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Editorial Cytology interpretation bias in the era of HPV primary cervical screening

Andrew Evered

Interpreting cervical cytology slides from samples that test positive for high risk HPV is likely to become routine practice in the near future. Two factors could affect the predictive value of cervical cytology in this scenario. The first is the higher prevalence of cervical abnormalities in the population who test positive for HPV compared to the adult female population as a whole. The increased frequency of exposure of cytologists to dyskaryosis will be welcomed in terms of alleviating the drudgery of screening a low prevalence population; the sensitivity of cervical cytology might even increase. There is a dark side to this so-called 'prevalence effect' however. In vision science the prevalence effect describes a cognitive bias in which observers are more likely to report the presence of a target when it is encountered frequently, even when the target is not there! In short, high prevalence conditions tend to increase the false positive rate. That cytologists are susceptible to the biasing effects of target prevalence was demonstrated in a neat experiment several years ago.¹ So HPV primary screening will be a double edged sword for cervical cytology; the possible improvement in sensitivity may come at the cost of a decrease in specificity.

Cognitively speaking there is a second profound threat to the sustainability of cervical cytology as we move into the era of HPV primary screening. *Confirmation bias* describes the natural human tendency to seek out evidence that confirms our implicit biases rather than seeking disconfirming evidence. Translating this into cytological language, I predict that the mere knowledge of a positive HPV test result could be sufficient to instil in cytologists an urge to report equivocal cases as positive, thus risking further loss of specificity.

To summarise, the introduction of primary HPV screening will have the twin effect of increasing the prevalence of dyskaryosis in the population of women who are subjected to cervical cytology, while providing cytologists with a priori knowledge of the HPV status of screened women. This may result in a systematic shift in cytology interpretation thresholds such that the sensitivity for detecting cervical abnormalities increases while the specificity and positive predictive value of cervical cytology declines. The predicted increase in the frequency of overdiagnosis and its negative effects on women who participate in screening should not be ignored. We should not sit back and let this happen. I am hoping to conduct research in this area in the very near future, with a view to testing novel debiasing strategies that might help cytologists to overcome, or at least reduce, their vulnerability to reporting biases should HPV primary screening become a reality.

Andrew

¹ Evans KK, Tambouret RH, Evered A *et al*. Prevalence of Abnormalities Influences Cytologists' Error Rates in Screening for Cervical Cancer. *Arch Pathol Lab Med* 2011;135(12):1557–1560.

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INFORMATION FOR CONTRIBUTORS

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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

BAC British Association for Cytopathology



President's piece

Allan Wilson



"Learn everything you can, anytime you can, from anyone you can, there will always come a time when you will be grateful you did." Sarah Caldwell

Due to other apparently more important national issues, the news that NHS Lanarkshire has merged two cellular pathology labs to create a single lab has not made it into the national media, perhaps unsurprisingly. I am fortunate that despite my almost 40 yrs experience in cytology (I started very young...); this is the first merger of this scale that I have been involved in. I am fully aware that mergers have sadly become "the norm" in cytology over the last 5–10 years and collateral damage from the move to larger and larger departments is the loss of staff and the establishment of labs whose workload has required considerable "re-engineering" to cope with workloads that until recently have been foreign to the UK.

The lab merger in my own patch highlighted to me the importance of training for all staff in new equipment and procedures. It also made me think about training for the cervical screening programme of the future. The quote above could never be more applicable to cytology staff. The changes we are facing are undoubtedly challenging but do offer an opportunity to train in areas that offer additional broader skills that will increase career options. The potential of HPV testing has forced us to look outside our traditional boundaries to new areas such as molecular pathology which is fast becoming core to most laboratory disciplines, particularly microbiology.

Congratulations to John Crossley who is the new Chair of the IBMS/RCPath cytopathology conjoint board (CJB). John has worked tirelessly in the background to ensure the success of the CJB and the examinations managed by the board. This board manages the IBMS cytology exams, which include the Advanced Specialist Diplomas (ASD) in gynaecological and non-gynaecological cytology and the Diploma of Expert Practice (DEP) in non-gynaecological cytology. As I have mentioned in previous editions of SCAN, the interest in the non-gynae exam has greatly increased over the last year and there are now 17 candidates for the DEP exam and three for the ASD in non-gynae. However, there are only two candidates for the ASD in gynae cytology. The deadline for applications passed in February for the June exam but I hope this is only the start of a steady increase in candidate numbers for the non-gynae exams. The extended roles now available to biomedical scientists in non-gynae cytology makes the DEP an attractive option for all biomedical scientists working in cytology. This should also provide an opportunity for the training centres to diversify further into non-gynae cytology to meet the growing demand.

On the subject of advanced roles for biomedical scientists, there are now a handful of biomedical scientists who have been awarded the Certificate of Equivalence by

the Academy for Healthcare Science (AHCS) upon successful completion of an assessment process against outcomes of the Modernising Scientific Careers Scientist Training Programme (STP). In slightly plainer English this allows biomedical scientists to be registered with HCPC as clinical scientists. At the moment it is not clear what advantage this confers on those who hold the Certificate of Equivalence. The process is onerous and time consuming and largely done in the applicants own time and at best can be seen as an "insurance policy" in the face of the career changing issues that have been discussed in previous editions of SCAN. One thing is certain about the equivalence process; the requirements are broad; practice in cervical cytology alone will not evidence the STP outcomes. This represents another driver for non-gynae cytology training and practice.

Due to the uncertainty around the future of cervical cytology, recruitment of new staff has virtually ceased in many areas. This has impacted on the Cytology Training Centres and some centres have not delivered introductory courses for several years. I must admit I was in the camp that suggested that recruitment was unfair to new employees in an uncertain world. On reflection, I think I got this wrong, we need to start recruitment and training again but we need to think carefully about what we are training new staff to do and ensure they are skilled for the world I described above. Non-gynae cytology must be core to training new and existing staff.

It may seem to many like turkeys voting for Christmas if we appear enthusiastic for the move to "HPV first" (i.e. primary cervical screening by HPV testing), but the service is currently so stressed that the recent announcement by the UK National Screening Committee did not go far enough — we need a timeframe for implementation. The longer the delay in providing a clear plan to introduce HPV primary screening the greater the risk to service delivery and to the women who participate in the screening programme.

The move to HPV first brings another challenge to the cytology community. The total cost of cytology contracts has been relatively "small beer" compared to the other laboratory disciplines. Even the move to LBC did not bring cytology into the same league as blood sciences. The move to HPV first will for the first time involve senior staff in cytology labs in decision-making in multi-million pound contracts. This brings challenges and pressures; commercial pressures will be intense but it is vital to the success of the screening programme that the choices and decisions made are based on science and rigorous assessment of evidence, not commercial pressure or studies with a commercial bias.

The approach to HPV first in Scotland has been slightly different than England. The screening community in Scotland has been asked to submit a full business case to

the Scottish Government. As health is a devolved matter in Scotland and there is a Scottish Government election in May this year, the difficulty is in the timing of submission of the business case to try and ensure the case is assessed as quickly as possible. The business case will recommend that the laboratory service will be delivered from only two laboratories rather than the existing eight. Both laboratories will carry out the primary HPV test and cytology triage. A selection process will start later in 2016. Procurement for a single HPV test for Scotland has already started but it is difficult to provide accurate timescales as it is dependent on political decisions by the new Government after the election in May. Wales and Northern Ireland are also progressing along slightly different lines, however, it is important that there is open communication between the four nations to ensure a joined up approach to this major change to the programme.

The HPV sentinel sites and many other labs that have skilfully absorbed HPV testing into their routine workload have clearly demonstrated the skills, knowledge, flexibility and willingness to adapt and change. We must continue with this move to a molecular pathology world because the skills learned and experience gained will be of great benefit not just in cervical screening but also in non-gynae cytology and in establishing cytology professionals in delivering a screening programme based on molecular testing and cytology.

