well established. The aim of our study was to evaluate outcome of patients with AGC found during pregnancy.
Method: Study included 12 patients who were referred to our colposcopy outpatient clinic in early pregnancy with cytological diagnosis of AGC (AGC – NOS (n=7), AGC – NEO (n=4) or AIS (n=1)). HPV high risk positivity was confirmed in 4 patients with AGC – NOS. All women were initially examined by expert colposcopy and transrectal ultrasound to exclude invasive endocervical cancer. Follow up controls proceed every 8 weeks and if there were no signs of progression, reevaluation was scheduled 6 weeks after delivery.
Results: Mean age of women was 32 years (26 - 38). Cone biopsy in one patient (AGC-NEO group) was performed in 16th week of pregnancy due to colposcopy signs of microinvasive squamous cancer. Progression to invasive cancer was not found in any of other 11 cases from which 8 (all with AIS and AGC-NEO and all HPV positive AGC – NOS patients) underwent cone biopsy after puerperium. Histopathology results were as follows: AIS (n=1), CIN3/CIS (n=3) (one case with concomitant high grade CGIN) and benign changes (n=4).

Conclusion: Conservative management of women with AGC in pregnancy is safe if invasive cancer is excluded. As histopathology verification of glandular precancerous lesions by minibiopsy is not reliable, postpartum regression rate can not be exactly determined.

PS-01-071

Position of HPV-typization in the protocol of cervical intraepithelial neoplasias treatment

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Objective: The goal of this article was to investigate the frequency of appearance of the oncogenic types of Human Papilloma Viruses (HPV) in the low grade squamous intraepithelial lesions (LSIL) of the cervical cells. HPV presence in the LSIL alterations determines the course of its further development and makes to be important parameter i the Protocol of its treatment.
Method: Investigation has been performed during the period of 15 years /1994.-2009./, where 1985 patinets' samples were collected from all areas of Serbia. Aplied methods: colposcopy, cytodiagnostic, histopathological PVU tissue analysis, obtained by targeted biopsy and HPV typization /method :in situ hybridization/. Data processing has been performed by usage of standard statistical procedures
Results: Results of HPV typization proved absence of HPV infections in LSIL cervical pathological changes in 457 patients /23%/, while HPV types with low oncogenic potential were presented in 774 patients /39%/ , and HPV types with high oncogenic potential were presented in 754 patients /38%/. These patients have presented risk group in which lesions' progresion toward HSIL and cervical carcinoma could be expected. Therefore, exsisting lesions in these patients have been treated by CO2 –laser vaporisation. Analysis of colposcopic results showed that LSIL was presented mosty as mosaic in 36% of patients, joined colposcopic findings were presented in 21%, and punctation in 18%. Cytodiagnostics showed regular finding in 73% of examined subjects, while in 27% of patients this finding was pathological.
Conclusion: Performing HPV typization in women with cervical LSIL made possible to detect patients with increased risk of disease progression and appearance of malignancy. In the LSIL cells of these patients, HPV types with high oncogenic potential have been detected. They have been treated and CO2-laser vaporization proved to be very efficient method of treatment of these lesions. HPV typization present irreplaceable part of the protocol for detection, prognosis and treatment cervical LSIL.

PS-01-072

Apical end of cone and lateral resection margins in patients with squmous intraepithelial lesion treated by the Cold Knife Conisation and LLETZ

