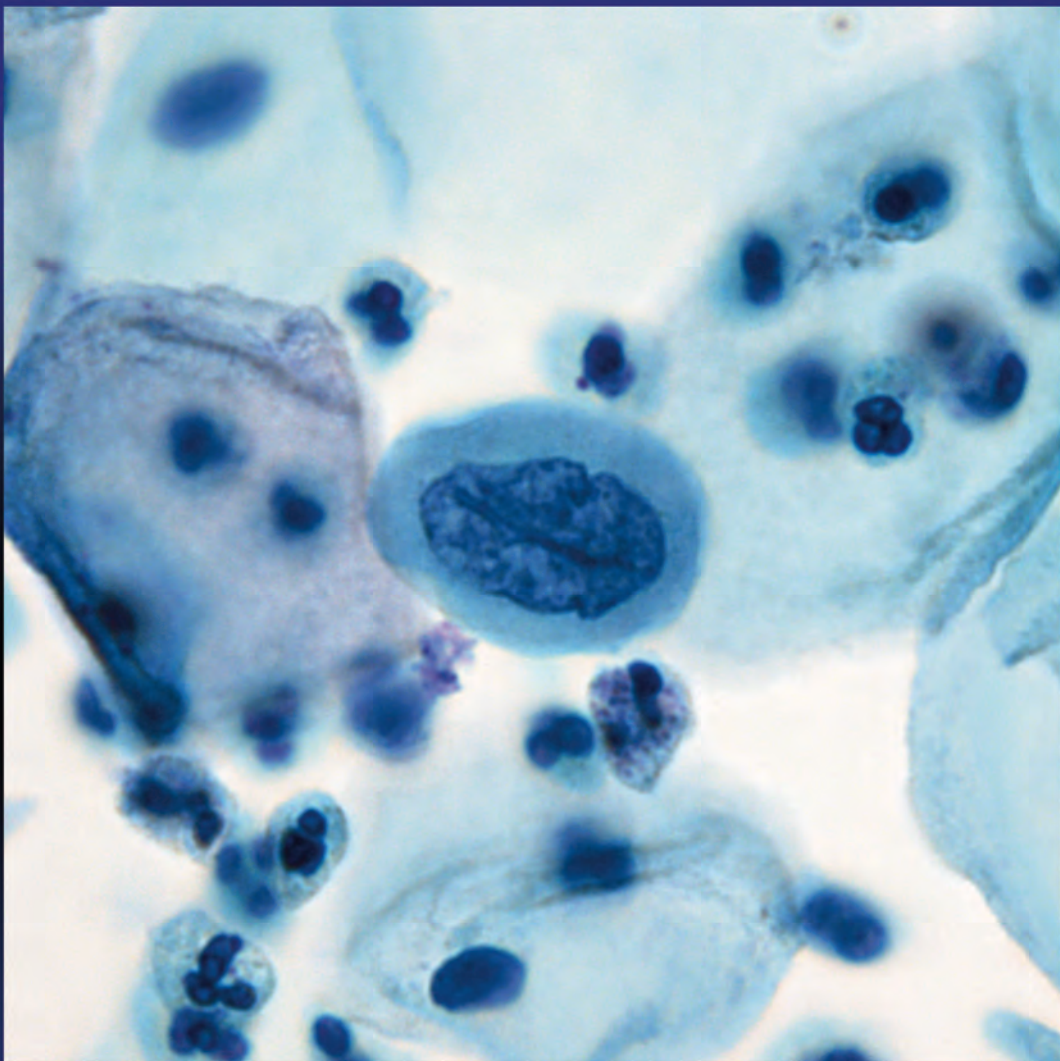


SCAN

VOLUME 25:1 April 2014



B A C

**British Association
for Cytopathology**

BAC Executive Committee

President



Dr Karin Denton Consultant Pathologist, Lime Walk building, Southmead Hospital, Bristol. BS10 5NB
Tel: 0117 323 5645
Email: karin.denton@nhs.net

Chair



Mr Allan Wilson Pathology Department, Monklands Hospital, Monkscourt Avenue, Airdrie. ML6 0JS
Tel: 01236 712087
Email: allan.wilson@lanarkshire.scot.nhs.uk

General Secretary



Sue Mehew Cytology Laboratory and Scottish Cytology Training School. Pathology Department, Royal Infirmary of Edinburgh, 51 Little France Crescent, Edinburgh. EH16 4SA.
Tel: 0131 2427149 Fax: 0131 2427169.
E-mail: Sue.Mehew@luht.scot.nhs.uk

Treasurer



Kay Ellis ABMSP/Cytology Manager, Cytology Department, Floor E, Royal Hallamshire Hospital, Glossop Road, Sheffield S10 2JF
Tel: 01142 713697 Fax: 01142 261213.
Email: kay.ellis@sth.nhs.uk

Members



Alison Cropper Cytology Department, 5th Floor, Derby Hospitals NHS Foundation Trust, Derby City General Hospital, Uttoxeter Road, Derby DE22 3NE
Tel: 01332 789327
Email: Alison.Cropper@derbyhospitals.nhs.uk



Dr Paul Cross Depart of Pathology, Queen Elizabeth Hospital, Gateshead, Tyne and Wear. NE9 SX
Tel: 0191 445 2603
Email: paul.cross@ghnt.nhs.uk



Jenny Davies Manchester Cytology Training Centre, Cytology Department, P.O. Box 208, Manchester Royal Infirmary, Oxford Road, Manchester M13 9WW
Tel: 0161 276 5114
Email: jenny.davies@cmft.nhs.uk



Claire Geary Cytology Department, Cambridge University Hospitals NHS Foundation Trust, West Anglia Pathology Services, Westbrooke House, 3 The Oaks, Fordham Road, Newmarket, Suffolk, CB8 7XN Tel: 01638 569187 | Ext: 59627 | Mobile 07718120414 |
Email: claire.geary@addenbrookes.nhs.uk



Dr Thomas Giles Dept of Pathology, Royal Liverpool University Hospital, Prescot Street, Liverpool L7 8XP
Email: Thomas.giles@rlbuht.nhs.uk



Jackie Jamison Cytology Department, Antrim Area Hospital, County Antrim BT41 2RL.
Tel:
Email: jackie.jamison@northerntrust.hscni.net



Dr Fraser Mutch Dept of Cellular Pathology, Bedford Hospital NHS Trust, Kempston Road, Bedford, MK42 9DJ
Tel: 01234 792325
Email: fraser.mutch@bedfordhospital.nhs.uk



Dr Louise Smart Department of Pathology, Medical School Building, Foresterhill, Aberdeen. AB25 2ZD
Tel: 01224 553794
Email: louise.smart@nhs.net

Editorial

The future of cervical cytology: critical thinking needed

Andrew Evered

Despite what now seems to be the inevitable demise of cytology as the primary screening test in cervical screening, cytology continues to be a source of fascination for biomedical science undergraduate students. As an educator in the subject I have no conflict in continuing to enthuse students in the art and science of cytology.

The subject is a wonderful example of the fruitful marriage of qualitative and quantitative science, and there is much that developing scientists can learn from it.

As cytology grows ever stronger bonds with molecular biology I believe we are entering an era when cytology finally finds a place for itself in a truly multidisciplinary diagnostic environment. Of this I have no doubt, at least for non-gynaecological cytology. But what is to become of cervical cytology? Undeniably, cervical cytology can provide the specificity that all currently available molecular tests lack, which means that we will continue to need highly trained and capable cervical cytologists for the foreseeable future. But this new breed of cytologist will have a different mind-set to today's screeners, and we must think very carefully about how they are recruited and trained.

According to conventional wisdom, a non-medical trainee in cervical cytology must examine at least 5000 slides over two years to become competent. But as someone once said, "he who conforms to the rules of conventional wisdom makes himself as featureless as a potato field". Cytology educators and programme managers must be more innovative, but more importantly they must call upon the best available evidence rather than blindly accepting the status quo. Obvious to anyone who has spent time with cytology trainees is the huge variation in

ability and speed of learning among this group of staff. Individual differences are noticeable from the very start of training and in many cases persist throughout a career. These observations send a strong message to employers that recruitment procedures must become more selective. Alongside robust selection processes must come more intelligent training programmes, designed to build on the tacit skills that carefully selected new recruits bring with them. In much the same way that medical trainees in histopathology are "fast-tracked" through cervical cytology training, we must seek ways of safely accelerating the training of non-medical cytologists. A major problem is the lack of research in this area, but there are a few tantalizing clues in the field of perceptual learning and some interesting preliminary results have recently appeared in the cytopathology literature.^{1,2} Cytology educators, curriculum developers and screening programme managers must join forces to find a sensible way forward. It would be a terrible mistake to discard cervical cytology with the cervical screening bathwater.

Andrew

References

1. Evered A, Walker D, Watt A, Perham N. (In press). Untutored discrimination training on paired cell images influences visual learning in cytopathology. *Cancer Cytopathol*. Online: 18 Nov 2013. DOI: 10.1002/cncy.21370.
2. Evered A, Walker D, Watt A, Perham N. To what extent does non-analytic reasoning contribute to visual learning in cytopathology? *Cancer Cytopathol*. 2013;121:329–38.

Copy date for October 2014: 5th August 2014,
Editor Sharon Roberts-Gant.



INFORMATION FOR CONTRIBUTORS

Articles for inclusion in SCAN can be emailed to the editor if less than 1MB in size or supplied on CD/DVD or memory stick. Text should be in a standard text format such as a Word document or Rich Text Format (rtf file). Please supply images as separate files in tiff or high quality jpeg files at a resolution of not less than 300 dpi (600 dpi if the image includes text). 35mm slides and other hard copy can be supplied for scanning if no electronic version is available. Graphs are acceptable in Excel format.

If you are unable to supply files in the above formats or would like advice on preparing your files, please contact Robin Roberts-Gant on 01865 222746 or email: robin.roberts-gant@ndcls.ox.ac.uk



Chairman's Report

Allan Wilson

Within the UK we are rightly proud of the achievements of the UK screening programmes and are often told that we have the best programme in the world. This is mainly due to the hard work and dedication of screening professionals across the programme from call recall offices to colposcopy. The UK programmes have worked hard over the last 25 years to create a "joined up" programme with excellent quality standards and monitoring that is the envy of the western world. We must also recognise the government funding through the NHS that has driven the programmes to deliver the high standards and reduction in incidence and mortality.

Before we start to feel the warm glow of satisfaction and self congratulation it is worth considering other countries struggle against cervical cancer. In January, Nick Dudding and I were invited to lecture at a Cytology course in Stellenbosch University, Cape Town. It was my first visit to Africa and I would like to share some of the challenges faced by screening professionals.

Although our base was Cape Town, the course delegates were from across Africa and included cytologists from Burundi, Kenya, Namibia, Rwanda, South Africa, Tanzania and Uganda. Perhaps not surprisingly, almost half the delegates were from South Africa and it was the South African cytology scene that we learned most about.

It is difficult to map our experience of the UK programme to African nations when women in one of the wealthiest African nations (South Africa) can wait for up to a year for a colposcopy appointment or elective surgery (including LLETZ) can be "cancelled" for six months due to lack of funds; where Kenya (population 44 million) has only 30 histopathologists to serve the entire country. Follow up of women with abnormal smears is extremely difficult, we could feel the frustration of laboratories where high grade disease is detected on smears but the women cannot be found for follow up or colposcopy referral. The quality of the smears arriving in the labs is variable; high from the private sector but often poor from rural settings where reagents such as fixative are often re-cycled.

Nick has highlighted the high quality of the South African cytology labs in his more detailed report in this edition of SCAN and this is laudable given the challenges they face. However, the investment in staff, training and standards in the cytology lab will not greatly impact on incidence and mortality from cervical cancer unless similar investment is made in smear taker training and IT systems. When faced with such challenges it is easy to see why African countries are considering alternatives to cytology such as HPV testing and mass vaccination.

Another issue the African screening programmes face is loss of trained staff, particularly nurses, who leave to work overseas.

There are many African nurses working in the NHS and this "talent drain" from African countries further impacts on their ability to deliver even a basic screening programme. The UK is one of the most generous countries in the world with regard to overseas aid but the active recruitment of African health workers to the NHS must negate some of the benefits of overseas aid. I know it is simplistic but it is tempting to suggest that if we trained and employed more UK based students we would reduce unemployment in this country and reduce the drain of experienced staff from African countries.

One final comment from Africa: as Nick has mentioned in his report, the contrast between the delivery of the non-gynaec service in the UK and Africa was very clear. This is particularly noticeable in the use of FNA cytology. However, before we start to depress ourselves about the reduction in samples in many UK labs, perhaps we should ask why FNA cytology is so widely used in Africa. FNA cytology is particularly suited to low resource settings. It is inexpensive and can be used in a one stop clinic or mobile lab to make rapid diagnoses, for example, TB versus lymphoma. This is vital where the population is mobile and may not return for follow-up visits. In addition, in the absence of histopathology services as mentioned above, it is easy to see the attraction of diagnosis by FNA. In the UK where we have easy access to high quality histopathology services with rapid turnaround, clinicians often choose core biopsy over FNA. We need to ensure the obvious advantages of cytology are clearly communicated to our users and encourage the use of non-gynaec cytology wherever the opportunity arises.

Now to UK based activities. Since the last edition of SCAN the BAC executive has been making steady progress on a range of fronts. One area has been the Birmingham scientific meeting in October. The programme is virtually complete and promises to be a fascinating meeting with something for everyone. I must thank Alison, Paul and Kay for all their hard work not just on the scientific programme but the numerous meetings with the conference organisers and the venue management to ensure a successful meeting. Registration is already open and we hope to see as many of you as possible in Birmingham. Registration is also open for our non-gynaec tutorial in London in July and I must thank Ash Chandra for his hard work in putting together this meeting.