Chairman's Column

Paul Cross

As the high winds of storms Henry and Imogen die away, the winds of change however are still blowing through the world of UK cytology. The decision of the UK National Screening Committee (NSC) to recommend the use of HPV testing as the primary tool in cervical screening with reflex cytology¹ is the most significant change in the cervical screening programme since the introduction of liquid based cytology. Currently however the NSC recommendation is just that - a recommendation. The mechanics of the screening programmes is that the UK NSC makes recommendations on screening (both cancer and many other non-cancer ones) to the respective UK governments.² It is then up to the UK governments to adopt them or not, and then up to each country to actually introduce it if adopted. This distinction may be lost on many, but is an important one. This is not, as yet, a done deal, but I think we would be naive to think that it is unlikely to be adopted, but this could happen. The history of the UK NSC would be that it recommendations are adopted, but not always immediately. And that may be the problem here. The use of primary HPV testing is being evaluated at the pilot sites, and their experience must be used to help identify how we can convert and what the actual issues are. There are many potential problems, but the most pressing must be not to allow harm to befall women who present for cervical screening. This point again may seem obvious, but with changes likely in laboratory delivery and configuration, HPV test platforms and in the need for an IT system (old or new) that can cope with the demands of this change, there are many points that need resolving. The changes are so large that changes to commissioning may also be required. Whilst all these are major challenges, we must all work to ensure that during any transitional period that we deliver the highest quality of service we can, but the likely changes and to a degree uncertainty, will make some working in laboratories look for alternative roles. The BAC is working with all relevant bodies to help ensure that any changes, if and when they come, have all these points considered. Two articles in this edition of *SCAN*, raise many of these points. Watch this space...

Whilst the NSC decision has been long awaited for, many other things are happening. The BAC is still working hard with the IBMS and RCPath on a joint statement on the roles of biomedical scientists within non-gynaecological cytology. This has, despite much effort, taken significantly longer than we would all hope. All parties do agree on the basic points, and also on the vital and important role that scientific staff play in service delivery, but navigating such agreements through the various organisational structures does seem to take a long time. One would hope that in the future closer and more co-ordinated working between all relevant bodies, and in the sphere of cytology, that would primarily be the BAC, IBMS and RCPath, would benefit all of us.

The BAC is progressing the science of cytology by funding relevant research — congratulations to Andrew Evered who is the first recipient of the BAC Discretionary Research Fund which was announced during last year. The BAC is keen to promote research in cytology that will benefit cytology. We await with interest the outcomes of Andrew's research.

The new BAC website is now well established, and whilst again there is much we want to do with it, it is, I hope you feel, a vast improvement on the old one. I am very grateful to Christian Burt who looks after the day to day running of it and BAC membership queries. We are always on the lookout for news and material for it — please do let us know if you have something or want to contribute!

The BAC Executive must be congratulated on yet another successful scientific meeting held last October in Liverpool, more of this again elsewhere in this edition. Work is also ongoing with the European Congress of Cytology meeting for later this year (2–5th October), again in Liverpool. As I write the website for this meeting is going live, and with various speakers from all over the UK, Europe and further



afield this will be the "must attend" cytology meeting of) 2016. Please use the loose insert advert in this SCAN to publicise the meeting in your laboratory. Do attend, and do consider submitting an abstract for it. All details can be found on the ECC 2016 website – www. Cytology2016.com.

As always I must thank the BAC Executive for all their hard (unpaid) work and efforts which they do on top of their very busy day jobs. The BAC like most professional societies depends on motivated and dedicated members to operate – without their input the BAC would be nothing. They make my job as Chairman much easier, and the level of experience, motivation and knowledge we have around the Executive is amazing. Long may it last!

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- 2. UK National Screening Committee Terms of Reference. 2015. URL: https://www.gov.uk/government/groups/uk-nationalscreening-committee-uk-nsc#terms-of-reference-updatednovember-2015 (accessed 10/2/16)

An investigation of the anticancer properties of thymoquinone using cultured cervical cancer cells

Philip Markham, MSc in Biomedical Science, Cardiff Metropolitan University

Thymoquinone (TQ), a chemical component of the herbal flowering plant Nigella sativa, has been investigated for its action against the major hallmarks of cancer in many cell types, and shows promising chemo-protective potential. TQ downregulates metastasis-related genes such as N- and Ecadherins in vitro and may also promote apoptotic cell death by inhibiting the synthesis of survivin, a protein that plays a role in regulating cell death. TQ also activates PPARy (peroxisome proliferator-activated receptor γ), a nuclear hormone receptor that downregulates survivin. PPARy is known to be downregulated in cervical cancer, an effect that is probably mediated by HPV-16 E7 protein. These are just a few of the proposed mechanisms by which TQ may exert its effects, but despite the link between TQ and survivin regulation we do not know whether TQ would be effective for the prevention and/or treatment of cancer.

A major obstacle to the use of TQ in medicine is its limited bioavailability, which is caused by the molecule's hydrophobic properties. In a few trials, TQ it was found to perform better than placebo in reducing refractory epileptic seizures in children. Furthermore, TQ was tolerated at a dose of 2600mg/day without toxicity when offered to patients with advanced metastatic disease who had declined chemotherapy. Attempts have been made to improve the bio-distribution of TQ by encapsulating the compound in synthetic nanoparticle and liposome carriers. Encapsulation has notably improved TQ's efficacy in several studies, showing increased apoptosis of target cells compared to unencapsulated TQ, with some evidence for more effective downregulation of key cancer genes. Dedicated antisurvivin therapies have also been administered by these methods, for example in the liposomal delivery of survivin siRNA to prevent translation to the active protein.

To date there has been little research relating to the effect of TQ on the expression of survivin in cervical cancer cells. I recently carried out an experimental study using RT-PCR to evaluate survivin gene expression in HeLa cervical cancer cells following exposure to TQ. The project was in part-fulfilment of a Masters degree in Biomedical Sciences at Cardiff Metropolitan University. Surprisingly, I found that neither the dose nor the duration of exposure to TQ affected survivin expression (P=0.24 and P=0.07, respectively). My results do not concur with studies in other types of cells, where TQ has been found to reduce survivin expression, usually in tandem with other antiapoptotic proteins such as XIAP (X-linked inhibitor of apoptosis protein). These encouraging? results have been noted in osteosarcoma, breast cancer and pancreatic adenocarcinoma cell lines, among others. My results were disappointing, but as scientists we must always consider the possibility of experimental error, particularly regarding PCR technique. Proper handling of PCR primers is essential in order to avoid reagent degradation. For future experiments I would suggest using micromixing rather than traditional blending techniques for more efficient conversion of limited quantities of mRNA to cDNA. Micromixing utilises simple audio components to induce oscillatory chaotic flow using ultrasound, mixing reagents more effectively and thus resulting in less mRNA degradation before it can be converted to stable cDNA.

I would like to thank the staff at Cardiff Metropolitan University for their guidance and for giving me the opportunity to carry out this important research.

First year as Editor-in-Chief of Cytopathology

Mina Desai

One year ago, when I took on the role of editor of *Cytopathology*, I anticipated that it would be a challenge harder than running with the Olympic torch. I was right! I thought that I had a clear vision of where the journal was and what I wanted to achieve as editor. Yet for the first few months, I had a rollercoaster ride.

My first challenge was to find peer reviewers. In the modern NHS, spending time on peer review is no longer costeffective. Young pathologists and Biomedical Scientists are working hard and seeking a work-life balance. Finding a young, UK-based peer reviewer ended up being next to impossible, posing a challenge for both me and my enthusiastic and talented team of new editors. I started to worry that turnaround times for manuscripts would be much higher under my editorship than under my predecessors. Dr. Amanda Herbert is a hard act to follow!

However, I soon I realised that there are ups and downs on the editorial rollercoaster ride. It was exciting to see the first issue of the journal with its appealing and young looking colours of the cover page, Henry Kitchener's editorial on HPV primary cervical screening and new initiatives e.g. InCyt and Enigma Portal.

When I embarked upon my editorial role, I had set the following objectives to enhance the journal's reputation. With the help of a truly excellent editorial team, I think that I have achieved most of them.