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Objective: The height and the width of cone obtained by cold knife conisation and LLETZ vary in many studies. These attributes of cone are very important because of follow up the patient. According to the literature the height of the cone varies between 5 to 25mm.
The aim of this study is to compare the height and the apical and lateral resection margins in specimens after cold knife conisation and large loop excision of transformation zone (LLETZ) in patient with squamous intraepithelial lesion-SIL and to discuss the possible options for further management.
Method: The detailed hystopathological findings were analyzed in 144 patients in 2009 with SIL treated with cold knife conisation and LLETZ. The height of cone, apical and lateral margins analyzed, too. Statistical analysis that used was Pearson Chi-square test-X2 test to determine the difference between this two approach of treating.
Results: 73 patients treated with cold knife conisation and 71 with LLETZ. According to the clinical diagnosis before treatment (SIL), conisation performed in 68 patients (93.2%) with high grade squamous intraepithelial lesion-H-SIL and 1 with low grade squamous intraepithelial lesion-L-SIL, and LLETZ in 34 patient (47.9%) with H-SIL and 7 (9,9%) with L-SIL. According to the final HP diagnosis SIL was treated by conisation in 52 cases (71.2%) and with LLETZ in 39 cases (55%). The average height of specimen obtained by cold knife conisation was 18.99 mm and by LLETZ was 5.52 mm what is statistically significant difference. Apical end of cone was positive in 5 cases (6.78%) in patients treated by conisation and it was positive in 18 patients (25.8%) treated with LLETZ. This is statistically very significant difference –Pearson Chi-square-9,422. Lateral margins were positive in 3 cases (4.1%) in patients with conisation and positive lateral margins were found in 21 cases (29.6%) in patients treated with LLETZ. This finding is very statistically significant difference-Pearson Chi-Square-16,809.
Conclusion: To make an adequate treatment for patient with SIL, we have to make exact measure of lesion on cervix. Appropriate colposcopy exam with measuring the lesion and especially microcolpohysteroscopy in cases when the lesion is spreading into cervical canal is an adequate approach to treat SIL and to prevent high percentage of positive apical and lateral margins and recurrence of disease.

PS-01-073

Immunohistochemical Features in the Cervical Glandular Intraepithelial Neoplasia of Various Degrees

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Objective: Aim of our investigation was to determine immunohistochemical diagnostic criteria of atypism of various degrees of endocervical glandular cells.
Method: Cytological cervical samples of 136 patients with the diagnosis of "atypism of endocervical glandular cells" have been investigated. Depending on the degree of lesion patients were divided by three groups. The curettage of endocervix was carried out with the histological examination (immunohistochemical method) in all cases.
Results: Comparative analysis of obtained data shown that the Ki67 expression is appeared in CGIN2 and sharply increased in CGIN3 ($p<0.05$). It is indicated the elevation of proliferative action of glandular cells of endocervix with the increase of atypism degree. The expression of MNF116 and EMA in groups did not significantly differ in groups ($p>0.05$). The expression of CEA and EpAg proteins was significantly increased in CGIN2 and CGIN3 in comparison with CGIN1 ($p<0.05$). It is indicated their possible role in the carcinogenesis.
Conclusion: Endocervical intraepithelial neoplasia might be classified as: endocervical intraepithelial neoplasia of low degree - CGIN1 and endocervical intraepithelial neoplasia of high degree - CGIN2 and CGIN3.

PS-01-074

Effect of condom use after CIN treatment on HPV positivity and other biomarkers: a randomised controlled trial.

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Objective: So far, no study has investigated whether consistent condom use after treatment of CIN reduces HPV positivity post-operatively and possibly as a result, the risk of treatment failure.
Method: Design: Single-blinded randomised controlled trial. Inclusion criteria: Women planned to undergo LLETZ for CIN. Intervention:

Women randomly allocated to Group A were given recommendation for condom use, whilst women in Group B received routine information. An LBC sample was tested for HPV typing, E6 & E7 mRNA (NASBA technique), E6 & E7 mRNA by flow cytometry, p16INK4a and microspectroscopy at 0 (pre-treatment), 6 and 12 months. A questionnaire to assess compliance was also completed. Outcomes: The relative risk(RR) and absolute RR(ARR) were calculated in an intention-to-treat analysis. The number needed to treat(NNT) and compliance were also assessed.
Results: A total of 113 women were recruited. Fifty-four have completed 6 and nineteen 12 months follow-up. The positivity for all the tested markers at follow-up was significantly reduced in Group A. In particular, 22% of women tested positive for HPV in Group A in comparison to 57% in Group B [RR:0.39(95%CI:0.24-0.54), ARR:0.343(95%CI:0.064-0.622). The NNT was 3. Analysis of HPV positivity in relation to the excision margins, treatment failures and compliance rates as well as histological data for both groups will be presented.
Conclusion: Post-treatment condom use significantly reduces HPV positivity. It remains to be confirmed whether this will also result in decreased number of treatment failures.