The nominations for the Executive yielded two interested Cytologists for two places and an election was therefore unnecessary. I would like to thank Melanie Buchan and Mina Desai for all their hard work on the Executive and welcome Jackie Jamison and Claire Geary. I am certain Jackie and Claire will be powerful advocates for Cytology during their term on the Executive. These changes to the Executive are the first of a rolling programme of nominations and elections which will continue in 2014. Nominations will be sought again in the

summer and elections, if required, held before the AGM. Please consider a nomination for the Executive.

The Gynae code of practice continues to make progress and the first draft of the revised document will be considered by the executive at our next meeting on 3rd April.

Jenny Davis has replaced Melanie on the group established by the MSC team to look at band 2-4 staff. This is vital work as we need to ensure that MLA's and cytoscreeners are not

"overlooked" in this process. MSC continues to move slowly forward and an update on progress is included in this edition of SCAN. It is tempting to bury our heads in the sand when we hear the MSC acronym but this national initiative has wide reaching implications for our profession and we must engage wherever we can to ensure the Cytology voice is heard clearly. Your Executive has representation in all the major decision making groups and continues to work quietly in the background with the MSC team and other professional bodies in what is often a frustrating "political game".

Report from BAC Annual Scientific Meeting 2013

Marlene Quintal, BMS 1
Aberdeen Royal Infirmary



Sometimes meetings fall short of expectations, but not the BAC Annual Scientific Meeting held on 24th October 2013 at the University of Manchester Innovation Centre. Introduced by Dr Karin Denton, BAC President, as provocative and controversial, it certainly proved to be both.

The first speaker was Dr Jesper Bonde from Denmark, introduced to the audience as the face of the HORIZON study. He presented findings of his work evaluating HPV testing platforms in the clinical/laboratory settings. The food for thought started here. Discordance was observed between the four HPV tests utilised. If you are implementing HPV testing in your laboratory, which test would you choose? Which criteria will you use for the selection? What level of error will you accept and who will take responsible for it?

This was followed by Mr Allan Wilson also with a thought provoking presentation on what screeners send for checking and how checkers are monitored. Inflammation, enlarged nuclei, koilocytes and reactive endocervical cells top the list of reasons for referral. He also presented results from an audit of checkers at Monklands Hospital and from a recent BAC survey on the checker role in which 75% of the UK laboratories participated, as well as giving guidance on how to monitor checker practice. His presentation ended with a stimulating and encouraging interactive session with images of features commonly sent for checking and the audience voting for their favoured diagnosis.

Continuing the cervical cytology theme, Dr Paul Cross gave a very practical and helpful presentation on the Colposcopy/Histology/Cytology multidisciplinary meeting.

He recommended which cases to include/not include in MDT meetings and tips on how to ensure a successful and productive MDT, such as naming a lead person, revision of the case and patient history before the meeting and encouraging honesty and openness, bearing in mind that none of the three modalities are foolproof, including the "gold standard" of histology.

Following the AGM, there was lunch. Delicious food to keep us happy and feed our brains after a thought provoking morning. For those still hungry for knowledge, there were four informative posters displayed, covering the topics of endometrial cells in LBC preparations, flow cytometry immunophenotyping and pancreatic EUS-FNAC. Mrs T Johnson won the Best Poster prize with the poster "Audit of Endometrial Cells in LBC samples".



The afternoon offered a choice of three workshops. "The Problem with Atrophy" was my selection as I'm working in Scotland and the screening age is expected to increase from 60 to 65; what I learned has proved useful already! The session started with a cleverly illustrated PowerPoint presentation reviewing the process of atrophy, the difficulties associated with it and what to look out for when screening such cases. This was followed by a practical screening session with examples of the full range of features possible in atrophic samples, including squamous and endocervical dyskaryosis, non-cervical disease and inflammatory processes. Participants reviewed the cases with the clinical details and the results were revealed only at the end.

Making good use of the day, my two colleagues each attended one of the other workshops. In the workshop “EBUS-FNAC and ROSE” participants were treated to a comprehensive overview by Dr Durgesh Rana of the enviable set-up in Manchester for rapid on-site assessment of EBUS samples; she highlighted the benefits of confirming sample adequacy and providing a preliminary diagnosis to ensure collection of sufficient appropriate material for ancillary tests. Dr Ivan Robinson, eloquently described his recent experience of SurePath preparations in head and neck FNA, illustrating both the diagnostic challenges and successes in using this methodology.

The third workshop “Interactive workshop — invasive cancer audit cases” was led by Dr John Smith. In his presentation, he revealed that 22.9% of cancer cases had a negative cytology test 0-5 years from diagnosis and that 32.8% had dyskaryotic cells on review. A review by the East Pennine Training School confirmed the usual suspects in such cases: hyperchromatic groups, small cells, few cells on a dirty background, diathesis, stroma and cells with ragged, fragile cytoplasm. In the interactive session, images of cases were projected together with a differential diagnosis and audience votes recorded electronically. The

images and magnifications shown revealed how opinion changed with increased objective power. My colleague was intrigued to learn if she was in line with the consensus opinion and found it a memorable exercise.

To close the meeting, Dr John Smith presented results of the multistranded HTA adequacy study. The study confirmed that low cellularity reduces the likelihood of dyskaryotic cells being detected and concludes that the minimum number of squamous cells necessary in a LBC preparation in order to detect dyskaryotic cells is 5000 cells for ThinPrep but 15000 cells for SurePath preparations.

In conclusion, this experience was extremely valuable even for a recently qualified BMS like myself. The topics discussed were current, relevant and stimulating and of interest to all individuals working in the discipline. Not forgetting that meetings are an opportunity to meet colleagues, exchange experiences and to get to know the face behind the name. I was very glad that I had chosen to attend.

I would like to express my gratitude to the BAC and the SACC for sponsoring me to attend this BAC scientific meeting and I recommend colleagues to apply for this opportunity — you will find the experience rewarding.

Poster presentations from the BAC Annual Scientific Meeting, October 2013

Audit of the significance of the presence of endometrial cells in LBC samples

Trudy Johnson* Martin Jones*, Diane Hemming#

*Biomedical Scientist, # Consultant Cellular Pathologist

Department of Pathology, Queen Elizabeth Hospital, Gateshead, Tyne and Wear, NE9 6SX

Introduction: Endometrial cells are often seen in cervical samples. National guidance since 2008 has been to report samples where such cells are seen, out of the expected date range and over the age of 40. In 2008 there was evidence based local agreement in the Northern region that apparently benign endometrial cells in any women under the age of 50 years would not be reported, irrespective of the presence of known high risk factors, but that the presence of apparently benign endometrial cells in women who are 50 years of age or greater, with or without symptoms, would be reported. However it was agreed that the presence of apparently benign endometrial cells between the ages of 40 and 50 would be noted for future audit purposes. We undertook an audit of all cervical LBC samples where endometrial cells were identified, and correlated with histology outcomes (where known).

Method: the The Winpath Laboratory Information system (LIMS) was searched from 2008 to June 2013 for the total numbers of samples taken, and the number of samples where the presence of normal or abnormal endometrial cells was recorded. An extract was produced with full patient history of all cases where endometrial cells were recorded and this extract was imported into excel for analysis.

Results: A total of 4667 out of 129,763 (3.6%) samples in total contained endometrial cells. 2345 (50.2%) were under the age of 40. Of the women aged 40-49 there were 1795 cases (38.5%), women aged 50-59, 478 cases (10%) and >60 years 49 (1%). Subsequent endometrial histology was found in a total of 223 (4.8%), the majority

of which 169 (76%) showed normal endometrial histology. Of the cases with significant pathology there were 5 hyperplasias, of which only 2 were atypical and these were both over 50+ and 19 polyps (3, 8 and 8 in each age band). A total of 32 cases (0.68%) were reported with *abnormal* endometrial cells and 34% of these were cancer. Of these cancers, 2 were women aged 40-49, 7 were women aged 50-59 and 2 >60 years. A total of 11 cancers were diagnosed, all of which were identified in cases referred with *abnormal* endometrial cells. No cancers were identified in the normal endometrial group.

Conclusion: Endometrial cells are common in NHS CSP samples in patients over the age of 40, but few contain significant pathology, especially those under the age of 50. The rationale for using a national age of over 40 for reporting and potential referral would appear to yield little, if any, meaningful pathology, where referring over 50 would be more targeted. Atypical endometrial cells should always be reported regardless of patient's age and further evaluation is required as per the current NHSCSP Guidelines. The authors feel that with current times of austerity the national guidelines should be changed to prevent unnecessary costly referral of these women to gynaecology.

The clinical significance of inappropriate endometrial cells in a liquid-based cervical cytology specimen

Sarah Fish, Specialist Biomedical Scientist,
University Hospital of North Staffordshire

Endometrial cells seen in cervical cytology specimens of women over the age of 40 and after day 12 of the menstrual cycle ('out of phase') have historically been shown to indicate possible abnormal uterine pathology, including endometrial adenocarcinoma. This has led to the reporting of these cells and subsequent referral, following national guidelines. However, more recent research on this protocol has suggested that these 'inappropriate endometrial cells' do not indicate abnormal uterine pathology (Moatamed *et al.*, 2011). As

such, data spanning a five-year period from July 2007 to June 2012 of inappropriate endometrial cell cervical cytology specimens from the University Hospital of North Staffordshire (UHNS) has been collated in order to determine the clinical significance of these cells within the NHS Cervical Screening Programme (NHSCSP).

• Moatamed, N.A., Le, L-T., Levin, M.R., Govind, R. & Apple, S.K. (2011) In Papanicolaou Smears, Benign Appearing Endometrial Cells Bear no Significance in Predicting Uterine Endometrial Adenocarcinomas. *Diagnostic Cytopathology*, 41(4), 335-341.

To evaluate the utility of flow cytometry immunophenotyping in the cytological diagnosis of clinically suspected lymphoproliferative disorders

Ebadi-Askari, R. FIBMS, MSc, BSc; Moonim, MT MD FRCPath

Introduction: Determining the cause of lymphadenopathy is essential for patient management.

Objective: Investigating whether the addition of flow cytometry (FC) to fine needle aspiration cytology (FNAC) improves the ability to distinguish between reactive and neoplastic lymphoid populations and improves stratification of lymphoproliferative disorders (LPD) into low and high grade Non-Hodgkin lymphoma (NHL).

Study design: A retrospective study involving 430 consecutive patients with persistent lymphadenopathy and clinical suspicion of LPD who underwent FNAC and FC between 2006 – 2009. The study consisted of 2 arms; A) The

original arm compared the results of the original cytology report (OC) against FC as well as the combined use of OC + FC. B) The blinded arm, blindly re-evaluated cytology (BC) and compared this result with the combined use of BC and FC.

Results:

- Considering all lymphoid lesions:
OC had a sensitivity of 0.81 which increased to 0.88 when OC was combined with FC (p-value= 0.03).
BC had a sensitivity of 0.75; this was significantly increased to 0.90 when combined with FC (p-value= 0.001).
 - For low grade LPD a significant difference in sensitivity & accuracy was noted between BC alone and combined BC + FC, rising from 0.72 to 0.93.
-

- No significant difference was seen in diagnostic accuracy for high grade LPD.

Conclusion: Combined use of C & FC significantly improved the sensitivity for the overall diagnosis of LPD and reliably distinguished between benign and malignant lymphoid lesions. It also significantly improved the diagnostic accuracy of low grade NHLs.

References

- Bangerter, M., Brudler, O., Heinrich, B. And Griesshamner, M. (2007). Fine needle aspiration cytology and flow cytometry in the diagnosis and sub classification of non-Hodgkin's Lymphoma based on the World Health

Organization classification. *Acta Cytol.* **51**(3). 390–8.

- Barroca, H., Marques, C. and Candeias J.(2008). Fine needle aspiration cytology diagnosis, flow cytometry immunophenotyping and histology in clinically suspected lymphoproliferative disorders: a comparative study. *Acta Cytol.* **52**, 124–32.
- Colorado, M., Cuadrado, M.C., Insunza, A., Mazorra, F., Acinas, O. And Insunza, A. (2010). Simultaneous cytomorphologic and multiparametric flow cytometric analysis on lymph node samples is faster than as valid as histopathologic study to diagnose most non hodgkin lymphomas. *Am J. Clin. Pathol.* **133**, 83–91.
- Zeppa, P, Vigliar, E., Cozzolino, G., Troncone, G., Picardi, M. De Renzo, A.D., Grimaldi, F., Pane, F., Vetrani, A. and Palombini, L. (2010). Fine needle aspiration cytology and flow cytometry immunophenotyping of non-Hodgkin lymphoma: can we do better. *Cytopathology*.

An intra-pancreatic Accessory Spleen diagnosed by endoscopy ultrasound (EUS) guided fine needle aspiration cytology (FNAC)

María Martino, M.D.*, Clara Caballero, M.D.*, Beatriz Castro, M.D.**,
Ana Toledo, M.D.* , Isabel Lastra*

(*Pathology Department and **Digestive System Department, Hospital Universitario Marqués de Valdecilla (HUMV) , Santander, Spain)

Introduction: Intra-pancreatic accessory spleen (IPAS) forms a well-defined nodule within the tail of the pancreas and is commonly mistaken by imaging studies as a neuroendocrine tumor.

Case Report: We report a case of a 62-year-old female with abdominal pain and a nodule in the tail of the pancreas. This lesion was clinically suspicious of pancreatic neuroendocrine tumor. EUS-guided FNAC reveals predominantly small lymphocytes with a subset of eosinophils, neutrophils, histiocytes and plasma cells. There is also characteristic CD8 positive immunostaining of endothelial cells in cell block sections.

Conclusion: IPAS is a benign lesion that usually presents as an incidental finding by imaging appearances.