- 1) I formed a new editorial board structure consisting of pathologists and cytotechnologists.
- 2) We launched a new section called "InCyt", aimed at cytotechnologists from across the globe. It is designed to provide a forum for discussion on all aspects of cytology.
- 3) We established the Enigma Portal, an important educational resource for cytologists, pathologists and cytotechnologists. It provides a rich source of continuing professional development material in gynaecological and non-gynaecological cytology.
- 4) We attracted experts from across the globe in the fields of gynaecological and non-gynaecological cytology, as well as molecular cytology, to write some of the best editorials and review articles. Hopefully, this will enhance the journal's citation index in future.
- 5) We provided a forum for clinicians to write reviews on cytopathologists' input to clinical and management decisions in the Clinical Perspectives section.

I must confess that there are still some unfinished jobs. We would like to finish publishing professional standards from the UK and Europe, and enhance our social media presence (for which we have recently hired a young, enthusiastic social media editor from Oxford).

I have been lucky to have a great team of professionals helping me enhance the image of *Cytopathology* nationally and internationally. I have listed their names at the end of this article. Without their help, I would not have survived this first year, nor achieved all that we have for the journal. I am also grateful to my family especially my grandchildren Nayan and Maya, who accept that when grandma has journal-related jobs, they are not allowed to disturb her!

My thanks to the *Cytopathology* Editorial team and Wiley staff.

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Would you like to be considered as a reviewer for *Cytopathology*? We always need new reviewers to help assess material submitted to the journal. If you feel you can assist, send your name, position, contact email address and areas of interest/expertise to Delia Smith at the Wiley publishers. Her email address is delia@malimrobin.co.uk

Reference

1. Desai M. Cytopathology: a new approach. *Cytopathology* 2015; **26**(1):3.

Our day out in Liverpool

Fiona Robertson and Sharon Heggie, Cytology Laboratory, Forth Valley Royal Hospital.

The 2015 BAC Annual Scientific Meeting lived up to our expectations and was as informative and interesting as we had hoped.

Firstly, we have to commend the facilities. The AAC in Liverpool is a lovely venue — new, clean, bright and comfortable. It is ideally placed on the Mersey for hotels and restaurants. Sharon and I had a great view from our hotel window of the Mersey River and the Liver building. It was easy for us to walk around safely and to find a restaurant the evening before the conference. It was then only a short walk to the ACC from the hotel on the morning of the conference. The BAC has made an excellent choice of the ACC as the venue for next year's 40th European Congress of Cytology.

The conference commenced with a welcome from Allan Wilson, president of the BAC and introductions from the commercial partners...enticing us to the trade show.





The first presentation was by Mr John Crossley on the Advanced Specialist Diploma (ASD) in Non- Gynaecological Cytology. This qualification was developed to mirror the ASD in Cervical Cytology. The ASD is the most advanced qualification for biomedical scientists offered by the profession and was developed by the conjoint board of the



BAC 2015

RCPath and IBMS. John Crossley described the 'drivers' that brought about this new qualification. In 2013 a subgroup was established to decide the exam structure and curriculum. The final result was put to the IBMS congress and was well received. The exam was finalised as a written paper with 4 questions out of 6 in 90 minutes, 12 short cases in 72 minutes and 5 complex cases in 100 minutes with discussion and correlation. The first exam was held on the 11th and 12th of June 2015 — the sole candidate passed. It is hoped more people will be interested in achieving this qualification.

The next presentation was titled 'Andrology in 2015'. Professor Allan Pacey, who works between the University of Sheffield and the NHS, gave a very informative and, at times, humorous talk on the problems and pitfalls of developing an effective male infertility service, with an amusing look at providing 'help' in the guise of pornographic material to assist men attending the clinic in providing the best semen sample possible. The WHO has been writing the guidelines on andrology analysis for years but, due to differences in male fertility between developing and developed countries, they are bowing out and new guidelines will be written by other interested organisations. Professor Pacey also touched on the introduction of analysers in sperm analysis and problems with quality assurance (QA). NEQAS results have improved over the years but he was concerned that due to UKAS accreditation some laboratories would want to offload their fertility service; regionalisation and reorganisation into specialist centres may be the way forward. However, some laboratories are putting their Andrology service 'out of scope' for accreditation — what are the implications for QA and the future of the service?

After coffee and a walk around the commercial stands, helping ourselves to the freebies, the next talk by Dr Jesper Bonde addressed rethinking the screening of nonresponders. The Copenhagen self -sampling initiative was a unique approach to encouraging women whom, for one reason or another, are not accessing the cervical screening



Main foyer ACC Liverpool

service, to 'opt in' after invitation and to self-sample at home. Dr Bonde provided a thorough explanation and reasoning behind the project with the rationale that, if the pilot was successful, self-sampling could be rolled out generally to screening non-responders. The non-attenders in the 30–60 age group included those in a low socio-economic/income group, poorly educated and difficult to reach women, but also 'regular' women who just forget to attend for a smear.

Dr Bonde explained how they tried a new approach to communication using 'Apps', electronic and paper scanning with QI codes and instructions in Danish, English, French, and Arabic. There were RFID chips in each sample brush for easy identification. Other factors looked at were test protocol, sample quality and HPV prevalence. Early conclusions to the pilot were that opt-in self-sampling was well received amongst all age groups, regardless of screening history. Communication strategies worked well and were more cost effective. The pilot detected 5 cancers and 72 women with CIN2 or more, with more than 6,500 women of the 25,000 invited being screened. Hard to reach groups such as the disabled and sexually abused, were helped by the pilot and there was a very low rate of inadequate samples.



The morning program concluded with the BAC Annual General Meeting.

Lunch was excellent and an opportunity to network with other laboratory staff as well as catching up with former colleagues.

Allan Wilson and Jenny Davies

The afternoon program began with an update of HPV testing in the UK by Dr Karin Denton. Some interesting data were shown in relation to the HPV primary screening test. Pilot sites in England showed HPV positive rates to be highest in Sheffield, where there is a younger and more 'deprived' population, with the lowest HPV rate being in Norfolk where the population is older and more rural. I imagine that few delegates were surprised by these results. HPV primary screening raises many questions which will require consideration, such as what to do with HPV positive/cytology negative women, the role of genotyping and optimum recall intervals. Since the BAC conference, the National Screening Committee recommended the implementation HPV primary screening in the UK.

Following on from this was a talk on the impact of HPV primary screening on colposcopy by Dr Julia Palmer. Introduction of primary HPV screening in Sheffield began in 2013. In subsequent years amendments have been made to the protocol which has significantly increased the number of referrals to Sheffield colposcopy clinics. It was clear to see that effects such as HPV triage, the Jade Goodie effect, HPV primary screening and the introduction of symptomatic clinics impact on colposcopy referrals.

The next presentation — "Are cytologists born perpendicular?" had a curious title which gave nothing away! Dr Andrew Evered gave an intriguing talk on the influential effect of bias in cytology. Dr Evered has been involved in cognitive science for the past 4 years, looking at cytology reporting behaviours. For instance does knowing HPV results influence cytologists' reporting? Dr Evered went on to explain the use of Signal Detection Theory in looking at bias. I have to confess that I had to look up Signal Detection Theory on Wikipedia to help me understand what to write here. 'SDT is a means to quantify the ability to discern between information bearing patterns and random patterns that distract from the information'. When it is humans that are the detecting system, experience, expectation and physical state such as tiredness can have an effect. Hearing Dr Evered's presentation on this topic has prompted me to find out more and hopefully will make me think more carefully of my own bias when reporting.



Andrew Evered

After coffee break there was a summary of the BAC Code of Practice in Cervical Cytology from Dr Louise Smart. This updated version involved a significant rewrite due to numerous changes in cervical cytology in the last five years.



There was also information from Dr Paul Cross, chairman of the BAC, on the new BAC website about to go live, and on the 40th European Congress of Cytology meeting here in the ACC Liverpool on the 2nd – 5th October 2016.