PS-01-075
Management of women with high-grade cytological abnormalities: a comparison of triage options
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Objective: A proportion of women referred for high-grade cytology will be proven to have only low-grade histology. This study aims to investigate possible combinations of tests that could safely identify these women.
Method: Design: Diagnostic study Inclusion criteria: Women referred with high grade cytology. Intervention: An LBC specimen obtained prior to colposcopic evaluation was tested for HPV typing, E6 & E7 mRNA (NASBA), E6 & E7 mRNA by flow cytometry, p16INK4a and microspectroscopy. All women underwent LLETZ (gold standard). Outcomes: The sensitivity, specificity, PPV, NPV, positive and negative likelihood ratio(LR) were calculated for each parameter alone or in combination for CIN2+ histology.
Results: A total of 118 women have been recruited. The colposcopic assessment appeared to have the best sensitivity [96%(95%CI:90-100)], NPV [67%(95%CI:29-100)] and negative LR [0.10(95%CI:0.02-0.49)]. NASBA had the best specificity [78%(95%CI:51-100)], PPV [94%(95%CI:87-100)] and positive LR [3.23(95%CI:0.94-11.11)]. The combination of colposcopy with high-risk HPV had the best sensitivity [88%(95%CI:78-97)] and negative LR [0.21(95%CI:0.08-0.51)]; flow cytometry with p16 had the best specificity [97%(95%CI:91-100)], negative PV 79%(95%CI:66-91) and positive LR [20.70(95% CI:2.92-146.71)], while NASBA with p16 the best PPV 98%(95%CI:91-100).
Conclusion: Some of the combinations might have significant accuracy for the prediction of high-grade histology. This could allow conservative management for women at low risk and avoidance of unnecessary intervention and/or treatment.
All the above markers should be evaluated in a cost analysis and could be integrated in high-grade triage prediction scoring system, allowing tailored selection for treatment. The above findings need to be confirmed in larger cohorts.

PS-01-076
Management of women with low-grade cytological abnormalities: a comparison of triage options
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Objective: A proportion of women referred for low-grade cytology will be proven to have a high-grade histology. However, the majority will have lesions of low malignant potential and this study investigates possible methods that could identify these women.
Method: Design: Diagnostic study Inclusion criteria: Women referred with ASCUS or LSIL cytology; histological diagnosis was available for all women (punch biopsies or LLETZ). Interventions: An LBC specimen obtained prior to colposcopic evaluation was tested for HPV typing, E6 & E7 mRNA (NASBA), E6 & E7 mRNA by flow cytometry, p16INK4a and microspectroscopy. Outcomes: The sensitivity, specificity, PPV, NPV, positive and negative likelihood ratio(LR) were calculated for each parameter alone or in combination for CIN2+ histology.
Results: A total of 282 women were included. High-risk HPV testing showed the highest sensitivity [94%(95%CI:80-98)], moderate specificity [65%(95%CI:51-77)] and positive LR [2.70(95%CI:1.8-4.0)]. HPV16-specific typing showed the best specificity [96%(95%CI:87-99)], PPV (87%) and positive LR [10.7(95%CI:2.58-44.25)]. Amongst the various combinations, p16 with high-risk HPV testing showed a specificity of 100% and a sensitivity of 50%.
Conclusion: High-risk HPV testing has the highest sensitivity, whilst HPV 16-specific genotype achieves the best specificity for the detection of high-grade lesions. These test and some of the above combinations could discriminate women at high-risk that need referral to colposcopy +/-treatment from those at low risk that do not require further unnecessary intervention. All the above markers should be evaluated in a cost analysis and could be integrated in low-grade triage prediction scoring system, allowing tailored management of women.