However, because imaging characteristics are not specific and the differential diagnosis includes neuroendocrine tumor, tissue sampling is recommended. We report a case reliably diagnosed by EUS-guided FNAC, leading to a benign prognosis and avoidance of unnecessary pancreatic surgery.

Bibliography:

1. Intra-pancreatic accessory spleen: a case report and review of literature. Rodriguez E, Netto G, Li QK. *Diagn Cytopathol* 2013;**41**(5):466–9.
2. Intra-pancreatic accessory spleen: mimic of pancreatic endocrine tumour diagnosed by endoscopy ultrasound-guided fine-needle aspiration biopsy. Schreiner AM et al. *Diagn Cytopathol* 2008;**36**(4):262–5.
3. Endoscopic ultrasound-guided fine needle aspiration biopsy of the intra-pancreatic accessory spleen: a report of 2 cases. Hutchinsonson CB et al. *Acta Cytol.* 2010 ;**54**(3):337–40.



Can HPV Primary Screening reduce cervical cancer incidence and mortality?

R. Marshall Austin MD, PhD
Magee-Womens Hospital of University of Pittsburgh Medical Center, USA

Background

The purpose of cervical screening is to reduce morbidity and mortality due to invasive cervical cancer by either detecting precancerous lesions that can be ablated or by early diagnosis and downstaging of prevalent invasive cervical cancers.¹ Numerous randomized controlled clinical trials have now explored introducing Human Papillomavirus (HPV) testing as a possible replacement for cytology as the primary cervical screening test.² However, the degree of benefit in preventing cervical cancer cannot be determined in test performance studies alone, as trials have been forced to rely on more prevalent CIN2/3+ as a surrogate outcome rather than far rarer data on invasive cervical cancer outcomes.³ Therefore, it has been acknowledged that the effect of HPV testing as an alternative to periodic cytologic screening on the incidence of invasive cervical cancer has not been adequately assessed.⁴

In response to this information gap, an analysis entitled “Efficacy of HPV-based screening for prevention of invasive cervical cancer: follow-up of four European randomized trials” was published in *Lancet*⁴ and was the featured article at the recent manufacturers’ Eurogin 2013 meeting. This analysis focused on four European randomized controlled trials from Holland, Italy, Sweden, and the UK in which a substantial number of invasive cervical cancers (107) were detected by screening and diagnostically confirmed by histopathology in either the experimental HPV arm or the control cytology arm of the trials. Because none of the four trials was powered to show a reduction in invasive cervical cancer incidence, the data was pooled. However, when the authors ascertained that the data (inconveniently) documented that cervical cancer diagnostic rates were no different between the HPV and cytology arms during the first 2.5 years after enrolment, the authors sought to explain this unexpected finding by suggesting that cancers diagnosed during the first 2.5 years after enrolment “mainly includes prevalent cases.” By this somewhat questionable manoeuvre, the authors unfortunately had to eliminate nearly half (52 of 107) of the pooled cervical cancers available for comparison, even while acknowledging that “we would (have) expect(ed) cancer detection to be higher in the experimental arm in the first 2.5 years.” Not dissuaded, the authors go on to argue that “the best estimate for the gain in reducing incidence of invasive cervical cancers— i.e. the true gain in efficacy— by the HPV-based screening is

provided by the rate ratio recorded after 2.5 years.” It is in this group of 55 remaining cervical cancers that the authors claim to identify a benefit of reduced cervical cancer diagnoses, 19 cancers diagnosed during 419,500 screened person-years in the HPV experimental study arms versus 36 cancers diagnosed during 358,656 screened person-years in the control cytology arms. This difference forms the basis for the authors’ main conclusion that “HPV-based screening provides 60–70% greater protection against invasive cervical carcinoma compared with cytology.”

A closer look, however, at data on the 55 “more significant” cervical cancers diagnosed in the four trials more than 2.5 years after enrolment raises many troubling observations and questions. First, the data is dominated by the large Italian NTCC trial with 40% of the total screened person-years in the four trials; in this trial alone all women with a positive HPV test in either of the first two phases of the trial were referred to colposcopy, resulting in over double the number of biopsies in the HPV experimental arm compared to the cytology control arm. Furthermore, the argument that the “true gain in efficacy by HPV-based screening” is reflected in cancers diagnosed over 2.5 years after enrolment is undermined by the observation that no reduction in cancers were documented during this period in the much smaller Swedish and UK trials. In fact, during the UK ARTISTIC trial, the only trial utilizing liquid-based cytology, all 5 cervical cancers diagnosed over 2.5 years after enrolment were diagnosed in the experimental HPV arm, and none were diagnosed in the control cytology arm! These findings suggest significant differences in results achieved with conventional smear cytology compared to UK quality-controlled liquid-based cytology. The UK ARTISTIC trial investigators themselves earlier acknowledged in a 2009 technology assessment study: “It is difficult to escape the conclusion that LBC was more sensitive in ARTISTIC than earlier conventional cytology.”⁵

Some unexpected findings also emerge in HPV test performance in the *Lancet* paper. Of the 19 cervical cancers detected over 2.5 years after enrolment, only 11 of 19 (58%) were HPV-positive at baseline. Since “virtually all” cervical cancers are said to be due to persistent infections with carcinogenic HPV,^{6,7} this 42% false negative rate is surprising, especially in light of proposed extended screening intervals with HPV-based screening.

US Kaiser Permanente investigators have made similar observations in documenting a 31% HPV false-negative rate in 87 cervical cancers diagnosed within 5 years of follow-up after Pap smear and HPV co-testing.⁸ Similarly, 3 of 12 cervical cancers diagnosed in the first two rounds of the ARTISTIC trial were preceded by negative baseline Hybrid Capture 2 HPV results.⁵ Even among presumed “prevalent” cervical cancers in the Lancet analysis, 4 of 25 (16%) tested HPV-negative at baseline.⁴ These findings are similar to other reports which note that around 10% of diagnosed cervical cancers tested by Hybrid Capture 2 will yield negative false negative results.⁹ What is not as widely understood is that false-negative HPV test results preceding cervical cancer diagnoses can increase to such significant levels (25–42%) as cervical cancers develop over time (2–7 yrs before diagnosis), probably due to both the challenges of adequate sampling of infected lesional cells and low viral load.

The Lancet analysis raises as many questions as answers in addressing still largely unanswered questions concerning the efficacy of primary HPV screening on reducing cervical cancer incidence and mortality. Limitations of the randomized controlled trial in evaluating population-based health interventions have only recently begun to attract attention.¹⁰ Perhaps another “unfortunate experiment”¹¹ will soon be underway in Europe as financially overextended systems seek to cut healthcare expenditures by moving from medical history’s most successful cancer screening test to primary HPV screening at extended screening intervals. Data on the relative effectiveness of primary HPV screening to control cervical cancer morbidity and mortality is likely to accrue only after Holland’s proposed program is implemented in 2016.¹²

References

- 1) Andrae B, Andersson TML, Lambert PC, et al. Screening and cervical cancer cure: population based cohort study. *BMJ*. 2012;**344**:e900.
- 2) Rebolj M, Pribac I, Lyng E. The Problem of False-Positive Human Papillomavirus DNA Tests in Cervical Screening. *Current Pharmaceutical Design* 2013; **19**: 1439–1449.
- 3) Kulasingam SL, Havrilesky L, Ghebre R, Myers ER. Screening for Cervical Cancer: A Decision Analysis for the U.S. Preventive Services Task Force. AHRQ Publication No. 11-05157-EF-1. Rockville, MD: Agency for Healthcare Research and Quality; May 2011.
- 4) Ronco G, Dilner J, Elfstrom KM et al. Efficacy of HPV-based screening for prevention of invasive cervical cancer: follow-up of four European randomized controlled trials. *Lancet* 2014; **383**: 524–32.
- 5) Kitchener HC, Almonte M, Gilham C. ARTISTIC: a randomised trial of human papillomavirus (HPV) testing in primary cervical screening. *Health Technol Assess*. 2009; **13**: 1–150, iii–iv.
- 6) Walboomers JMM, Jacobs MV, Manos MM, et al. Human papillomavirus is a necessary cause of cervical cancer worldwide. *J Pathol* 1999; **189**: 12–19.
- 7) Schiffman M, Glass AG, Wentzensen N, et al. A long term prospective study of type-specific human papillomavirus infection and risk of cervical neoplasia among 20,000 women in the Portland Kaiser Cohort Study. *Cancer Epidemiol Biom Prev* 2011; **20**: 1398–1409.
- 8) Katki H, Kinney WK, Fetterman B, et al. Cervical cancer risk for women undergoing concurrent testing for human papillomavirus and cervical cytology: a population-based study in routine clinical practice. *Lancet Oncol* 2011; **12**: 663–672.
- 9) Wu Y, Chen Y, Li L et al. Associations of high-risk HPV types and viral load with cervical cancer in China. *J. Clin. Virol* 2006; **35**:264–269.
- 10) Sanson-Fisher RW, Bonevski B, Green LW, D’Est C. Limitations of the Randomized Controlled Trial in Evaluating Population-Based Health Interventions. *Am J Prev Med* 2007; **33**: 155–161.
- 11) Coney S. The Unfortunate Experiment: The Full Story Behind the Inquiry Into Cervical Cancer Treatment. Penguin Press, 1988.
- 12) Health Council of the Netherlands. Population screening for cervical cancer. The Hague: Health Council of the Netherlands, 2011; publication no. 2011/07E. ISBN 978-90-5549-866-6. Available at: <http://www.gezondheidsraad.nl/en/publications/prevention/results/taxonomy%3A189>, accessed 2/14/14.

Non-gynaecological cytology survey — can you help?

Hedley Glencross, Cytology Department, Level E, Pathology Centre, Queen Alexandra Hospital, Portsmouth PO6 3LY

I am conducting a short survey on non-gynaecological cytology practice in the UK. Principally, this is concerned with the extent of involvement by biomedical scientists in the preparation, evaluation and reporting of non-gynaecological cytology samples. I am also interested to understand the involvement of biomedical scientists in both their attendance at remote clinics and assessment of cytological adequacy by them in these clinical situations.

I anticipate this survey should take approximately 15 minutes to complete and it is intended to publish or present the results. Your participation is encouraged as this will help provide background information on such practices throughout the UK.

A link to the survey is here: www.cytology.co.uk

Many thanks in advance for your co-operation.

Hedley

Charity fundraiser

Rhona Currie

Cytology Screener, Royal Infirmary, Edinburgh



I work at the Royal Infirmary of Edinburgh, as a Cytoscreener and have been with the trust for 13 years. I am looking to do something different in July next year and make a difference by attending the Vine Trust, Tanzania Work Party, helping to build homes and centres for vulnerable and orphaned children in Moshi, Tanzania. Joining a Work Party will offer me the opportunity to witness and experience the stark realities of choices (or lack of them) in the developing world. I will play my part in the transition from the street to a loving home, which many of the children I will work with make. The Vine Trust does 2 week volunteering stints so it is practical for people who work full time, you can make a real difference using 2 weeks of your holidays and doing something different. I do feel I can help make a huge difference.



The Vine Trust is an international interdenominational volunteering charity, which seeks to enable volunteers to make a real and significant difference to some of the poorest children and communities in the world. Work party teams help local partners to build centres to provide some of the most vulnerable children with a home, and education. Connecting people to change lives is the Vine Trusts aim and their goal for both the overseas partners and volunteers alike. Through the short-term volunteer opportunities they seek to create “ambassadors for the poor” who in turn will bring back their experiences to our communities, schools and workplaces here in the UK. The Vine Trust does Work Parties, Medical Teams and School Trips they have an extensive experience of sending teams throughout the year to the projects and organising specific opportunities which quite literally can be life changing for all involved.

I will be working in the Moshi area, a region in the Northeast of Tanzania by the slopes of Africa’s tallest mountain, Kilimanjaro, and the border with Kenya. Whether I am helping with new buildings or ongoing maintenance I will live and work alongside the communities I am serving. All teams will be involved in basic building duties alongside local craftsmen and community volunteers. Tasks include: bamboo stripping, brick making, laying bricks and general labour.

Sample Itinerary:

Day 1 & 2

Arrive in Kilimanjaro airport following flights from UK via Amsterdam or Nairobi. Minibus will take group to Umoja Hostel in Moshi. Orientation and introductions.

Day 3–11

— Travel to the work sites each day, Work with local builders and volunteers to help construct the children’s homes/centers.

— Visit other children’s centers that are being supported by the Vine Trust. Possibility to work in local schools and visit vocational training centers.

Day 12 (Optional Safari Trip or continue building work).

Day 13 (Optional Safari Trip or continue building work)

Day 14

Last day in Moshi and catch flight back to UK

Day 15

Arrive back in UK

I think it would be an amazing and rewarding experience, I know there are so many great Charities and Causes out there, but I do feel it is such a worthwhile cause and the right project for me.

I have already started fundraising by selling 'Sweet Treats Bags' of fudge, tablet, truffles, coconut ice and jelly beans and am having a cake sale in February, I am planning a car boot sale, and have sent letters to a few of the big supermarkets regarding a bag packing day, plus I have lots of other ideas, I need to raise £1775 that includes my personal cost and fundraising for the projects, I have to raise a minimum of £300 for the projects but would love to raise so much more.

I would like to share my vine trust fundraising page with you all:

<http://www.vinetrust.org/fundraise/rhona-Tanzania-July-2014-fundraising>

You can also visit www.vinetrust.org for more information about the work they do.

Thank You

Rhona (Cytology Edinburgh)

Sub Saharan Cytology

Nick Dudding, Deputy Director of East Pennine Cytology Training Centre, Sheffield Teaching Hospitals.