Paul Cross

Finally, Allan Wilson gave his closing remarks, thanking everyone for their participation in another successful conference.

Sharon and I would like to say a big thank you to the SACC for sponsoring our attendance at the BAC ASM. I would also like to thank Sharon for helping me to write this and for correcting my spelling mistakes!

Human papillomavirus testing in the NHS Cervical Screening Programme – response to Public Health England screening consultation

Phil Bullock, Consultant Healthcare Scientist in Cytology, Gloucester Hospitals NHS Trust

Summary

There can be little doubt that a move to high risk human papillomavirus (HPV) primary screening holds significant attractions. The possibility of self sampling alone as a means of improving coverage bears further investigation as long as all other quality parameters can be maintained and that management continues to be based on the proven presence of disease and not HPV status.

There is significant risk in such a move however, which will be compounded if centralisation is attempted at the same time. Currently much interaction takes place between cytology laboratories, colposcopy clinics and the screening database. As this is now being centralised the need for increased vigilance in this area will be paramount until new systems settle down. Coupled with this is the laudable desire to re-write the screening database to address significant and long standing issues which will further magnify the risks if not implemented extremely carefully. This would best be done within the existing laboratory framework as that is where much expertise currently sits.

Existing laboratories are under pressure however; staff recruitment and retention is, to say the least, challenging. Both this and the IT risk could be minimised by forming hub and spoke networks of existing laboratories. The hub would need to be identified by a process — possibly competitive tendering — which takes organisational willingness and service delivery into account and would need to be able to support MDTs at all the spoke sites. If centralisation were to take place then it would logically be to these hubs over a period of time via a process of evolution. If primary screening were to be introduced in its completeness to such a network over the next three years then this would allow for the existing laboratories to deliver one screening round under primary HPV screening by the end of year six. At this time the HPV vaccinated cohort will be arriving and the centralisation process to the hub with perhaps further adjustment to screening intervals based on experience from the first screening round would seem to offer a strategy to minimise risk to the programme and the population it screens.

Introduction

The following paper represents an individual response by the author to Public Health England's request for consultation on the move to primary screening based on HPV testing in the NHS cervical screening programme. It was forwarded to both the Institute of Biomedical Science (IBMS) and the British Association for Cytopathology (BAC) as the author is a member of both organisations.

The National Screening Committee has now pronounced on the consultation; further updates can be found at http://legacy.screening.nhs.uk/cervicalcancer, including the evidence base to support the decision to recommend the move to HPV primary screening. Ministerial approval is now required; the speed at which implementation follows is likely to be influenced by the importance attributed to the provision of a replacement screening database to deal with the current issues in the Exeter system and the process by which any laboratory reconfigurations are to be managed.

The success of cervical screening

The NHS Cervical Screening Programme is a great success, as evidenced by the low incidence of cervical cancer in the UK. The introduction of an organised call and recall based programme together with quality assured cytology and colposcopy services have got us to this point, but there is more that could be done within this framework, particularly with regards to screening coverage and the need for robust quality assurance of cervical histopathology.

The introduction of HPV triage and Test of Cure (TOC) has had a very positive effect on the programme. While multifactorial influences are hard to separate (e.g. shift in disease incidence, effect of vaccine, etc), HPV testing has probably had a significant effect on detection rates and the age distribution of CIN3 (figs 1 and 2).



Figures 1 and 2. CIN3 detection rates in Gloucestershire between 2003 and 2015. Note that detection of CIN3 represents successful screening (compared to invasive cancer, which is a measure of screening failure, given that prevention is the aim of the programme).

Drivers for change

Having established this baseline let us consider the following drivers for change:

1. Coverage. The declining programme coverage represents a real risk to the success of the programme, since non-responders place themselves in an at-risk category. This would appear to be amplified by demographics. If introduction of an element of self sampling could improve coverage then this would be a significant quality gain.

2. Efficiency. The cost of HPV primary screening may appear cheaper than cytology but if, as seems likely, the HPV primary screening model retains cytology as triage then the infrastructure to support this will also have to be retained. This will significantly erode cost benefits if recall intervals remain the same. However, the robust negative predictive value of HPV testing should allow increased screening intervals and this is where the efficiency gains will come, both at laboratory and primary care levels.

3. Workforce. The workforce currently exists to provide the screening programme as it stands but is suffering death by default due to lack of a clear pathway and future service provision models. Furthermore, future staffing models are either unpopular with professional groups or do not align with current educational pathways, especially for non-medical staff.

4. HPV vaccination. The vaccinated cohort is reaching screening age imminently. If the evidence of the vaccination programme in SW Scotland is robust then a reduction of up to 50% in the incidence of CIN3 can be expected. This would have a profound effect on quality parameters as currently applied in a cytology based programme and robust quality assurance may prove more difficult in this environment.

Current strengths in the programme

1. Local service delivery. In many areas strong teams have been established that are robust and capable of delivering to all current quality standards. Where this may not be the case early action should be taken to deliver change. HPV primary screening should not be used as a tool to drive reconfiguration.

2. Well proven technology. Services currently delivering the programme have had significant periods of change over the last four years. Technology is well embedded and sufficient information is now available to drive better informed choices on service delivery models.

Current weaknesses in the programme

1. Variability in delivery, particularly on sites where there is currently no cytology laboratory. Often, multidisciplinary teams are highly dependent on cytology input for both clinical and programme pathway advice and decisions. Hospital Based Programme Coordinators are key to this but are often less active at these sites.

2. Information technology. The lack of either a single national database or a system recording all elements of a woman's screening pathway creates significant issues within the current service delivery structure.

3. Variable performance of HPV testing platforms.

The screening programme tends to treat all combinations of approved HPV and liquid based cytology technology as if they are one and the same, when published data shows that plainly they are not, with TOC failure rates over 20% higher at some sites than others. Recent papers by Moss *et al*¹ and Innamaa *et al*² give further context to this issue.

4. National data. The failure of the programme to amend national returns to better reflect current programme pathways is worrying. Many of the questions that arise as a result of this proposed change might be addressed with better national data.

Potential future strengths in a HPV primary screening programme

1. Increased screening intervals.

- 2. Improved turn round times for approximately 80% of screened samples (i.e. those with a negative HPV result).
- 3. Efficiency gains.
- 4. Reduction of dependency on highly skilled cytologists.

Potential future weaknesses in a HPV primary screening programme

- 1. Failure to identify the small number of cervical cancers that test HPV negative.
- 2. Failure to identify incidental findings, such as noncervical cancers, infections, and endometrial cells.
- 3. Failure due to address database issues due to insufficient laboratory resource in a centralised model.
- 4. Failure due to lack of robust local input in a centralised model.
- 5. Inability of educational systems to map to the needs of the new screening programme.

Conclusion

A low risk model under which the NHS cervical screening programme might move to HPV primary screening would be to plan to make the move in three years time within existing laboratories that robustly meet current guidelines. These three years could be used to rebuild the national screening database and to create local networks which could be used for planned centralisation in years four to six should that become the preferred model. This evolutionary process reduces the risk of programme degradation whilst making the most of current staffing expertise.

References

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Mysterious aliens!

Lisa Callaghan, Royal Gwent Hospital Newport.

In a nine month period from December 2014 to September 2015, 19 out of 84 cervical cytology samples (22.6%) at the Royal Gwent Hospital laboratory contained 'alien' material. The aliens arrived from a single family planning/sexual health clinic. Originally, the aliens (figures 1 and 2) was reported as molluscum contagiosum because of their close resemblance to cases reported in the literature.¹







Figure 3. More aliens.

Figure 1. Our little aliens.



Figure 2. Another alien on higher magnification.

There were no obvious factors linking the 19 strange samples. Collectively, the slides originated from seven different sample takers and a wide age range of women (age range 36–44 years). However, when two more samples containing the same alien entities were received three weeks later (figures 3 and 4), molluscum contagiosum seemed unlikely.



Figure 4. More aliens on higher magnification.

Oil immersion microscopy provided a closer look (figures 5–8).