PS-01-077
Review of patients with low-grade smear abnormalities referred for colposcopy
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Objective: To review the outcome of patients referred to colposcopy clinic with smear reported as Inadequate/Borderline/Mild dyskaryosis and to see how the smear reports correlate with histology of cervical biopsies.
Method: Retrospective analysis of records of all patients referred to colposcopy clinic with low-grade smear abnormalities to North tees and Hartlepool University hospitals over 12 months between 1st January 2008 to 31st December 2008. Retrieved the list of all patients referred to colposcopy clinic from computer-based database. Collected the data with regards to histopathology from the computer database. Analysed the data using the frequency tables.
Results: 380 patients with low-grade smear abnormalities were referred to colposcopy clinic during this period. Out of these we were not able to retrieve the data for 7 patients. The data for 373 patients was analysed 272/373(73%) of women were of reproductive age group. (Between - 21- 40) 2 (0.5%) of referrals were for inadequate samples. Colposcopic assessment of these patients revealed no abnormalities and subsequent smears done in the clinic were reported negative, and they were referred back to routine recall. 209/373 (56%) was referred for borderline smears. 10/209(4.7%) had normal colposcopic assessment. 197/209(94.2%) of these had colposcopically identified lesion needing punch biopsy at 1st visit. 2 did not attend the appointment. 115/197(58.3%) had miscellaneous results (squamous metaplasia, koilocytosis, inflammation, wart virus, endometriosis etc.), 29/197(14.7%) had CIN 1, 30/197(15.2%) had CIN2, 23/197(11.1%) had CIN3. 53/209 patients (25.3%) had CIN 2+3 and needed treatment. 162/373 (43.4%) was referred for mild dyskaryosis. 1 patient DNA'd the appointment. Rest of all the patients had colposcopically identified lesions needing intervention. 2 had direct lletz with results reported as CIN 2, CIN 3 each. 159/162 (98.1%) had punch biopsy at first visit. 61/159 (38.3%) had miscellaneous results (see above) and 41/154 (26.2%) had CIN1 43/154 (27%) had CIN2, 17/154 (11%) had CIN3. 58/162(35.8%) had CIN2+3 needing treatment. 2 of the patients with CIN 2 did not

attend the appointments. The patients with CIN 1 was followed up with repeat colposcopy, while CIN 2 and 3 (105/363 i.e. 28.9% of all referrals) underwent LLETZ. 3 patients with CIN 2 were not followed up and this is being looked into. Of the patients who had LLETZ biopsies 17/111 (15.3%) had miscellaneous results, 9/111(8.1%) had CIN1, 49/111 (44.1%) had CIN 2, 33/111 (29.7%) had CIN3. 3 (2.7%) patients had cervical cancer and there was no CGIN. Overall, of 373 patients referred to colposcopy, occurrence of CIN 2 was 49(13.1%,) and CIN3 was 33(8.8%) and cancer was 3(0.8%) from LLETZ biopsy.
Conclusion: 76.4% of patients with low-grade smear abnormalities had normal colposcopy or low-grade lesion on colposcopy. We also see that overall occurrence of CIN 2 was 13.1% and CIN3 was only 8.8% and cancer was 0.8%. Hence there is a good correlation between low-grade smear abnormality and findings at colposcopy and histology.