Allan Wilson, Lead Biomedical Scientist in Cellular Pathology, Monklands Hospital, Airdrie

In January this year Allan Wilson and I were fortunate enough to travel to Cape Town at the invite of an Australian Pathologist, Dr Andrew Field. Andrew has run a number of training events in Africa under the auspices of the Papanicolaou Society of Cytology, though this was one of his most ambitious projects. In addition to over 40 Cytotechnologists and pathologists from South Africa there were 22 Pathologist from Kenya, Tanzania, Burundi, Namibia, Uganda and Rwanda The tutorial ran over four days; the first two concentrating on diagnostic cytology, most notably FNA and the last two days concentrating on cervical cytology and delivered by Allan and myself.

There are over 80,000 cases of cervical cancer reported per annum in Africa and of course this is just those that are reported. There is no screening in many parts of sub Saharan Africa where HPV prevalence is much higher than in the west and normal epidemiology is modified by the large numbers of women that are HIV positive. HPV prevalence in South Africa for instance is over 60% in women aged 20 – 50.

Although we were to discover that LBC is used in parts of South Africa the training was completely in conventional cytology. The Turning Point interactive voting system was extremely useful and allowed us to assess the level of knowledge from the outset. This was extremely high, most interestingly with regard to glandular lesions where the audience performed very well despite suggesting that they saw very few such lesions.

Of most interest to us was how cytology worked in those parts of Africa represented. As you might expect there is no organised screening in East and Central Africa and screening is limited to those few that can afford to pay for the privilege.

In South Africa screening is organised, but certainly very differently to what we do here in the UK. In a country where cervical cancer rates are high, HIV is common and access screening limited by geography and cultural issues they have managed to develop a three pronged programme. At present the majority of most women screened present with either symptoms or with a HIV positive test. This would seem a little incongruous to us in the UK, but in a country

with limited resources this represents a useful way of identifying those most at risk. Within the group that are HIV positive those with a normal pap smear are rescreened in three years, those with a low grade or borderline repeated in a year and those with high grade referred to colposcopy. The third strand is those women that fall outside these groups. Such women, with no symptoms and not known to be HIV positive are supposedly offered screening three times in ten years starting at age 30, but we were to hear that of the three groups it is these women that are most poorly screened.

Despite the difficulties the programme faces individual labs in South Africa appear to be pretty much on a par with us in the UK. LBC is used in some centres as is the Focalpoint system which is used on conventional samples.

A special symposium about the way forward for South Africa on the Monday evening was attended by a number of key individuals within the South African Programme and the various options were discussed. Most of the discussion centred around the likely impact of HPV testing and the potential of vaccination, but it soon became very clear to Allan and I that western solutions would not work and we were left floundering at various times as we battled with a very different system.

There are enormous problems in particular within sample taker training and colposcopy. Despite intensive discussion around cytology we were bemused to discover that South Africa just doesn't have the number of trained individuals within primary care to take the samples. We were both left slightly embarrassed by informal discussions confirming that part of their problem is the constant poaching of trained nurses by countries like the UK. Whilst it fills a need for us in the west the impact on countries like South Africa is enormously damaging and we were both left reflecting that it borders on immoral. Gynaecology is also a huge issue. Despite my statement above that women diagnosed with high grade lesions are referred to colposcopy we were to discover that they could wait at least six months if not a year for investigation and that default rates are extremely high. Against this background discussion around moving the screening programme forward becomes very challenging.

What they are looking at for now is a combination of cytology where screening is already established and the introduction of HPV testing where it isn't. The plan is to start screening with cytology at age 25 or at the time of diagnosis for those women that are HIV positive following the same algorithm noted above and for non HIV women to start at 30, with three screens in a lifetime at age 30, 40 and 50. There was some very enjoyable debate around a proposal that where HPV testing was used HPV positive women with any cytological abnormality (ascus or above) would go onto LLETZ. One could see that this policy would be easier and simpler in a programme where repeat colposcopy / smears is challenging, but I think it's fair to say that not all in the audience were happy with this suggestion!

There are however ambitious plans for vaccination through the schools to start later this year and both Allan and I felt that it is difficult to see anything other than mass vaccination having the desired impact.

Although we weren't specifically involved in the non gynaecological days it was also interesting to hear how far behind UK Cytotechs are in terms of non gynaecological cytology and the degree that South African Cytotechs are involved in it. In Tygerberg hospital for instance Cytotechs attend ROSE daily in the theatres. Their Lung Unit alone has 450 patients annually for transbronchial, transthoracic or EBUS FNA and again Cytotechs attend all of those. There is also a FNA clinic that aspirate 15-30 patients daily with Cytotech attendance. In this regard there is much the UK could learn.

We would like to thank a number of people for making this trip possible. Firstly we must thank Dr Field for initial the invitation and his generous sponsorship. We must also thank Hologic for partly sponsoring the flights, the Scottish Pathology Network (SPAN) for paying for our accommodation in Cape Town and lastly all our training centre colleagues who kindly let us have copies of old presentations we could use for the morphology sessions.



**CEC Local
Officers
(Spring 2014)**



Alison Baseley
Cytology Dept
Royal Hampshire County Hospital
Winchester, Hants
SO22 5DG
Tel: 01962 825371
Fax: 01962 824664
e-mail: Alison.Baseley@wehct.nhs.uk

Viv Beavers
Manchester Cytology Centre
Central Manchester Healthcare Trust
P.O. Box 208, CSB 2
Oxford Road, Manchester
M13 9WW
Tel: 0161 276 5115
e-mail: Viv.Beavers@cmft.nhs.uk

Beverley Crossley
Cytology Dept
Royal Oldham Hospital
Rochdale Road
OL1 2JH
Tel: 0161 656 1742
e-mail: beverley.crossley@pat.nhs.uk

Andrea Styant-Green
88 Campernell Close
Brightlingsea
Essex CO7 0TA
Tel: 01206 744855
e-mail:
Andrea.Styant-Green@colchesterhospital.nhs.uk

Hilary Diamond
The Laboratories
Belfast City Hospital
Lisburn Rd, Belfast
BT9 7AD
Tel: 028 9026 3651
e-mail: hilary.diamond@bll.n-i.nhs.uk

Helen Burrell
Cytology Training Centre
Southmead Hospital
Bristol
BS10 5NB
Tel: 0117 959 5649
e-mail: Helen.Burrell@nbt.nhs.uk

WALES
POSITION VACANT
VOLUNTEERS REQUESTED

Rhona Currie
2nd Floor Pathology Dept
NRIE
51 Little France Crescent
Dalkeith Road
EDINBURGH EH164SA
Tel: 0131 242 7156
e-mail: rhona.currie@luht.scot.nhs.uk

LONDON
POSITION VACANT
VOLUNTEERS REQUESTED

**Please remember to make a copy of
everything before it is sent — there
have been one or two losses in the post.
Thankyou**

CEC News – Spring 2014

Jenny Davies

A very short report as the scheme continues to tick along nicely, with book submissions and JBLs being sent in on a regular basis, thank you. No major issues have come to light so the new rules seem to be working well.

I am about to start sending details of those members who have been active in the scheme in the last 3–5 years. **Please could you write to me and let me know if you no longer actively participate in CEC.**

If you are in a region that currently has a vacancy for a Local Officer, please do send books directly to me or an officer in a different region if you prefer.

When you submit your CEC book for validation, if you do not know your BAC membership number, I can chase up your records with Christian, so don't worry about that for the time being.

Remember — if you haven't already transferred to the new scheme, please send your book to me even if you haven't reached the 300 points — and I will bring them forward into the new one to maximize the use of the new scheme credits.

Well done once again to everyone participating in the scheme, please keep it up.

Journal Based Learning

Now on to this issue's JBL exercise. One JBL — **10 questions — 10 credits**. This issue's topic relates to cervical screening in South Africa, which has a high prevalence of HIV. For submission, same instructions as before — photocopy the page and send your answers to me, or your Local Officer, for marking — there is no need to send your book.

Please try to do the JBLs as they come up in each issue of SCAN. JBLs more than 12 months old should be considered closed. Only one submission of each JBL will count.

Remember to keep a copy. Please include your name, BAC membership number, and as we are not receiving your book, your return address

Membership Corner

Louise Smart

Chair, BAC Membership Subcommittee

Thank you all for renewing your membership subscription. We now have around 620 members and are pleased to report a steady stream of new members joining. Nevertheless, we are keen to encourage new members from all the professional groups involved in cytology, trainees as well as trained staff. Joining information is available on the BAC website: www.britishcytology.org.uk

Membership cards were not reissued this year; the membership number printed on your previous card and also your renewal notice will continue to allow access to the members' area on the website. If you have forgotten your membership number please contact the BAC at mail@britishcytology.org.uk

Cervical Squamous Intreepithelial Lesions and associate cervical infections in an HIV positive population in Rural Mpumalanga, South Africa

P.J. Swanepoel et al, *Cytopathology* 2013, **24**, 264 – 271

1. What is the HIV positive prevalence rate in South Africa?
2. What is the effect of HPV viral genome integration?
3. What are the consequences of the answer to "2" above?
4. Outline the management of abnormal cases in the Mpumalanga Lowveld region
5. At what age does the South African screening programme start?

-
6. What justification has been cited for the answer to “5” above?
7. How might female genital Bilharzia be linked to the development of HSIL?
8. What initial conclusion is highlighted by this study?
9. What hypothesis have the authors put forward in relation to Bacterial vaginosis?
10. What major concern have the authors raised as a result of this study?

10 marks available

Name..... CEC number (if known).....



Learning how to s

Andrew Evered, Darren Walker
Department of Applied Psychology, Cardiff

Experiment 1

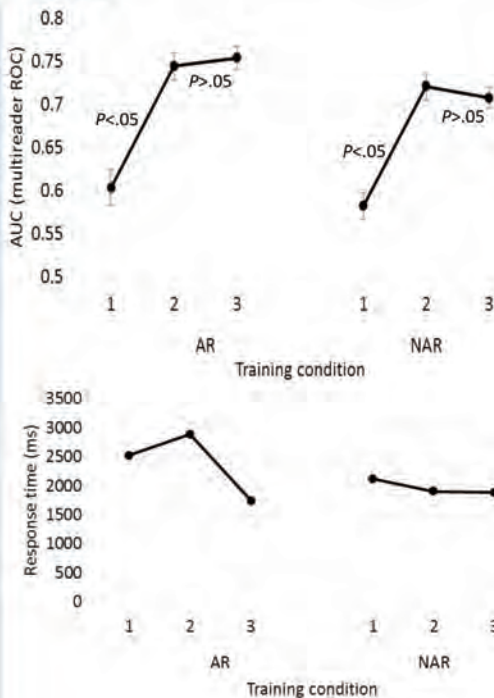
Background

A diagnosis of cancer is a life changing event, and one that the clinician must get right as often as possible. Cytologists are clinicians who must visually assess cells through a microscope for the tell-tale signs of abnormality. Surprisingly little is known about how they learn this important skill.¹ Traditional training programmes focus on teaching explicit diagnostic rules (analytical reasoning), a process that can be time-consuming and burdensome.² The ability of novices to learn these rules implicitly through passive exposure to exemplar images of normal and abnormal cells (non-analytical reasoning) has not been investigated.

Methods

Two groups of non-experts received cytology training using analytical (AR) or non-analytical reasoning (NAR) techniques. Diagnostic accuracy (area under the ROC curve) and response times were measured.

Results



Participants were tested before (test 1) and after (test 2) their respective training protocols. Non-analytical reasoning yielded diagnoses that were as accurate as analytical strategies. Instructions to combine AR and NAR strategies (test 3) were ineffective.

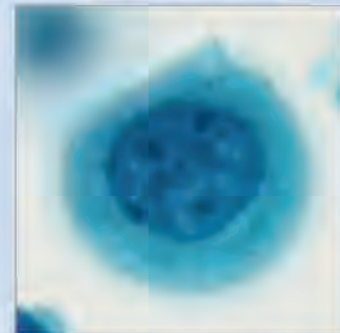
Response times were generally faster under non-analytical reasoning conditions.

Conclu

Two experiments showed that no... recognise abnormal cells:

- a) With remarkable accuracy a
- b) Without specific tuition
- c) By implicitly transferring wh... to more complex diagnoses

Normal cell



Is explicit training required to distri

Refer

1. Evered A, Walker D, Watt A, Perham N. To v... contribute to visual learning in cytopathology
2. Level 3 Diploma in Cervical Cytology Centre... 2007.
3. Evered A, Walker D, Watt A, Perham N. (In p... paired cell images influences visual learning in... 18 NOV 2013. DOI: 10.1002/cncy.21370.
4. Ahissar, M. and Hochstein, S. (1997) Task dif... learning. Nature. 1997;387:401-406.
5. Ahissar, M. and Hochstein, S. The spread of... effects of target distribution and task difficulty

Spot a cancer cell

er, Andrew Watt, Nick Perham
f Metropolitan University, Cardiff, CF5 2YB



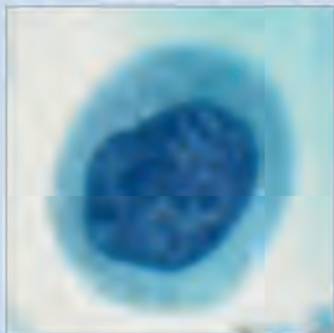
usions

n-experts can learn how to

and speed

that they learn from simple cases

Abnormal cell



nguish normal and abnormal cells?

ences

what extent does non-analytic reasoning
? Cancer Cytopathol. 2013;121:329-38.
Resource Pack. London: City and Guilds;

ress). Untutored discrimination training on
n cytopathology. Cancer Cytopathol. online:

difficulty and the specificity of perceptual

attention and learning in feature search:
y. Vision Res. 2000;40: 1349-1364

Experiment 2

Background

Do trainees require training on difficult images in order to recognise difficult cells, or does training on easy images effectively transfer to difficult diagnostic scenarios?³ Previous research suggests that training is more effective if subjects start with easy conditions and gradually move to more difficult conditions.^{4,5} As a follow up to experiment 1, the aim of experiment 2 was to determine whether the interpretive difficulty of training images under non-analytical reasoning conditions influences the efficiency of visual learning in cytology.