Figures 5–8. High magnification oil immersion microscopy.







Figure 7.



Figure 8.

Special stains failed to identify the aliens. Congo red (figure 9) did not show the apple green birefringence that is characteristic of molluscum contagiosum and Grocott staining was negative (figure 10), so whatever these entities were, they were unlikely to be fungal. A cell block was prepared but sadly no alien material survived the processing.



Figure 9. Congo red stain was negative.



Figure 10. Grocott stain was negative.

On visiting the offending clinic I was informed that a new lubricant was being used and that samplers were being stored in an open environment during the time that the aliens were being found in cytology slides. The sampling devices were subsequently stored under protective covering and no aliens have been seen since. Further internet research eliminated the idea that the aliens might be pollen grains,² but then a couple of publications caught my eye. Rivasi *et al* cites Galactomannan polysaccharide — present in Guar and Tara gums — as a source of strange aliens that look extremely similar to ours.³ Similar contaminants have been observed in urine samples from patients with ostomy bags.⁴ Guar gum is commonly used as an ostomy adhesive.

We have seen no aliens since September 2015. Will the mystery ever be solved?

References

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- 2 Cambridge University Palynological Online Database 2008. URL: http://www.quaternary.group.cam.ac.uk/pollen/ (accessed 6/2/16)
- 3 Rivasi F, Tosi G, Ruozi B, Curatola C. Vegetable Cells in Papanicolaou-Stained Cervical Smears. *Diagn Cytopathol*. 2006; 34(1):45–49.
- 4 Planinšek T, Kladnik A, Pohar-Marinšek Z, Fležar MS. Vegetable Cells in Urinary Samples of Patients with Bricker Ileal Conduit. *Diagn Cytopathol.* 2014; 42(2):120-124.

Comparison of the performance of HPV tests in women with abnormal cytology: results of a study within the NHS Cervical Screening Programme

Moss, S. et al Cytopathology 2015 26:373-380

1. What were the aims of this study? (2)

2. Explain the terms sensitivity and specificity in relation to HPV triage? (2)

3. List 3 disadvantages of having an HPV test with high sensitivity but low specificity. (3)

4. What data was sent from each site to the co-ordinating centre for analysis? (1)

5. For calculation of sensitivity, which samples were considered to have a positive outcome? (1)

6. What was the range for the proportion of samples positive on HC2 and how did this compare with the alternative assay range? (2)

7. Why was the total number of women referred to colposcopy higher than the total number of HPV positive samples? (2)

8. Overall, how did the alternative HPV assays compare to HC2 in terms of sensitivity and specificity? (2)

9. What conclusions were drawn about the alternative HPV assays? (1)

10. In your opinion which assay would be best suited for use in (a) TOC and (b)HPV primary screening and why? (4)

20 marks available

Name..... CEC number

Please return your completed JBL either by post or by email to:

Helen Burrell South West Regional Cytology Training Centre Lime Walk Building Southmead Hospital BRISTOL BS10 5NB

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Validation of a new cell block

Siar

Cellular Pathology Cardiff & Vale UHB. BSc (Hons) App

Aim: To investigate two methods for cell block preparation: Agar technique validated to investigate whethe

Introduction

Cell block preparation is an extremely useful method in cytology, as it allows tissue fragments and cell remnants to be processed in a paraffin embedded block to be used for histological analysis[1]. Cell blocks can then be used in conjunction with initial cytological preparation to investigate cell type and appearance.

This technique is one of the oldest methods used for the investigation of serous fluids. Cell blocks can provide multiple sections that may be needed for further investigations, such as immunocytochemistry (ICC) and molecular genetics[2].

Method

A total of 40 anonymised serous fluid specimens (20 malignant & 20 benign) were split into two universal containers for each cell block method. Serous fluids were chosen as the test material as these account for 60% of all cell blocks made within the cytology laboratory at Cardiff & Vale UHB.

Cytological preparation

Each sample was prepared by centrifuging at 3000rpm for 7 minutes. The supernatant was discarded to leave a pellet to be used for each cell block method. Each block was used to provide sections for Haematoxylin and Eosin (H&E) staining and ICC investigation (BerEP4 and Calretinin).



Fig 1: CytoFoam[®] disk process sequence. Fluid specimen (A); specimen pellet (B);CytoFoam ® disk (C); Absorbed pellet(D); disk in cassette ready for processing (E) [3].

This new method was validated against the 'gold standard' agar method, to ensure ease of use, increased diagnostic yield and suitability for ICC investigations. The new method must meet the needs of the service, ensuring results are correct for accurate patient diagnosis.

Agar method

This method involved heating a small bottle of 1% Oxoid agar to a molten state using the hotplate. Once the agar had liquefied and cooled, a number of drops were added to the pellet, mixed carefully with a pipette and allowed to cool and set.

CytoFoam® method

CytoFoam[®] cell blocks were prepared in accordance with the Exmoor Innovations 'process sequence' instructions included in the kit (fig1). Disks were placed into the bottom of the universal for 10 minutes to absorb the pellet. These were treated with alcohol for 30 seconds, then alcohol was replaced by 10% formalin for 12 hour fixation[3]. Both agar and foam were wrapped in tissue wrap, fixed in 10% formalin and processed as a routine histology specimen.

References

[1]. Shivakumarswamy U, Arakeri SU, Karigowdar MH, Yelikar BR. Diagnostic utility of the cell block method versus the conventional smear study in pleural fluid cytology. J Cytol 2012;29(1): 11–15.

[2]. Nathan NA, Naryan E, Smith MM, Horn MJ. Cell Block Cytology: Improved preparation and its efficacy in diagnostic Cytology. Am J Clin Pathol 2000;114: 599-606.

k technique in Cellular Pathology

n Norris

olied Biomedical Science: Cardiff Metropolitan University

and a new commercial kit - CytoFoam[®] disk. This new method will be r it meets current standards.

Results

The grading system described by Khan *et al* [4]. was used to produce quality scores 0-5 for H&E staining with regards to cellularity, morphological and architectural preservation (fig 2). 12 ICC cases were also analysed for positive colouration (0-6) and background staining (0-3) (fig 3)..

All score medians were analysed using the Wilcoxon signed rank test on Minitab17. P values for each method are shown in table 1 with regards to disease state.

The results indicated no statistical significance using either method for H&E of malignant cases (P=0.795). However, there was a statistical significance for benign cases (P=0.029). The statistical significance was therefore disease dependant. There was no statistical significance with regards to ICC analysis, however, this result needs to be considered carefully as only 12 cases were investigated.



Fig 2 H&E staining (X20 mag) both methods scored 5 for overall quality.



Fig 2 Boxplots for H&E and ICC quality scores.



Fig 3 BerEP4 analysis (X10 mag) both methods scored 6 for ICC. CBC produced less background.



Medium	Disease State	P value (H&E)	P value (ICC)
Agar	Malignant Vs Benign	0.067	1.000
CytoFoam®	Malignant Vs Benign	0.013	0.371
Agar Vs CytoFoam®	Benign	0.029	1.000
Agar Vs CytoFoam®	Malignant	0.795	0.600

[3]. Exmoor Innovations Ltd. Make cell blocks from cytology fluid specimens: 'Process Sequence' 2013. PUB/375/B/2.
[4]. Khan S, Omar T, Michelow P. Effectiveness of the cell block technique in diagnostic cytopathology. J Cytol 2012;29(3): 177–182.

Discussion / Conclusion

From comparison of both methods, agar was found to be superior in fulfilling the needs of the service, however there were problems with standardisation using this method. An advantage of using CytoFoam® method was that this was standardised therefore complying with ISO 15189. However, delayed turnaround times due to longer fixation periods, and increased cost were a major disadvantage using this method.

39th European Congress of Cytology, Milan 2015 – and ECC Liverpool 2016!!