PS-01-078
Cervical Stenosis and Conization
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Objective: To identify the reasons of cervical stenosis (CS) after conization.
Method: This is a prospective study including 282 patients who underwent conization between 1999 and 2007. The different parameters studied were at the moment of the surgical procedure: - patient's age -menopausal status -parity -height of removed tissue -diameter of the endocervical canal at the top of conization -and the size of the external os, three months after conization We have defined cervical stenosis as an external os diameter ≤2 mm
Results: We observed 34 stenosis on 282 cases (12,41%) We used a logistic model for predicting stenosis àInfluence of patient's age: The percentage of CS in women aged of <45 years old was 9,5% versus 47,5% for women aged of >45 years old. p= 0,005 . RR:2.95. CI [1.37-6.34] àInfluence of menopausal status: The percentage of CS en pre-menopausal women was 10,85% versus 57,14% for post-menopausal women. P= 0,001. RR:5.6. CI [2-15.6] àInfluence of number of pregnancies: The average size of the external os in patients who were never pregnant was 5,87 mm, 5,36mm in women who had few pregnancies, and 7 mm in women who had numerous pregnancies but with too few cases to be significant. àInfluence of the height of the cervical cone: The average height of the cervical cone was 14,3mm. In patients with CS, it was 16,48 mm whereas 13,98mm in the non-CS patients. p= O,04. RR: 1.08. CI [1.002-1.15] à Influence of the diameter of the cervical cone: The percentage of CS was respectively 6.61, 13.7 and 22.72% for loop of diameters 25, 20 and 15mm. àInfluence of the endocervical canal diameter at the top of excision: The average endocervical canal diameter for the overall patient group was 5,54 mm. In patients with CS, the average was 4,08 mm whereas 5,72mm in the non-CS patients. p= 0,0001. RR: 0.66. CI [0.53-0.82] The multivariate logistic analysis (AUC=0.78) highlights that the main factor is the endocervical diameter at the top of excision (p= 0.003) followed by diameter of the cone (p=0.02), before height of excision (p= 0.06).
Conclusion: In our study, the main risk factors for cervical stenosis are: age >45, menopausal status, and a narrow endocervical canal diameter.

PS-01-079
Follow-Up After Conization: When Does HPV Test Work the Best?
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Objective: HPV test has proven to be excellent as a follow-up method of conization. However, when practiced too soon after the surgical procedure HPV test often remains positive; conversely, if proposed too late, many patients will be lost to follow up. Determine the best date to perform HPV testing after conization.
Method: From October 2000 to October 2007, 582 conizations were performed. Hybrid Capture 2 (Quiagen) HPV test was taken most often just before the surgical procedure in the operating ward and in some cases a few weeks before. A follow up visit was proposed to the patients after 3 to 6 months in order to obtain Pap smear and HPV testing; 351controls only were performed, as many patients were seen by their private doctor and no HPV test was obtained.
Results: There is no significant difference at 3, 6 and 12 months. It justifies the first control at 3 months: so we can decrease the rate of lost to follow-up and treat without delay a synaechia of the cervical os. The viral load seems to have a little influence.
Conclusion: HPV testing 3 months after the conization is efficient, avoids poor follow up, and allows to detect ant treat complications.