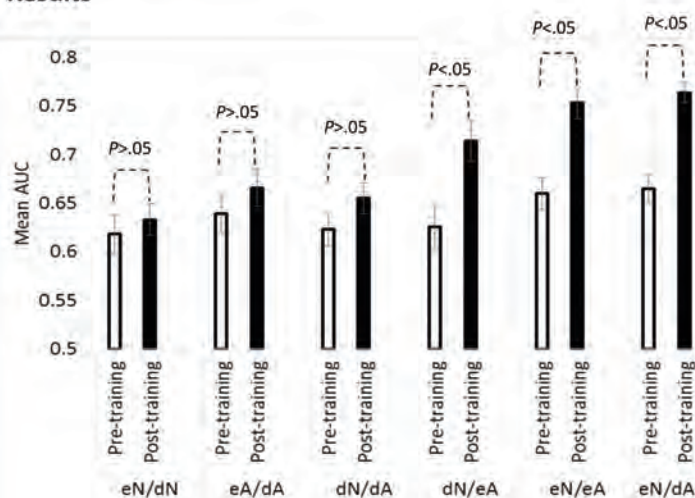
Methods

Six cytology training protocols were devised, involving exposure of separate groups of participants to the following image pair combinations.

1. Difficult normal paired with difficult abnormal (dN/dA)
2. Difficult normal paired with easy abnormal (dN/eA)
3. Easy normal paired with difficult abnormal (eN/dA)
4. Easy normal paired with easy abnormal (eN/eA)
5. Easy normal paired with difficult normal (eN/dN)
6. Easy abnormal paired with difficult abnormal (eA/dA)

Participants were given a difficult 60-slide image interpretation test before and after their respective training protocol and diagnostic accuracy measured as in the previous experiment.

Results



Training was most effective when participants were exposed to normal/abnormal image pairs in which at least one member of the pair was easy to interpret.

Current CEC Scheme Sponsorship

On behalf of the NAC Executive, and I am sure all the members, I would like to express my thanks to the following companies for the continued support they have shown in the development and growth of the CEC Scheme. Now that the scheme is changing, I hope that this support will continue, and indeed that the group will grow to support the ongoing developments of CEC.

Pioneer Research Chemicals Ltd Julie Jarman Tel: 01206 791781 e-mail: sales@pioneerresearch.co.uk website: www.pioneerresearch.co.uk 2013/14	Carl Zeiss Ltd (Paul Southey) 15 – 20 Woodfield Road Welwyn Garden City Hertfordshire AL7 1JQ Tel: +44 1707 871200 e-mail: micro@zeiss.co.uk website: www.zeiss.co.uk 2013/14
Source BioScience Healthcare Wilma Anderson Tel: 0115 973 9012 e-mail: Wilma.Anderson@sourcebioscience.com website: www.sourcebioscience.com 2013/14	Hologic (UK) Jo Frost Tel: 01293 522080 e-mail: ukreception@hologic.com website: www.hologic.com 2013/14

This list will be regularly reviewed for each issue of SCAN, and on the NAC Website. If any of the companies listed above have any changes of details to report at any time, please let Jenny Davies know by e-mail — jenny.davies@cmft.nhs.uk

Membership Details

Please email or write to Christian Burt if any of your contact details change.

Email: mail@britishcytology.org.uk

BAC Office, 12 Coldbath Square, London EC1R 5HL

Update on Modernising Scientific Careers (MSC)

Allan Wilson, on behalf of the BAC Executive

It is now one year since an article on MSC appeared in SCAN. That piece provided an overview and update of MSC. We would all hope for progress in all areas but the enormity of the change required means that rapid progress will inevitably be quicker in some areas than others.

The Academy for Healthcare Science (AHCS)

Despite a flurry of activity in the first half of 2013, the second half of the year was relatively quiet. There has been a merging of groups and functions and Cellular Pathology is now part of a larger grouping and this has led to a loss of focus.

The Academy has concentrated on the equivalence process and has recently asked for expressions of interest from Biomedical Scientists wishing to apply for equivalence to the learning outcomes of the Scientist Training Programme (STP). Several Consultant Biomedical Scientists have either expressed an interest in equivalence or have already applied for assessment. Successful candidates will be awarded a Certificate of Equivalence and will be able to register with HCPC as a Clinical Scientist. The Scottish Government and Welsh Assembly have announced separate initiatives to promote applications for equivalence.

Proposed Standards for Register of Healthcare Science Practitioners

The AHCS has recently had a consultation event on proposals for a register of Healthcare Scientists not currently regulated by the HCPC. For more information on the document please visit the AHCS website. The standards are basically very similar to those laid out by existing regulatory bodies, which have been used as a template. CPD will play a major part. A consultation event is being held on 19th February, with representation from the BAC.

National School of Healthcare Science (NSHCS)

The School has focused on supporting the STP candidates across all disciplines and the first Cytopathology and Histopathology candidates will have their final exams and assessments in 2014. The final assessment process is currently under development.

There are currently five STP candidates in cytology labs across the country but the role of the Clinical Scientists who emerge from this programme is still unclear. Unless candidates

already hold the City & Guilds Diploma (or equivalent) they will not have a role in primary screening within the UK NHS cervical screening programmes. Equally, unless candidates hold the ASD in cervical cytology they will not be permitted to authorise abnormal reports. It would appear therefore that their role may be limited to non-gynae cytology or HPV testing.

Advanced Specialist Diploma (ASD) in Non-Gynaecological Cytology

Progress has been slow mainly due to a review of the ASD in gynae cytology. The conjoint board will review both qualifications together to ensure a consistent approach. The next meeting of the board is on 27th February where proposals to review the gynae exam and approve the non-gynae exam will be discussed.

Pilot study for extended roles of scientists in Histopathology

The pilot scheme is progressing although some Consultant Biomedical Scientists have either deferred assessment for a year or opted to drop out altogether due to work pressures. Participation in this scheme is demanding and the review of a considerable number of cases while still doing the "day job" is extremely challenging and should only be considered after careful reflection. However, the outcome of this pioneering programme will inform the development of HSST in cellular pathology.

MSC Apprenticeships Career Framework (CF) 2-4 progress

Since Summer 2013, work has been undertaken through the MSC network to develop a training strategy for those staff falling into bands 2-4 on the career framework. This is being led by Shirley Fletcher of Fletcher Consultancy, and modules from all training programmes at this level have been collated to try to provide a common framework. The aim is to address the training needs across 50+ disciplines. Cytology screeners and MLAs will fall into this bracket. The BAC has ensured that there is a presence at meetings taking this work forward to ensure that the very specialised nature of cytology screening is recognised. There is a current reform of Apprenticeships as a Government directive; the aim is that all apprenticeships will be reformed by 2017. A more detailed account is difficult at present as this is very much in draft form and changes/additions are frequent.

Higher Specialist Scientific Training (HSST)

Implementation of the STP project has been marred by a failure to adequately define the roles which the training programme supports. Defining the roles through HSST remains a difficult area and is less developed than the STP project due to the expected lag between the two programmes. Unlike other disciplines where the role of Clinical Scientists is defined, this is not the case in cellular pathology. Currently, whilst it is tempting to consider roles in cytology in isolation, diagnostic cytopathology is undoubtedly a core component of cellular pathology and any route to HSST in cellular pathology will require expertise across the full range of cellular and molecular pathology. The histopathology pilot, mentioned above, which several colleagues have already enrolled on, and the extended roles developed through close collaboration between the Institute for Biomedical Science and the Royal College of Pathologists provides a strong basis on which to build this programme.

BAC and HSST

The BAC and its predecessor bodies, NAC and BSCC, have strongly supported advanced roles for senior Biomedical Scientists. The creation and further development of the role of Consultant Biomedical Scientist has undoubtedly added extra value to the UK NHSCSPs over the last ten years.

The evolution and modernisation of the pathology workforce has to be focused on what is best for patient care. The BAC will continue to support and promote roles that enhance the quality of healthcare available to the public. In the preceding SCAN article in April 2013 the question was posed — 'What do we need in a modern health service to deliver the service that patients need/expect?'

The answer provided is still fundamentally correct. We will need trained cytologists, irrespective of their professional background, who are competent, appropriately trained and supported in post. At senior levels, the expertise and knowledge to provide leadership and training are as essential as competence to deliver the routine service.

Perhaps with time the routes will become clearer, but there is no doubt that this will be a lengthy process and will involve protracted negotiations between the IBMS, RCPATH and Dept of Health. The BAC is committed to informing these debates in a mature and professional manner. Slow progress has been made but significant barriers still remain. Patience and perseverance will be required to influence the development of MSC and produce a cytology workforce that can continue to deliver a service that the people we serve deserve.

More fundraising

A team of 9 laboratory staff from Cellular Pathology at Kettering General Hospital NHS Foundation Trust are competing in a dance competition to raise vital funds for Cransley hospice, a local hospice in Kettering.

The group which includes 3 members of the BAC are up against 9 other teams. Each team has to perform two dances at Wicksteed Park, Kettering, Northamptonshire on Saturday March 22nd March in front of 5 judges and 1000 members of the general public. As part of the competition the teams also have to fund raise.

The Cell Path team have named themselves "Dolly Mixtures" and are being taught a flamenco and burlesque routine by Anthony Bazin from MaSH School of Dance. The team have been practicing since December, and are currently practising over 10 hours a week in addition to work and other commitments. Two members of the team are also training to take part in Cambridge Marathon 2 weeks before the show!!!

If you would like to support the team please go to:

<http://www.justgiving.com/dolly-mixture>

Information about all the teams participating can be found at:

<https://www.justgiving.com/teams/StrictlyGottoDance>



Team members (left to right)

Lesley Davies

Julie Smith

Laura Saberton

Sarah Black

Sharon Breckin

Steph Potter Nall

Carol Smith

Anthony Bazin in foreground

Jessica Leads (not pictured)

Jane Campbell (not pictured)

The competition takes part in three stages. Competitors are ranked according to judges scores on their performance and also on funds raised both before and on the night. The winners are the team with the highest overall score.

Fundraising events so far include Beauty treatments, Disco, Raffle and bag packing and "wear something red to work for Valentines Day".

Simple cell blocks

Dr Fred Mayall MB, ChB, MD, FRCPath.
Consultant Cellular Pathologist.
Taunton and Somerset NHS Trust.

“Good design is as little design as possible” — Dieter Rams¹.

I have always enjoyed experimenting with technology, with variable results; some glorious failures and occasional successes. One of my software projects was recently awarded a prize by The Secretary of State for Health in the UK. Emboldened by this, and at the request of the editor, I want to tell a story about another of my projects that spans two decades. It concerns the quest for the simple cell block.

There are innumerable methods for making cytology cell blocks that are described in most large cytopathology text books.² Even the simplest of these involve multiple steps, often with centrifugation, washing, resuspension, warming, cooling and a lot of manual handling. In addition they often use non-formalin fixatives, usually alcohol, which would be entirely acceptable if similarly fixed control tissue is used for any subsequent immunohistochemistry or molecular studies. However, the latter safeguard is not practical and is rarely implemented. Instead one usually uses a formalin fixed control and hopes for the best. However, this is being willfully blind to the obvious. Try running IHC for ER, TTF1 and WT1 on appropriate parallel formalin fixed and alcohol fixed tumour samples in your own lab and you will see the problem. Nuclear antibodies seem to fare worst. This issue becomes particularly important when the result of the IHC or molecular investigation is used to determine therapy, for example ER, Her2 and an increasing number of newer markers such as ALK in lung carcinomas.

I trained in the UK but my first consultant job was at Green Lane Hospital in Auckland, New Zealand in 1994. Having perform perhaps 20 fine needle aspirations (FNAs) in my entire career, I found myself travelling around Auckland in a taxi with a mobile phone (my first mobile phone), performing FNAs wherever they were needed, sometimes more than 20 a day. The funding model in New Zealand encouraged rapid diagnosis FNA cytology more than it does in the UK. At the time we used to wash our needles into formalin and then spin this down to make an agar cell block. I noticed that if one expelled the needle's contents on to the underside of a specimen jar lid and left it for a few minutes, it would clot. These clots would tend to get washed off the lid in transit but at least one got bigger fragments of clotted material in the agar cell block. Over time I refined this technique, replacing the formalin liquid in the specimen jar with a plug of formalin soaked tissue paper, and relying on formalin vapor to fix the material on the underside of the lid and form a solid 'limpet' of

material that could then be prised off. This was published in outline in 2003³ and then more fully in 2010⁴. This technique, the "Poor Man's Cell Block", seems to now be quite widely used around the world (Figure 1). It is certainly simple. However, it does rely on the specimen containing plenty of blood or protein to make the material fix into a solid pellet. It does not work well with watery samples such as cystic fluids or serous fluids. It also requires a trained operator to handle the specimen at the time that it is ejected from the needle, and is not really suitable for occasional use by a surgeon or radiologist.