Paul Cross



Milan Cathedral

The 39th ECC meeting was held in Milan (September 20–23), and once again lived up to the high traditions of these meetings. The meeting boasted a wide range of symposia, lectures seminars and workshops. The conference venue was a modern well-equipped and, more importantly, air conditioned auditorium! It was remote from the city centre, requiring some interesting navigation, by foot mostly, of the streets and tramlines of Milan. Given that the BAC is organising the 40th ECC meeting in Liverpool this year, we had arranged to have a



BAC stand, Milan

small stand within the commercial area to help advertise the meeting. We spent a lot of our time at the stand promoting and answering questions about the meeting, but did get to a wide variety of the scientific sessions. We were amazed at the interest in the 2016 meeting, with many keen to come to the UK, but in particular the lure of Liverpool could not be underestimated! We had promotional material, as well as the very popular screen cloths. We had naively thought that these would be useful for microscope lenses, but they turned out to be far more useful for cleaning of I-pads, I-phones and glasses!



ECC screen cloths

The congress officially opened on the Sunday evening, followed by a total of 56 sessions of all types. All the meetings were held in English, and the sessions ran well and invariably to time. The use of an on-screen clock which allowed the audience, chair and speaker to know exactly where they were in their timings certainly helped in this respect. We attended as many of the scientific sessions as we could, and two that stand out for me were sessions on the new Paris urology system as well as on thyroid cytology reporting.



BAC reception, Milan



QUATE Milan

Given the interest in the Liverpool meeting, we arranged an impromptu reception one evening, and the sight of the BAC president and chairman serving drinks to delegates, as well as the Beatles music that we were able to blast out from a small laptop certainly caused a stir. There was much discussion and engagement with people, and I am indebted to Mina Desai, Ash Chandra, Alison Cropper and Allan Wilson as well as a member of our conference organiser team, Grainne Ni Ghiollagain, for all the hard work and effort they put into promoting the meeting. Particular memories of the meeting itself will be the numerous colleagues and friends that we bumped into, who we may not see in between such meetings, as well as the high quality of the scientific presentations that we attended. We certainly noted several features that we would wish to incorporate into our planning for ECC Liverpool 2016, but we certainly do not plan to follow Milan's example of having three hour sessions without coffee breaks! Milan used electronic poster boards for all poster presentations, and this was not without technical difficulties. It was a tiring four days in total, and trying to carry our BAC roll-up banners as hand luggage did cause a few raised eyebrows at airport check in.

The ECC bandwagon now rolls on to the meeting in Liverpool later this year, for which you will see an advert in this edition of *SCAN* as well as a loose leaf advert for you to hopefully use within your own department. Do try and attend, fly the flag for UK cytology and also see the best that Europe and the rest of the world has to offer. We are keen to promote the best of UK cytology so do consider submitting a poster or an oral presentation. Visit the meeting website for further details and the evolving scientific programme: www.cytology2016.com. See you in Liverpool!!



Presidents x 3



Actual cells, Milan

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HPV testing as the primary test in cervical screening

Karin Denton, Regional head of screening quality assurance, national lead for HPV quality assurance, Public Health England and consultant cytopathologist.

On 12th January 2016 the minutes of the National Screening Committee (NSC), which met in November 2015, were published.¹ The committee was supportive of the proposed modification to the cervical screening programme (HPV primary screening).

Readers should note that the NSC is a pan-UK body and its terms of reference are listed below.² English ministers and their opposite numbers in the devolved nations then make the final decision on implementation.

NSC terms of reference²

The UK NSC will advise ministers and the NHS in all 4 UK countries about:

- the case for implementing new population screening programmes not presently provided by the NHS within each of the countries in the UK
- screening technologies of proven effectiveness but which require controlled and well-managed introduction
- the case for continuing, modifying or withdrawing existing population screening programmes. In particular, programmes inadequately evaluated or of doubtful effectiveness, quality, or value
- generic issues relating to screening programmes and policy

What are the drivers for implementing HPV as a primary screening test?

- Randomised trials show increase in sensitivity and duration of protection of a negative result even though UK cytology is the best in the world.
- An increase in the screening interval would be safe and lead to fewer screening episodes for each woman.
- Better fit for the HPV vaccinated cohort.

What are the challenges of implementing HPV as a primary screening test?

- Maintaining cytology expertise (for the triage of HPV positive samples).
- Extending recall intervals in a way which allows management of the workload.
- Understanding what will and what will not be detected by the new test.

Maintaining cytology expertise

The papers accompanying the NSC consultation identified this as the most dominant driver for centralisation. 200,000 HPV tests would generate an estimated cytology workload of 35,000, with the current screening interval. This would support a cytology "screening" workforce of between five and seven staff, which is the minimum required for resilience, quality control, professional development and training, etc. This means that we would need around 15 laboratories for England, one for Wales and two for Scotland (total number of samples/200,000).

Centralisation brings its own challenges, but these are not new or unfamiliar. There are now numerous centralised cytology services which link with multiple colposcopy and histology units. Large examples would include Derby, Manchester, Sheffield and Newmarket, but there are many others. In particular, the areas which need to be addressed to make centralised services work are IT connections and staff job plans, especially those required to support the colposcopy MDT.

It has been well known for many years that the Exeter system, while having given long and valuable service, no longer meets the needs of the programme, and a new system is under development. The new system will allow linkage of colposcopy and histology outcomes to recall history and cytology/HPV results. But we know that it is possible to safely implement HPV primary screening using the Exeter system, because this is what has been happening in the six pilot sites, some of which are centralised. It is more labour intensive, and all would agree that it is not ideal, but it is possible.

The challenge here is one of timing. Do we wait for the new IT system before moving to HPV primary screening, or would it be less risky to start implementation with the existing IT? The key factor is the impact on the cytology workforce. PHE understands that the biggest risk to continuity of the existing excellent cervical screening programme is the ability to recruit and retain highly trained cytology staff, and there is abundant evidence that this is becoming increasingly difficult, as people do not want to commit to what might be a very temporary move when the location of the future sites is unknown. Smaller laboratories which have no desire to become a centralised hub site are likely to have the biggest staffing challenges.

Managing the increase to the screening interval

If we decided to immediately extend all intervals from three/five years to six years, then in years four and five there would be very few women recalled. Numbers being tested would plummet and this would have impossible implications not only for cytology but also for general practice and colposcopy. While we could cope with the numbers dropping, what would happen when they went back up again? Many have recognised this problem, but finding a solution turns out to need a complex mathematical model, and this has been undertaken by ScHARR (School of Health and Related Research, Sheffield). There is a way to manage this with predictable falls in numbers of women tested, and only very slight short term upward blips which should be manageable within capacity. One aspect of this to remember is that all intervals need to be set at the time of the test, not changed retrospectively. The complex cohorts required in this model could not be managed manually and it is uncertain whether the Exeter system could cope. This may need to wait for its replacement.

Understanding what will and what will not be detected by the new test.

HPV testing as a primary screen is proven to significantly reduce the incidence of CIN 3, and our understanding of the natural history of the disease means that we believe this will also reduce the incidence of cancer. However, cervical cancer is so rare in the screened population that it is not feasible to use cancer as an analytical end point.

There is published evidence that some patients with even advanced cervical cancer have negative HPV test results, though this appears rare. However we do need to keep in mind that significant numbers of women with cervical cancer also have negative cytology, and in fact any analysis of the national cervical cancer audit will show that negative cytology preceding cervical cancer is a feature in a significant number of cases of invasive cancer. The six pilot sites have been continuing with this audit, and I am not aware of any case of interval cancer with a previous HPV negative result, after 2–2.5 years implementation and over 200,000 women screened.

What about non-cervical adenocarcinomas? Cytology reports of non-cervical carcinoma are very rare. No national data on the number and outcome of samples coded as 0 (non-cervical adenocarcinoma) are currently published but it is a rare diagnosis. Of these, perhaps 50% at most will have non-cervical carcinoma, mostly endometrial. Very occasionally, we will detect ovarian or metastatic carcinoma. In the future, cervical screening will not detect these, except in the unlikely event that a woman also has a cervical HPV-related lesion. This is not an argument against implementation of HPV testing, where benefits to many need to be weighed against benefits to a few, but it is something which needs to be picked up in training to sample takers and information to women.