PS-01-080
Study of Microinvasive Squamous Cell Carcinomas of The Cervix in Figo Stage IA1 in the Canaries University Hospital Maternity Ward
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Objective: Retrospective study of microinvasive squamous cell carcinomas of the cervix in FIGO stage IA1, diagnosed at the Pathology of the Lower Genital Tract Unit of the Canaries University Hospital Maternity Ward during the period 1991-2007.
Method: We analyzed 62 cases of microinvasive squamous cell carcinomas of the cervix in FIGO stage IA1. Patients were referred upon abnormal cytology results or upon high-grade histological findings. They underwent cytology, colposcopy examination and biopsy when necessary. Subsequently, excision treatment with diathermy loop cone was applied and all diagnoses were determined in the specimen. The studied variables included: age, initial reason for consulting, status of the specimen margins, fragment of the endocervical canal when biopsy was performed and the histological findings of patients who underwent a second treatment. Finally, we analyzed the post-surgery follow-up periods.
Results: Patients' average age was 41 years (26-68 years). The follow-up period ranged between 6 and 128 months, with an average time of 82 months. The most frequent initial reason for consulting was HSIL, with a total of 83% of high-grade lesions and 17% cases of low-grade lesions. All cases of microinfiltrating carcinomas were diagnosed on the first conization specimen, except for one case, which was diagnosed in the second cone (indicated by CIN III, involved margins). The margins were free of lesions in 49% and affected by the high-grade lesions in 51%: 28.2% of exocervical margin involvement, 37.5% of endocervical margin involvement and 34.3% of both margins involvement. Endocervical canal biopsy was carried out after conization in 46.7%. Results were negative for 86.2% of them. There were two cases (3.2%) of vascular invasion – both treated with radical hysterectomy – and in one case there was a diagnosis of synchronic endometrial adenocarcinoma. 64.5% of patients (40/62) underwent a second treatment; the most frequent one was hysterectomy (37 cases), followed by conization (4 cases) and radiotherapy in one case because of high risk associated to surgery. The second treatment was applied to 28 patients with involved margins (4 cases of involved margins with negative results of the endocervical canal fragment were followed-up with expectancy because of the patients' will of pregnancy), 4 cases with margins that could not be examined and 8 cases with margins free of lesions. The outcome of the second treatment was: 55% without residual tumor, 15% of CIN I, 15% of CIN III, 5% of microinvasive carcinoma, 5% of non-gradable CIN, 2.5% of isthmus adenocarcinoma, and 7.5% whose results could not be found. All high-grade lesions detected upon the second surgical treatment corresponded to patients whose specimens had already showed involved margins upon the first conization. In general, only 22.5% of treated cases presented high-grade lesions.

Conclusion: Microinvasive epidermoid carcinomas stage FIGO IA1 can be managed with a conservative treatment, independently of the patient's will of pregnancy, so that if the specimen's margin remain uninvolved, a second excision procedure is not necessary. In case of involved margins, individual circumstances should be considered in evaluating the suitability of a second conization.

PS-01-081

The importance of colposcopy in diagnostics of SIL

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Objective: The objective of this paper is to determine the value of colposcopy, sensitivity and specificity in the diagnosis of cervical SIL.
Method: Because of abnormal colposcopy finding at 1301 women the biopsy was done on Colposcopy ambulance in Gynecology and Obstetrics Clinic Narodni front Belgrade. Data processing was done using standard statistical procedures.
Results: Benign histology lesion were found in 73,9% biopsy, abnormal histology lesion were found in 26,1% biopsy, (LSIL 53%, HSIL 32,7%, cancer invasive 14,3%) according to the colposcopy examination a positive predictive value was 26% and false positive findings value 74%. Sensitivity and specificity are 68,4% and 88,6% respectively.
Conclusion: Low specificity, positive predictive value 26% and false positive findings value 74% are cause to many unnecessary biopsies. Our data confirm the role of the colposcopy in the detection of SIL. While cytology is more reliable then colposcopy, histological examination of colposcopy directed biopsy with previous knowledge of abnormal cervical smear, together give best results.

PS-01-082

Should cervical conization be performed by specially qualified gynecologists?

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Objective: The European Federation for Colposcopy (EFC) has developed guidelines for quality assurance and certification of specialists. The status of the resection margin is a quality feature for cervical conization and influences subsequent management. We reviewed the rate of positive conization margins according to the qualification of the surgeon (resident, staff/specialist, or certificated specialist).
Method: This was a retrospective cohort analysis of 363 consecutive patients undergoing conization for histologically verified cervical intraepithelial lesions or carcinoma in situ between November 2005 und December 2009. Standardized preoperative colposcopy was performed to localize and document the transformation zone and the field of the lesion.
Results: The rate of positive margins did not differ between residents and specialists (22% vs.15%); a certificated specialist had a significantly lower rate (8.9%, $P<0.002$).
Conclusion: Quality-assured preoperative colposcopy contributes to a modest non in sano rate for gynecologists and residents. A certificated specialist can further improve these results. This may confirm adaptation of the EFC quality assurance program in Austria.

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