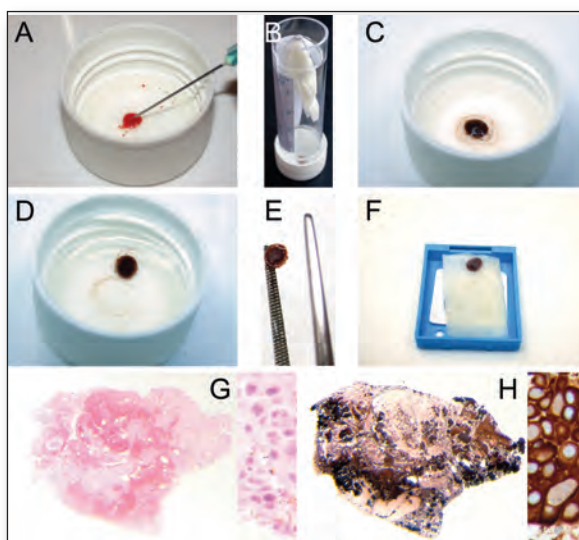


Figure 1. Images demonstrating the main steps in the preparation of a vapour fixed cell block. (A) The fine needle aspiration material is expelled to form a blob. (B) The universal container is left inverted for at least 6 h to allow the material to vapour fix. (C) The material is now solid. (D) The lid is flooded with a small amount of formalin so as to help gently break the "limpet" suction. (E) The solid cell block can be picked up, being careful not to let it dry out. (F) The specimen should be wrapped in tissue paper for processing. (G) H&E section showing the low-power appearances and high-power detail (metastatic breast carcinoma). (H) Low-power appearances and high-power detail of a cytokeratin 7 immunostain showing that the cells are densely distributed in the cell block. Copyright BMJ Publishing Group Ltd, used with permission.

In 2008 I started using gelatin foam to make cell blocks from watery samples. Gelatin foam has been used in medicine and dentistry for at least 80 years for haemostasis and wound dressing. The cell block method was to spin the sample down, decant off the supernatant and then use a crouton of gelatin foam to absorb the

cellular deposit. The crouton was then paraffin processed like a biopsy (Figure 2). This simple method⁵ worked very well and was particularly useful for serous fluids such as peritoneal fluids and pleural fluids. However, the adoption of the method was limited by the practical difficulties related to gelatin foam. I was using Gelfoam® (Pfizer, New York City, USA), that I had acquired with help from my hospital pharmacy, but after the method was published in the *Journal of Clinical Pathology* I started receiving a lot of emails from pathologists in the UK telling me that they could not get a supply. It was not a licensed medical device in the UK and not for sale in the UK, although it could be purchased online from the USA and posted to the UK.

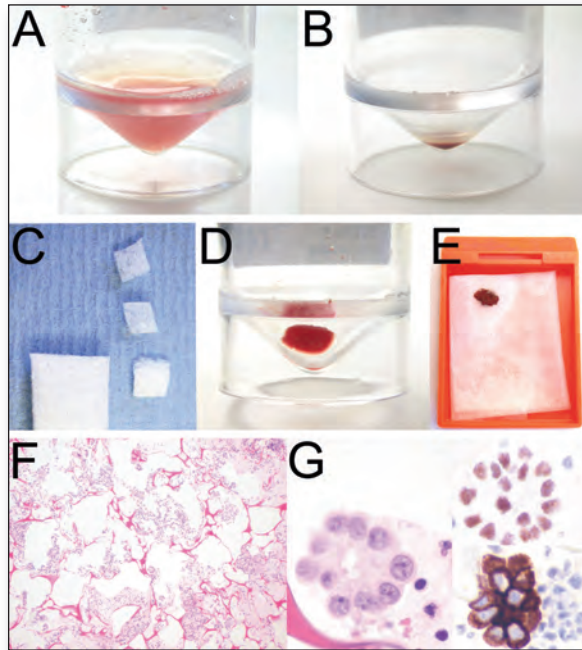


Figure 2. (A) Residual cytology fluid sample after material has been taken for smear preparation. (B) The sample is centrifuged and the supernatant is removed. (C) Small blocks of gelatin foam are cut from a sheet of dressing material. (D) Foam absorbs the fluid to form a solid sample. (E) The solid cell block is wrapped in tissue paper for processing. (F) H&E-stained section; the wall of the gelatin bubbles are deeply eosinophilic. (G) High-power H&E detail, together with TTF1 nuclear staining and CK7 cytoplasmic staining of lung adenocarcinoma cells. Copyright BMJ Publishing Group Ltd, used with permission.

I did find an alternative supply of gelatin foam that was available in the UK; Surgispon™ (Aegis Lifesciences, Gujarat, India). However, there were a myriad of other problems too. Gelfoam® was sold in quite large blocks that were expensive. The user had to cut these blocks down into smaller croutons to be used for cell blocks. The user then had to find a way to keep the croutons clean and dry until they were needed. This was not an insurmountable difficulty for the enthusiast but was a barrier to routine use. I contacted a medical device manufacturer and discussed having them make some cell block sized gelatin foam discs for use in cytology labs, but it soon became apparent that for gelatin foam to be distributed commercially in this new form it would have to undergo certification as a medical device for this particular

use. Also if the device was derived from animal products and was to come into fluid contact with a patient (as in the needle hub application below), then it would be regarded as a Class 3 medical device under the European Medical Device Directive 93/42/EEC. Class 3 medical devices are particularly strictly regulated partly because of the possibility of transmission of prion disease. There are also various religious and cultural issues relating to the mixing of human cells and gelatin, which is derived from cattle and pigs, that are best avoided.

Then started a search for a synthetic material that had properties similar or superior to gelatin foam. Most commonly used synthetic foams, such as polyurethane foam, are not suitable. In order for the cell block material to be successfully paraffin processed and produce high quality sections, it is necessary that the paraffin is able to penetrate not only into the cavities in the cell block material but also into the solid matrix of the walls of the cavities in the cell block material. If this is not achieved, the sections tend to break apart, fracturing at the interface between the wax and non-wax regions. For paraffin processing to cause paraffin wax to penetrate into the solid matrix of the cell block material, it is necessary for water to be present in the solid matrix when processing starts. Thus the material needs to be a “hydrogel”. Processing then replaces the water with ethanol, ethanol with xylene and finally xylene with paraffin wax. In addition, the cell block material should be resistant to the solvents used during paraffin processing, including water, ethanol and xylene, and should have a melting point above about 64 °C. In these ways the cell block material ideally closely resembles the respective properties of the organic tissue in the sample. Furthermore the material should have sufficient strength and rigidity to allow it to be machined into shaped forms and resist deformation and disintegration during processing and sectioning. The material should be “fast wicking”. “Wicking”, in this context, is the hydrophilic property of a material that causes it to draw up water. Finally it should not be soluble in warm water (in the way that gelatin and agar are), as we have learned that this can interfere with DNA extraction and electrophoresis. The latter requirement was something that we were not aware of at the time of development, but was achieved by accident nonetheless. It is also desirable that the material should be translucent or transparent in histological sections, and that it has an established medical use that would make certification more straightforward.

After some consideration we proceeded with poly vinyl alcohol (PVA) foam. This foam has been used for decades as a nasal packing material and also and an intravascular embolic agent. PVA meets all of the desirable criteria set out above. It can be manufactured with a small pore size, around 50 to 100 microns, and, when dry, it is hard and rigid, allowing it to be machined into shapes. The latter property is a notable improvement over gelatin foam.

It was possible to form PVA foam into discs 2 mm thick and either 6 mm or 16 mm in diameter that performed the same function as gelatin foam. These could be used to make cell blocks from serous fluids and other watery samples.

It was also possible to machine this foam into a narrow core, 2.5 mm in diameter and 18 mm length, that could be incorporated into a plastic housing with a male Luer-Slip® taper connection at one end to connect to the needle hub and similar female connection at the other end for the syringe. The device then allows cell blocks to be made as the FNA sample is being taken by absorbing the material as it enters the needle's hub. The material in the hub of an FNA needle is often wasted during conventional FNAs as it is difficult to eject on to a slide. We have now been using this type of foam core device for hundreds of samples.

This method of collection of an FNA sample has some notable features. The foam acts as a partial graduated filter so that the largest fragments of material come to rest closest to the needle hub end, while smaller particles penetrate further before being trapped. Blood and fluid passes through the foam with ease. This property is useful when aspirating cyst fluids. Another notable feature is that the core can retain a record of the way that the character of the sample fluid evolved during sampling. The standard method of collecting an FNA sample causes all of the material that is collected at various stages of the procedure to be blended together; a high quality diagnostic sample might be obtained early in the procedure, but as sampling progresses the sample becomes increasingly contaminated with haemorrhage. An example of this would be the aspiration of a colloid cyst of thyroid; early on in the procedure clear golden colloid fluid is obtained, but later the fluid becomes haemorrhagic. Using the standard method, the haemorrhage will be blended through the entire sample by the time it is examined, giving the misleading impression that the entire sample was haemorrhagic. However, when using the device the sample can be retained in the cell block material in the order in which it was obtained, with the early sample being most distant from the needle hub and the late sample being closest.

The PVA disc and in-hub core device are available as CytoFoam® Disc and CytoFoam® Core (Exmoor Innovations Ltd, Taunton, UK).

In a highly specialist area like diagnostic cytology there is limited commercial interest in innovation, because the potential market is small. Consequently, some of the best ideas will be to “home grown” by cytopathology professionals who have the knowledge and motivation to improve their techniques. The best innovations are often simple. There must be some other simple ideas in the minds of cytology professionals that could flourish into something worthwhile.

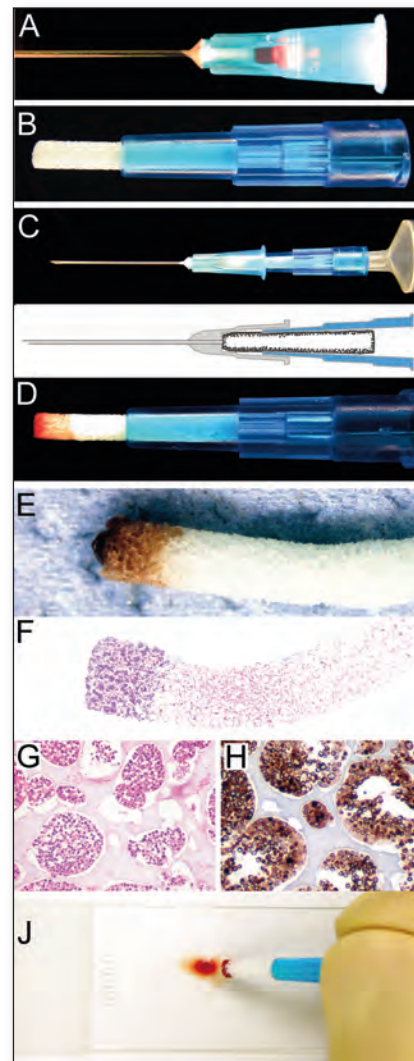


Figure 3. (A) Residual fine needle aspiration cytology material is often left in the hub of the needle after the specimen has been ejected. (B) The foam residue device consists of a core of polyvinyl alcohol foam housed in a Luer type plastic adapter. (C) The device attaches to a needle and syringe. (D) The sample is absorbed into the tip of the foam core. (E) After formalin fixation the core is removed from the adapter, paraffin processed and sectioned (F) in the usual way. (G) Adenocarcinoma cells within the polyvinyl alcohol foam. (H) Adenocarcinoma cells immunostained for cytokeratin 7. (J) The tip of the foam core can also be used to collect material from the surface of a slide. Copyright BMJ Publishing Group Ltd, used with permission.

References

1. Dieter Rams: As Little Design As Possible, S. Lovell, Phaidon Press Limited, 2010, ISBN-13: 9780714849188.
2. Koss' diagnostic cytology and its histopathologic bases, Volume 2, Leopold G. Koss, Lippincott Williams & Wilkins, 2005, 1590-1592, ISBN/ISSN: 9780781719285.
3. Mayall F, Darlington A, Harrison B. Fine needle aspiration cytology in the diagnosis of uncommon types of lymphoma. *J Clin Pathol* 2003;**56**:11 821–825 doi:10.1136/jcp.56.11.821.
4. Mayall F, Darlington A. The poor man's cell block. *J Clin Pathol* 2010;**63**:9 837–838 Published Online First: 29 July 2010 doi:10.1136/jcp.2010.078410.
5. Mayall FG, Wood I. Gelatin foam cell blocks made from cytology fluid specimens. *J Clin Pathol* 2011;**64**:9 818–819 Published Online First: 2 February 2011 doi:10.1136/jcp.2010.088542.
6. Mayall FG. An FNA cytology foam core device for making cell blocks. *J Clin Pathol* doi:10.1136/jclinpath-2012-200858.

Student projects 2014

Lisa Shepherd, Jamie Old, Ronaldo Filho and Duncan Inwood

We are final year undergraduate Biomedical Science students undertaking cytology-related research projects at Cardiff Metropolitan University. Below is a summary of the work we have done so far.

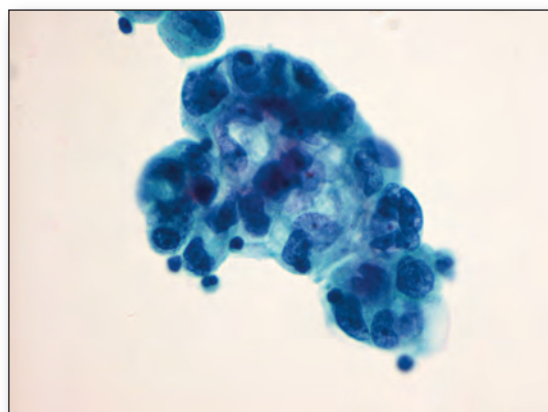
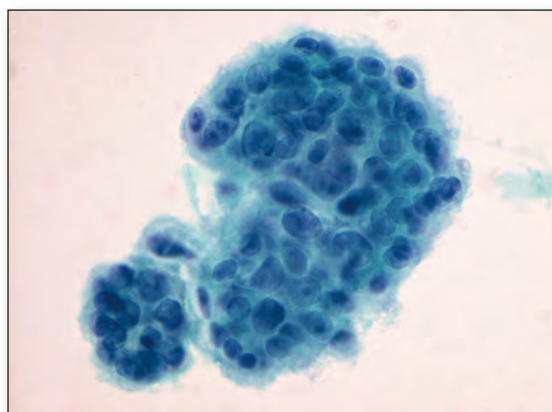
Using image analysis to help diagnose malignant mesothelioma

Lisa Shepherd

Mesothelioma is a highly malignant form of cancer which primarily affects the respiratory tract. This cancer is restricted to the cells that line the pleural, peritoneal and pericardial cavities. My research project focused mainly on pleural mesothelioma. The main cause of the disease is inhalation of asbestos dust, which can still be found in old buildings due to its insulating and lightweight properties. Mesothelioma is considered to be an occupational risk in various industries involving asbestos exposure.