Commissioning

Commissioning of screening services can seem quite remote to some staff working in laboratories, but others will be extremely familiar with the processes. Prior to 2013, screening was commissioned by PCT's — organisations typically with a small footprint often covering one cytology laboratory only. Negotiating mergers was challenging as it required multiple PCT's to work together and this made rationalisation to implement minimum laboratory sizes for HPV triage problematic in some areas. However, in recent years a number of large services have been subject to competitive tender, not related to HPV primary screening. For example, services based in Manchester, Sheffield and Derby have all experienced this. NHS England commissions this service, advised by PHE staff who are embedded with them, and using the Section 7a service specification. This specification covers the whole of the screening pathway. Where these large centralised services are in place, all aspects of screening are covered, including attendance at MDT meetings and sharing of data. So it would be wrong to combine the issues of centralisation and HPV primary screening — centralisation is going ahead anyway.

The way forward

At the time of writing, a decision on the implementation of HPV primary screening has not been made in any of the UK countries. In England, PHE has set up an implementation group to try to "hit the ground running" if this announcement comes. Key strands of work include, but are not limited to:

- Defining the whole pathway from initial invitation to the diagnosis of cancer, including resolving all the queries arising from the pilot sites' experience.
- Defining a detailed service specification to include the whole pathway, including for example colposcopy MDT meetings.
- Agreeing programme and quality standards and means of measuring them.
- Agreeing a new QA process/operating model.
- Working with relevant bodies on qualification and training implications for all staff in cytology.
- Working hard to develop and implement a new IT system, and to ensure that existing systems continue to work effectively during transition.
- · Modelling any proposed extension of screening intervals.
- An intention to produce implementation/best practice guidance.
- Noting the need for revisions to patient information and sample taker training.

Conclusion

The cervical screening programmes in the UK are the best in the world and offer a really good service to women who participate. But the evidence now suggests that in the future, especially once the vaccinated cohort enter the screening programme, HPV testing as the primary screen is more clinically and cost effective. It is completely recognised that the biggest risk to successful transition is maintaining the excellent cytology based service up until HPV primary screening can be implemented beyond the existing pilot sites. There is much work to do, and PHE is calling on the expertise of many from all parts of the programme, including cytology, to make any transition as safe and effective as possible.

- The UK NSC recommendation on Cervical Cancer screening in women. 2016. URL: http://legacy.screening.nhs.uk/cervicalcancer (accessed 10/2/16)
- 2 UK National Screening Committee Terms of Reference. 2015. URL: https://www.gov.uk/government/groups/uk-nationalscreening-committee-uk-nsc#terms-of-reference-updatednovember-2015 (accessed 10/2/16)

First ECC delegate from the UK!!

At the BAC ASM held in Liverpool last October, we offered a free place to one lucky delegate for the ECC 2016 meeting.

And our lucky winner was BAC member Katharine Ferry, pictured here with the President of the BAC Mr Allan Wilson FIBMS.



Katharine said:

"This year, I have had the pleasure of attending the BAC ASM. It had been a while since I last attended conference, and my happy experiences then were returned at Liverpool.

The programme was varied, covering everything from the Non gynae Diploma to HPV primary screening to Andrology, the latter providing many a knowing chuckle. HPV testing via the postal service was an interesting concept for reaching women who were perhaps unable to access screening in the usual way. Other topics included the impact of HPV primary screening on colposcopy and cognitive bias in cytology. All in all it was a thought provoking conference.

As the meeting drew to a close, the draw was made for the ECC pass. We all sat waiting for the announcement with great anticipation, and no one was more surprised than I to hear my name.

Everyone was generous in their congratulations. Having been involved with cytology for nearly 30 years, this will be the pinnacle of my professional life, and I am looking forward to October and the ECC immensely"

A walk on the wild side

Dr Tom Giles, Consultant Pathologist, Royal Liverpool University Hospital

I care about cytology. I want to see cytology services help our patients live the best life possible but being isolated in a laboratory can make us forget what it means to be a patient. At some point, each of us will be reminded of how vulnerable our aspirations can be as we become patients ourselves.

I have dilated cardiomyopathy, which was diagnosed in February 2015. I have been left with an implantable cardioverter defibrillator (ICD) and hypersensitivity to symptoms that may be a failing heart. Despite family concerns over a 'weak heart', my superb cardiology team have strongly supported a return to full physical activity. I have been given a licence to continue challenging myself. Despite my illness I can carry on living.

So it is that seven months after discharge from our 'Heart Emergency Centre' I find myself waiting to start my longest walk on the banks of the river Thames with a mixture of apprehension and excitement. People mingle, talk and fiddle with kit until there is no more time to prepare. The 100Km route follows the river Thames from Putney bridge to Henley. My aim is to walk this in less than 24 hours. I know that during the journey I will feel great, I will feel lousy, I will help others and they will help me. I will reach the finish by concentrating on doing what is needed to simply keep moving forward, breaking the task into stages and focusing on each goal.

As the walk starts there is an atmosphere of celebration. The journey we have just begun mirrors life. Plans have been made but these can be undermined. Success is anticipated but not guaranteed. Following an initial period of congestion, the walkers soon spread out. Walking becomes a celebration of the freedom of rhythm. Freed of the restraints of work or planning, thoughts turn to reflection and rejoicing. This is my opportunity to remember when I would wake breathless every night, and the week when I was restrained by cardiac monitor wires worried if I would walk in the countryside again. Now I enjoy each free moment to simply stride.

For the first stages, the river is dominated by rowers. Families, joggers and cyclists share the path even when it is clogged by walkers. During the first half of the route those who have chosen to attempt 25 or 50Km options walk with us. After half way the atmosphere changes. The light fades and the number of companions reduce. Now everyone has tired legs yet maintains a drive to move forward. There is no place for reflection now. Problems need to be managed not dwelt on. I meet people hobbling with blisters and laying down in the grass exhausted. I have de-roofed and taped my own blister.



My gait is becoming stooped but not yet fully bent. From a party on a passing boat music pulsates '... I will walk 500 miles and I will walk 500 more...'

As the hours of darkness increase the challenge is testing, whispering, 'do you really want to do this? You could stop. A shuttle bus will take you to the finish'. There is only one answer. 'I will carry on. I will finish!'

My metabolism adapts to burning fats as all the carbohydrate has gone. Exertion becomes harder and breathing is laboured. I am now walking through 'the wall' so often talked about in marathons. The effects of carbohydrate depletion are most apparent following a fix of chocolate at a checkpoint. The surge of sugar gives my muscles energy to shiver, and the reason for my drop in motivation becomes apparent as I shake visibly, recovering from my chilling. Through the shroud of night, when I see only a bubble of light from head torches, I walk with three others. We become a team, four strangers united by a will to succeed. Fatigue hits at different times. Those feeling positive gently support quiet, determined strugglers who slip behind and onward we progress. For 10 hours of deepest darkness we trudge along a ribbon of worn grass and gravel. The only discoveries now are of what is inside us, all scenery having gone. My mind becomes my enemy as negativity pushes at every crack in my resolve trying to overwhelm my ambition until, just as the eastern sky brightens, the lights of Henley come into view. Emotion rises as the realisation that I will succeed builds inside. The struggle to reach here has penetrated to my deepest darkness so success means so much more.

I have cardiomyopathy. I also have a medal that shows I can challenge myself and still achieve things that I am proud of. My heart disease may limit my physical abilities, but I will not let a negative outlook limit me further. As professionals we are expected to reflect on adverse events. As a patient there is no place for reflection. As a patient my life is driven by looking ahead to a future that at times seemed in doubt.

The BAC Recommended code of practice for cytology laboratories participating in the UK cervical screening programmes 2015

Paul Cross

The BAC Code of Practice was launched in October last year, and will be available in the February edition of *Cytopathology*. It will also be available as a free download from the Wiley *Cytopathology* website

(See: http://onlinelibrary.wiley.com/doi/10.1111/cyt.2016.27.issue-1/issuetoc)

and also on the BAC website

(see: http://www.britishcytology.org.uk/go/publications/other-publications).