Due to the cytological similarity of mesothelioma and metastatic adenocarcinoma in pleural effusions (see figure), there are numerous problems associated with its

differential diagnosis. This research project involved digital image analysis of cytological images of histologically confirmed cases of mesothelioma and adenocarcinoma. The aim was to determine whether the two types of malignancy can be discriminated on the basis of various parameters such as cell shape, area, lacunarity and staining intensity. My hypothesis is that there is a statistically significant difference between specific cell features of mesothelioma and adenocarcinoma. Data analysis is not yet complete but will help to determine whether there is a place for image analysis in the clinical laboratory to aid in the cytological diagnosis of malignant mesothelioma.



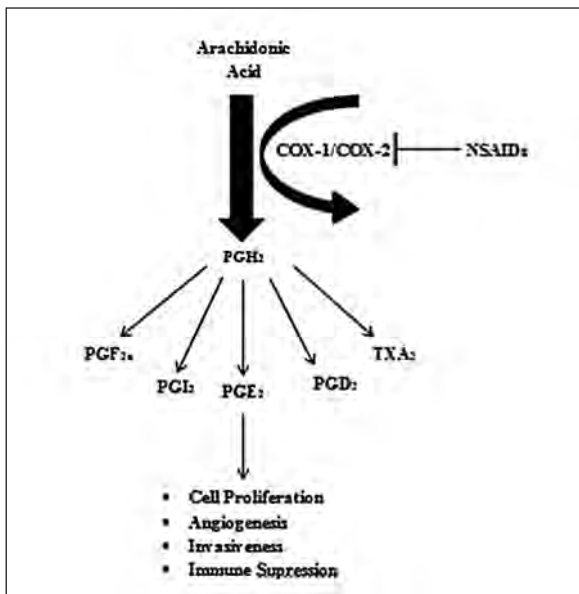
Mesothelioma (left) and adenocarcinoma (right). Can image analysis help?

Aspirin and cervical cancer

Jamie Old and Ronaldo Filho

The undoubted success of cytology-based screening programmes has not deterred continued research into alternative methods of preventing cervical cancer, which continues to claim over 270,000 lives each year around the globe. For years research has demonstrated the link between aspirin use and a reduced risk in colorectal cancer. However, any beneficial effect of aspirin in relation to cervical cancer is yet to be demonstrated. We investigated the effects of aspirin on two proteins involved in the apoptotic pathway and cancer progression; cyclooxygenase-2 (COX-2) and p53.

COX-2 is an enzyme responsible for catalysing the formation of prostaglandin H_2 (PGH₂) from arachidonic acid. PGH₂ is the precursor to four further prostaglandins; prostaglandin E₂ (PGE₂), prostaglandin D₂ (PGD₂), prostaglandin F_{2α} (PGF_{2α}), prostaglandin I₂ (PGI₂) and thromboxane A₂ (TXA₂). PGE₂ derived from COX-2 has been shown to play a key role in tumour progression by initiating intracellular pathways leading to cell proliferation, angiogenesis, invasiveness and suppression of the immune system (see figure).



Aspirin and other NSAIDs exert their anticancer effect partly by inhibiting COX enzymes

P53 is a tumour suppressor protein which has been linked to 50% of human cancers, and regulates genes involved in growth arrest. P53 protein levels are normally quite low in unstressed cells, but can increase in response to toxins, mechanical damage and other adverse cellular events. High levels of p53 protein are known to induce apoptosis in cultured cervical cancer cells, such as HeLa and HT3 cells.

Non-steroidal anti-inflammatory drugs, such as aspirin, exert their effects by inhibiting COX-2 production and also by the upregulating p53. These mechanisms contribute to aspirin's anti-cancer properties, making this readily available and inexpensive drug an appealing candidate for the primary prevention and as an adjuvant for treating cervical cancer. As a step towards determining aspirin's potential, we incubated HeLa and HT3 cells with various concentrations of aspirin and its metabolite salicylic acid and determined the effects these have on COX-2 and p53 gene expression. After 16 hours incubation, we extracted RNA from the cells and converted this to complementary DNA. Finally, polymerase chain reaction (PCR) was undertaken using p53 and COX-2 primers. Gene expression was visualised using DNA gel electrophoresis.

As expected, we demonstrated overexpression of the p53 gene at all but the lowest concentrations of aspirin, indicating that the drug is detrimental to the survival of cervical cancer cells. Counterintuitively, aspirin failed to reduce COX-2 gene expression, which would favour the survival of cervical cancer cells. We should emphasise that these changes in gene expression do not necessarily result in altered levels of functional p53 and COX-2 protein. To further elucidate the mechanisms underlying the effect of aspirin on cervical cancer cells, future studies should evaluate p53 and COX-2 gene expression and protein levels simultaneously.

Image analysis for detecting dyskaryosis

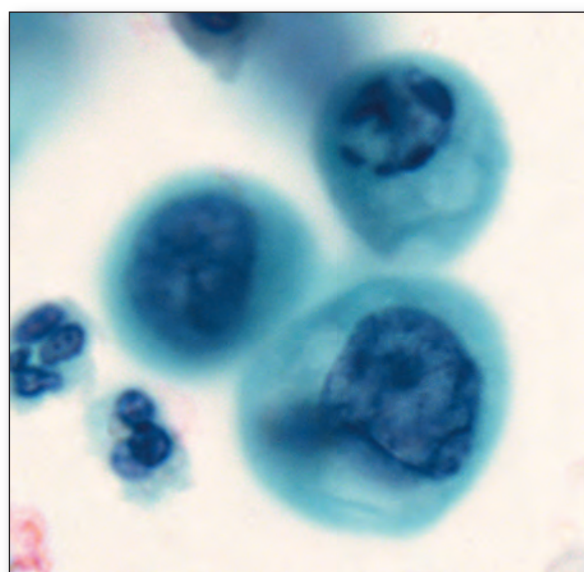
Duncan Inwood

Cervical cancer is a preventable disease, and with the use of successful cytology screening programmes there has been a significant decrease in both mortality and morbidity. Current methods of cervical screening require the visual skills of experienced cytologists. The process is monotonous and requires long periods of intense concentration. As such, there is an increased susceptibility to screening error, which can be detrimental to the health of women who participate in screening.

A possible solution to this problem is the implementation of computer assisted screening (CAS) technologies. The use of computer vision algorithms potentially provides a platform for detecting cellular abnormalities automatically and without the frailties associated with human vision. Although CAS systems exist, they are not currently considered appropriate for use in the NHSCSP. In cervical cytology, nucleocytoplasmic (NC) ratio is one of the determining factors used in the detection of dyskaryosis. My research is based on exploring alternatives to NC ratio for distinguishing normal and neoplastic cells.

An open source java based image processing program, ImageJ, was used to analyse a total of 700 images of normal

and dyskaryotic cervical epithelial cells. Data collected from these images included NC ratio, cell area, area of nucleus, and the fractal dimension of nuclear chromatin. The data collected from the cell images will provide an insight into the value of novel parameters for incorporation into CAS systems.



Chromatin analysis. Can fractal geometry help?

Spring will be late this year!

The traditional Spring Tutorial will this year be a Summer Tutorial, to be held on Friday 11th July 2014 at the Hodgkin Building, King's College, Guy's Hospital, London SE1 1UL

Presentations from eminent speakers will be on:

Cytology and Carcinoma of Unknown Primary (CUP) — Anna Green, London
EUS FNA Pancreas — Darshana Jhala, Philadelphia
FNA liver, kidney and adrenal — Nirag Jhala, Philadelphia

Microscopy workshops will be on:

Urinary tract cytology — Darshana Jhala
Serous effusions — Mufaddal Moonim, London
FNA pancreas — Darshana Jhala
FNA liver, kidney and adrenal — Nirag Jhala



The BAC is grateful to Dr Ashish Chandra for putting together such an interesting programme for the tutorial, which is sure to be popular. Places will be allocated on a 'first come, first served' basis and as last years' tutorial was a sell out early booking is definitely recommended!

The full programme and registration details can be found on the BAC website <http://www.britishcytology.org.uk>

Scottish Cytology Training School

Programme 2014/15

No course fee is charged for Gynae cytology courses to employees of Scottish NHS Trusts

Training School Director

Dr Edward Duvall
Tel: 0131 242 27123
Email: Edward.Duvall@luht.scot.nhs.uk

Training School Manager

Sue Mehew
Tel: 0131 242 7149
Email: Sue.mehew@luht.scot.nhs.uk

*Application forms available on request
from:*

Mrs Linda A Cooper
Training School Administrator
Pathology Department
Royal Infirmary of Edinburgh
51 Little France Crescent
Edinburgh
EH16 4SA
(Available mornings Mon-Thurs)

Tel: 0131 242 7135
Fax: 0131 242 7169
Email: Linda.Cooper@luht.scot.nhs.uk

NHSCSP Accredited Training Centre

Courses held at Royal Infirmary of Edinburgh
unless states (SGH) Southern General
Hospital Glasgow.



Introductory Course

8th Sept – 3rd Oct 2014
£1000

23rd February – 22nd March 2015
£1000

Introductory Course Part 2 tbc

10th November – 14th November 2014

Update Course

23rd – 24th April 2014
11th – 12th June 2014 (SGH)
4th – 5th November 2014 (SGH)
3rd – 4th December 2014
3rd – 4th February 2015

£100 per day

Pre-Exam Course

19th – 21st Aug 2014 (for Oct Exam)
£250

Workshops

21st Nov 2014 – Medical Staff tbc
£100

Non-Gynae Course for Trainee Medical (ST3) & BMS staff

4th – 6th March tbc 2014
23rd – 26th September 2014

£100 per day

Course for Colposcopists

January 2015 tbc

*Non-NHS Labs – price on application
All courses are in Liquid Based Cytology (Thin Prep)
Courses are CPD accredited*

2014 Course Schedule

Date	Gynae Courses	Fee*
29 Sept-24 Oct	Introductory in Gynae Cytology	NHS £1000 Other £1200
TBC	Prep for C&G Diploma in Cervical Cytology	NHS £250 Other £300
17-19 June 9-11 September 2-4 December	Update in Cervical Cytology for Technical Staff	NHS £300 Other £350
11 November	Update for Cytology Checkers	£100
20 May	Update in Cervical Cytology for Pathologists & Consultant BMS's & Holders of the Advanced Specialist Diploma in Cervical Cytology	£100
21 May	Gynae Histology for Technical Staff	£100
23-25 June	Gynae for Trainee Pathologists	£300
28-29 April	Gynae Pathology for Trainee Colposcopists	£200
12-13 May 15-16 September	Cervical Sample Taker Training	£250
26 June 19 November	½ Day Update in Cervical Screening	

Date	Non-Gynae Courses	Fee*
30 April	Serous Fluid Cytology	£100
3 June	Respiratory Cytology	£100
12 November	FNA Cytology	£100
25 November	Urinary Tract Cytology	£100
1-4 July	Non-Gynae for Trainee Pathologists	£400

For further course details & application form please visit our website: www.cythology-training.co.uk

Department of Cellular Pathology
Lime Walk Building
Southmead Hospital
Bristol BS10 5NB
Tel: 0117 323 5649
Fax: 0117 323 5640
Email: SWRCTC@nbt.nhs.uk

Dr P Tidbury
Director
Mrs Helen Burrell
Manager

Mrs Helen Hoskins
Deputy Manager
Mrs Louise Storie
Course Administrator

BIRMINGHAM CYTOLOGY TRAINING CENTRE

All BCTC courses are provided in **SurePath and/or ThinPrep LBC**

INTRODUCTORY COURSES FOR CITY & GUILDS DIPLOMA IN CERVICAL CYTOLOGY

3-14 March 2014 & 24 March—4 April 2014

This course provides students with a theoretical and practical introduction to cervical cytology. A five-day Follow-on Course is offered free of charge to all those attending our Introductory Course.

FOLLOW-ON COURSES FOR CITY & GUILDS DIPLOMA IN CERVICAL CYTOLOGY

12-16 January 2015

The aims of this course are to revise the topics taught on the Introductory Course, consolidate skills and identify problem areas

PRE-EXAMINATION COURSES FOR THE CITY & GUILDS DIPLOMA IN CERVICAL CYTOLOGY

27-29 August 2014

A 3-day course for those preparing to take the City and Guilds Diploma in Cervical Cytology

UPDATE COURSES IN GYNAECOLOGICAL CYTOLOGY (ThinPrep & SurePath)

18 March 2014 (Checkers' Update) 29 April 2014 (Metaplasia/Hormonal effects)
19 May 2014 (Pitfalls in Squamous Reporting) 5 June 2014 (Pitfalls in Glandular Reporting)
11 July 2014 (topic tbc) 2 October 2014 (topic tbc) 26 November 2014 (topic tbc)

NON-GYNAECOLOGICAL CYTOLOGY FOR TECHNICAL STAFF

10-11 April 2014

Ideal for those completing their portfolio for the Specialist Diploma

WEST MIDLANDS AUTOPSY PATHOLOGY COURSE

1-2 October 2014

For trainees in preparation for the Autopsy element of the FRCPath exam and Consultant Pathologists involved in coronial / procurator fiscal work as an update for annual appraisal and revalidation.

BIRMINGHAM HISTOPATHOLOGY COURSE

16-27 June 2014

The programme provides topic based lectures on systemic pathology, slide review of selected cases followed by discussion and a revision session including mock exam in preparation for the FRCPath Part 2 exam.

GYNAECOLOGICAL CYTOLOGY FOR TRAINEE PATHOLOGISTS (StRS)

8-9 September 2014

The programme for this course is a combination of lectures workshops and multiheader sessions. This course includes a mock exam and is particularly suitable as revision for the FRCPath Part 2 exam

NON-GYNAECOLOGICAL CYTOLOGY FOR TRAINEE PATHOLOGISTS (StRS)

2-5 September 2014

The programme for this course is comprehensive and includes the salient aspects of diagnostic non-gynaecological cytology. This course includes a mock exam and is particularly suitable as revision for the FRCPath Part 2 exam

INTRODUCTORY COURSE FOR ST1s

1-5 December 2014

Gynaecological and Non-Gynaecological Cytology including Autopsy element

LBC Conversion Courses, Ad hoc workshops and Off Site workshops can be arranged on request—please contact BCTC

Please see our website for further details and for reservations please contact Louise Bradley or Amanda Lugg

Birmingham Cytology Training Centre

Birmingham Women's Hospital

Birmingham B15 2TG

Phone: 0121 627 2721

Fax: 0121 627 2624

Email: Louise.Bradley@bwhct.nhs.uk or Amanda.Lugg@bwhct.nhs.uk

Website: <http://www.bwhct.nhs.uk/cytology-training-centre>



Directorate of Laboratory Medicine

Central Manchester University Hospitals **NHS**

NHS Foundation Trust

THE NORTH WEST CYTOLOGY TRAINING CENTRE COURSES 2014

Bespoke training available on request

Please contact the Centre with your requirements



Head and Neck Adequacy Assessment for BMS staff

11th March 2014

Course fee: £100 / £80 for NW regional staff

Beginners Non - Gynae (BMS staff)

Thyroid – 18th March
Serous Fluids – 13th May
Respiratory – 14th May

Course fees:
see website for details

LBC Update Course in Gynae Cytology for BMSs/Cytoscreeners (SurePath)*

£100 per day

Topic A – Borderline
Topic B – Atrophy
Topic C – Pitfalls and lookalikes

February	June
25 th (Topic C)	3 rd (Topic C)
26 th (Topic A)	4 th (Topic A)
27 th (Topic B)	5 th (Topic B)

September
29th (Topic C), 30th (Topic B), 1st Oct (Topic A)

Pre-Examination Course for the C&G Diploma in Cervical Cytology (Surepath)*

Bespoke training on request

FRCPath COURSES 2014

Non Gynaecological Cytology Revision Course

February 3rd – 7th

August 18th – 22nd

FRCPath Pre – Exam course

March 3rd – 7th

September 15th – 19th

20% discount for regional trainees

Non-Gynae Master Classes for Medical Staff

EBUS (6 RCPATH CPD credits)

11th November 2014
(note change of date)

Course fee: £150 / £120 for NW staff

Introductory Course for C&G Diploma in Cervical Cytology*

21st July – 15th August 2014

Fee £1000

Primary Care ½ day Update Event

17th January
13th February

Further dates to be arranged by popular demand

Fee £30

Gynae Master Classes*

Courses tackling difficult areas aimed at Medical, BMS Consultant and experienced staff wishing to challenge their knowledge.

Check our website for upcoming dates

***Mandatory Courses Are Free Of Charge to North West Region Technical Staff.**

Please note that all gynae courses are based on Surepath morphology

Novice Sample Taker Training

2014 Dates to be announced

Director

Dr. Miles Holbrook
Clinical Lead for Cervical Cytology
0161 276 6727
Email: miles.holbrook@cmft.nhs.uk

Manager:

Mrs Jenny Davies
Tel: 0161 276 5114
Email:
jenny.davies@cmft.nhs.uk

Administrator:

Miss Jen Bradburn
0161 276 8804
Email:
jennifer.bradburn@cmft.nhs.uk



Training Centre Manager:

Mr N Dudding

0114 226 8691

Nick.dudding@sth.nhs.uk

Website: www.cytologytraining.co.uk

Administration:

Mrs K Hawke

0113 246 6330

Kathryn.hawke@nhs.net

One-Day Update Courses in Cervical Cytology for Consultant Medical Staff

These one-day courses are limited to Consultant Medical Staff. This year we will concentrate on cases identified through the NHSCSP cancer audit and recent developments regarding the introduction of HPV testing including the progress of HPV primary screening.

20th May 2014

Course Fee*: £95

Call Recall, Failsafe and the Impact of ABC 3, HPV testing and NHS re-organisation on the NHSCSP

A broad, one day course that should be of value to anyone who is involved in Call Recall, the failsafe process and anyone needing a broader understanding of these functions within the NHSCSP. It would be of particular value to those new to the screening programme, but also useful to those individuals involved in call / recall & failsafe process and who do not normally have access to other forms of update training.

9th October 2014

Course Fee*: £95

One-Day Course for Hospital Based Programme Coordinators

This one-day course is aimed at all Hospital Based Programme Coordinators (HBPCs). It would be particularly suitable to anyone new to post but should also appeal to those who have been in post for many years as an update and an opportunity to network with fellow HBPCs.

14th July 2014

Course Fee*: £120

One-Day Update specifically for Checkers & Experienced BMS Staff

A One-day course aimed specifically at those intending to, or already acting as Checkers. Includes a session on basic histopathology, new NHSCSP evaluation criteria and microscopy sessions on what can be called negative and what can't!

8th July 2014

Course Fee*: £120

Three-Day Update Course for AP/Consultant BMSs

Includes sessions on cervical histopathology, recent developments in colposcopy, HPV triage and test of cure and a whole session on the NHSCSP cancer audit.

Suitable for Thinprep[®] or Surepath[™] users

9th – 11th September 2014

Course Fee* : £230

**Participants from the North East, Yorkshire and East Midlands will incur £15 administration fee per day on all courses above except those marked * where full fee applies. All prices are subject to change. Further information and application forms are available from our Administration Team: Kathryn.hawke@nhs.net.*



2014 COURSES

All course information and online booking form can be found on our website
www.lrctc.org.uk

Pre-Registration Gynaecological Courses

INTRODUCTORY COURSE IN GYNAECOLOGICAL CYTOLOGY (Thinprep®)

- 3rd – 28th February
- 6th – 31st October

Course fee:

- Contracted London regional students: No charge
- All other students: £1100

FOLLOW UP COURSE (Thinprep®)

- 31st March – 4th April
- 28th July – 1st August

Course fee:

- Those who attended the Introductory Course at LRCTC: No charge
- Other participants: £400

PRE – EXAM COURSE (Thinprep®)

- 6th – 10th January
- 1st – 5th September

Course fee:

- Contracted London regional students: Free
- Non-Contracted students: £400

Medical Practitioners Courses

PATHOLOGISTS COURSE – GYNAE

This two day course covers gynaecological cytology.

- 5th – 6th + 7th (Optional Mock Exam) **March**

Course fee: - £200 Mock exam - +£50

PATHOLOGISTS COURSE – NON GYNAE

This four day course covers non-gynaecological cytology.

- 10th – 13th + 14th (Optional Mock Exam) **March**
- 15th – 18th + 19th (Optional Mock Exam) **September**

Course fee: - £ 400 Mock exam - +£50

Please indicate on the online booking form if you wish to attend the mock exam.

MEDICS 1-DAY UPDATE COURSE

A refresher course for consultant pathologists/APs

- 23rd May
- 26th September
- 20th November

Course fee

- Contracted London regional participants: Free
- Non-Contracted participants: £150

Post Registration Courses

BMS/CYTOSCREENER UPDATE COURSE

- 14th – 16th January
- 18th – 20th March
- 15th – 17th April
- 20th – 22nd May
- 9th – 11th June
- 22nd – 24th September
- 25th – 27th November
- 10th – 12th December

Course fee:

- Contracted London regional participants: Free
- Non-Contracted participants: £350

Introductory Non-Gynae Courses

RESPIRATORY CYTOLOGY COURSE

- 16th – 17th June

SEROUS FLUID CYTOLOGY COURSE

- 11th – 12th September

URINE CYTOLOGY COURSE

- 17th – 18th November

Course Fees

- Contracted London regional participants: Free
- Non-Contracted participants: £200

Medical Laboratory Aides (MLAs) Courses

INTRODUCTORY MLA COURSE

This is an Introductory course designed to cover topics such as overview of the NHSCSP, terminology, role of an MLA and audit.

- 24th April
- 19th November

Course Fee

- Contracted London regional participants: Free
- Non-Contracted participants: £150

Book online at www.lrctc.org.uk

All courses above are CME, IBMS CPD and NAC CEC accredited.

Further details/information can be obtained by contacting 0208 869 5270 or emailing nwlh-tr.lrctcbooking@nhs.net or by visiting our website.

The BAC is pleased to announce further details of the

**2014 Scientific Conference, AGM and Trade Exhibition
9 – 11th October 2014
Crowne Plaza hotel, Birmingham city centre**

Suitable for Pathologists, Biomedical Scientists and Cytoscreeners of all levels of experience, the scientific programme will provide a mix of both gynaecological and diagnostic cytology, with topics including:

Various aspects of HPV	Anal screening
Use of P16	Lymph node
Small cell ca of cervix	Respiratory / molecular
Medico-legal issues	BMS histopathology reporting

**Confirmed overseas speakers include Professor Marshall Austin (USA)
and Dr Christine Bergeron (France)**

The Erica Wachtel memorial lecture will be delivered by Dr Christine Waddell

Proffered papers and posters are requested and there will be a cash prize for the best overall presentation – see the BAC website for full details. All proffered paper and poster presenters will receive a voucher for a discount off the registration fee for a future BAC scientific meeting, funded by the BAC educational bursary fund.

The social programme will commence on the evening of Thursday 9th October with a drinks and canapé reception for the opening of the Trade Exhibition by Mr Dennis Williams.

The conference dinner at the Crowne Plaza on Friday 10th October will be followed by after dinner entertainment and a disco.

Registration fees have been held at very competitive rates for both the full package and day delegate rates. The full package does not include accommodation but this is available at the Crowne Plaza or one of the many other nearby city centre hotels.

For the full programme and booking details please see the BAC website
<http://www.britishcytology.org.uk/>

A discount for early booking applies until April 30th so don't delay and register today!

STOP PRESS

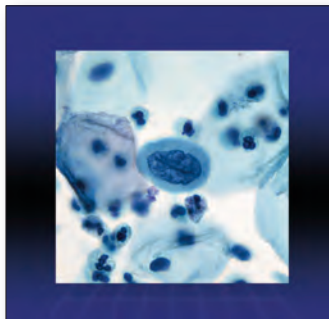
The BAC is delighted to announce that it will be hosting the participant feedback sessions for both the Interpretative Non-Gynae EQA (Chaired by Dr Sally Hales) and the Non-Gynae Technical EQA schemes (run by UK NEQAS CPT) on the afternoon of Thursday 9th October at the Crowne Plaza, prior to the main conference. Details of both meetings will be circulated by the respective scheme organisers. Delegates attending either of these meetings will be welcome to register for the full conference.

SCAN is published by the British Association for Cytopathology (BAC) in England and produced by the Medical Informatics Unit, NDCLS, University of Oxford.

©BAC MMXIV No part of this publication may be reproduced in any form without the prior permission in writing of the Editor. Editorial prerogative to shorten or amend material may be exercised where necessary. The Editor and the Executive Committee do not accept responsibility for opinions expressed by contributors or correspondents.

Material for publication should be sent direct to the Editor; all other correspondence with the Association should be addressed to the Secretary.

Cover Image: One of 60 test images presented to naïve observers in a study by Evered et al (2013). Remarkably, participants performed significantly better than chance with no prior training, suggesting the existence of implicit pattern recognition skills.



CONTENTS

Vol 25 No 1 2014

EDITORIAL <i>Andrew Evered</i>	1
CHAIRMAN'S REPORT <i>Allan Wilson</i>	2
REPORT FROM BAC ANNUAL SCIENTIFIC MEETING 2013 <i>Marlene Quintal</i>	3
POSTER PRESENTATIONS FROM THE BAC ASM, OCTOBER 2013 <i>Various</i>	4
CAN HPV PRIMARY SCREENING REDUCE CERVICAL CANCER INCIDENCE AND MORTALITY? <i>R. Marshall Austin</i>	7
NON-GYNAECOLOGICAL CYTOLOGY SURVEY — CAN YOU HELP? <i>Hedley Glencross</i>	8
CHARITY FUNDRAISER <i>Rhona Currie</i>	9
SUB SAHARAN CYTOLOGY <i>Nick Dudding</i>	10
LOCAL OFFICERS	12
CEC NEWS <i>Jenny Davies</i>	13
CEC JOURNAL BASED LEARNING	14
LEARNING HOW TO SPOT A CANCER CELL <i>Andrew Evered, Darren Walker, Andrew Watt and Nick Perham</i>	16
UPDATE ON MODERNISING SCIENTIFIC CAREERS (MSC) <i>Allan Wilson</i>	19
MORE FUNDRAISING	20
SIMPLE CELL BLOCKS <i>Fred Mayall</i>	21
STUDENT PROJECTS 2014: USING IMAGE ANALYSIS TO HELP DIAGNOSE MALIGNANT MESOTHELIOMA <i>Lisa Shepherd</i>	24
ASPIRIN AND CERVICAL CANCER <i>Jamie Old and Ronaldo Filho</i>	
IMAGE ANALYSIS FOR DETECTING DYSKARYOSIS <i>Duncan Inwood</i>	
BAC EDUCATIONAL EVENTS IN 2014	26