The revised and updated CoP are a standard reference for all laboratories operating within the various cervical screening programmes across the UK. Although many things are and will be changing in service delivery in the foreseeable future, the CoP are still be highly relevant.



Editor's indulgence: five top stories

Andrew Evered

- 1. The UK National Screening Committee recommends the adoption of HPV testing as the primary cervical screening test. http://legacy.screening.nhs.uk/cervicalcancer
- 2. A snapshot of cervical screening practice in the US reveals that: (1) most cytology laboratories do not limit cytotechnologist screening workload during the work shift; (2) one third of laboratories use image-assisted screening devices; (3) rapid prescreening as a quality assurance measure is used by only 3.5% of laboratories; (4) most laboratories screen a mix of ThinPrep, SurePath and conventional Papanicolaou tests. http://www.archivesofpathology.org/doi/full/10.5858/arpa.2015-0004-CP
- 3. A comparison of the performance of the Roche Cobas and Hybrid Capture 2 tests for the detection of high-risk human papillomavirus using both ThinPrep and SurePath preparations shows no statistically significant difference in the percentage of positive high-risk human papillomavirus results between the 2 liquid-based preparations with either assay. http://www.archivesofpathology.org/doi/full/10.5858/arpa.2015-0027-OA
- 4. Japan faces HPV vaccination crisis as government continues its negative position. http://www.thelancet.com/journals/lancet/article/PIIS0140-6736%2815%2961152-7/fulltext?rss%3Dyes
- 5. A new biotechnology company aims to develop a 'liquid biopsy' test for the early detection of cancer in asymptomatic individuals within three years.

http://www.thelancet.com/journals/lanonc/article/PIIS1470-2045%2816%2900016-4/fulltext? elsca1=etoc&elsca2=email&elsca3=1470-2045_201602_17_2_&elsca4=Surgical%20 Oncology|Internal%2FFamily%20Medicine|Radiation%20Oncology|Oncology|Lancet

Julietta Patnick's retirement

After a long and distinguished career, Julietta Patnick retired from her role for overseeing the Breast, Cervical and Bowel Cancer Screening Programmes and the Prostate Cancer Risk Management Programme during 2015.



Julietta Patnick's retirement, NHSSCP

Julietta first joined the NHS in 1979 and became involved in screening with the establishment of the Breast Screening Programme in 1987. In 1990 she was appointed National Coordinator of the Breast Screening Programme and, subsequently, National Coordinator of the Cervical Screening Programme. She later took responsibility for implementing additional programmes in cancer screening. Julietta graduated in Ancient History and Classical Civilisation from The University of Sheffield. She is a Fellow of the Faculty of Public Health. We wish her well in her retirement from all her friends in the BAC!



SOUTH WEST REGIONAL



2016 Course Schedule

Date	Gynae Courses	Fee*
13 June – 8 July	Introductory in Gynae Cytology	NHS £1000
		Other £1200
8-10 March	Update in Cervical Cytology for Technical Staff	NHS £300
7-9 June 13-15 Sentember		Other £350
6-8 December		
18 May	Update for Cytology Checkers	£100
19 April - cancelled	Undate in Cervical Cytology for Pathologists & Consultant	£100
18 October	BMS's & Holders of the Advanced Specialist Diploma in	
	Cervical Cytology	
27 April	Cervical Histology for Technical Staff	£100
12-13 April	Gynae Pathology for Trainee Colposcopists	£200
18-19 January	Cervical Sample Taker Training	£250
9-10 May 19-20 September		
21 January	¹ / ₂ Day Update in Cervical Screening for Sample Takers	
12 May		
12 September		
Data	Non Curros	Foo*
16 Fohrwary		100
16 February	Serous Fluid Cytology	£100
2 March	Respiratory Cytology	£100
11 October	FNA Cytology	£100
15 November	Urinary Tract Cytology	£100
15-18 March 6-9 September	Non-Gynae for Trainee Pathologists	£400

*PLEASE NOTE THAT NO FEE IS APPLICABLE FOR NHS STAFF BASED IN THE SOUTH WEST REGION

South West Regional Cytology Training Centre Department of Cellular Pathology

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

www.cytology-training.co.uk

Birmingham Women's NHS

BIRMINGHAM CYTOLOGY TRAINING CENTRE

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

Please see our website for full list of courses: www.bwnft.nhs.uk/professionals/cytology-training-centre/courses/course-calendar IBMS RCPath CPD accredited courses as appropriate

> INTRODUCTORY COURSES FOR NHSCSP DIPLOMA IN CERVICAL CYTOLOGY 4-week course— 8-19 February 2016 & 7-18 March 2016

FOLLOW-ON COURSES FOR NHSCSP DIPLOMA IN CERVICAL CYTOLOGY 11-15 July 2016

PRE-EXAMINATION COURSES FOR THE CITY & GUILDS/NHSCSP DIPLOMA IN CERVICAL CYTOLOGY 18-20 January 2016, 1-2 September 2016, 6-7 February 2017

UPDATE COURSES IN GYNAECOLOGICAL CYTOLOGY (ThinPrep & SurePath)

25 January 2016 (Checkers), 22 March 2016 (HPV), 21 April 2016 (Atrophy, latrogenesis), 16 May 2016 (Metaplasia), 27 June 2016 (Small cells), 21 July (HPV), 15 September 2016 (Atrophy, latrogenesis), 17 October 2016 (Metaplasia), 29 November 2016 (Small cells)

NON-GYNAECOLOGICAL CYTOLOGY MASTERCLASS—Dr Glen Dixon

19 April 2016 (fully booked) Ideal for BMSs or medical staff requiring an update

GYNAE PATHOLOGY COURSE FOR BMS UNDERTAKING RCPATH/IBMS ASD IN HISTOPATHOLOGY REPORTING 5 February 2016, 4 March 2016 & 15 April 2016

BIRMINGHAM HISTOPATHOLOGY COURSE

6-18 June 2016

(course includes optional Saturday & Sunday am for personal revision) This two-week course 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)

29 February-1 March 2016 12-13 September 2016

The programme for this course is a combination of lectures workshops and multiheader sessions. Includes a mock exam and is particularly suitable as revision for the Certificate in Higher Cervical Cytology Exam

NON-GYNAECOLOGICAL CYTOLOGY FOR TRAINEE PATHOLOGISTS (StRS)

22-26 February 2016 (fully booked), 5-9 September 2016

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

WEST MIDLANDS AUTOPSY PATHOLOGY COURSE

2 November 2016 (provisional)

INTRODUCTORY COURSE FOR ST1s 5-9 December 2016 (provisional)

Introduction to Gynaecological and Non-Gynaecological Cytology including Autopsy element

LECTURE SERIES IN GYNAECOLOGICAL PATHOLOGY

Pathology of Cervical Tumours 16 September 2016

Update for consultant pathologists and senior trainees with an interest in gynaecological pathology.

TRAINING OFFICERS' MEETINGS: 10 May 2016, 25 November 2016

LBC Conversion Courses, Ad hoc workshops and Off Site workshops can be arranged on request—please contact BCTC LBC Sample Taker Introductory and Update Training sessions are arranged regularly throughout the year

For further details and 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@bwnft.nhs.uk or Amanda.Lugg@bwnft.nhs.uk Website: http://www.bwnft.nhs.uk/professionals/cytology-training-centre



London Regional Cytology Training Centre

The North West London Hospitals MHS

2016 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•)

1st – 26th February 3rd – 28th October

Course fee:

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

FOLLOW UP COURSE (Thinprep•)

- $11^{th} 15^{th}$ April
- 25th- 29th July

Course fee:

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

PRE – EXAM COURSE (Thinprep•)

4th – 8th January 5th – 9th 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.

2nd - 3rd + 4th (Optional Mock Exam) March

Mock exam - +£50 Course fee: - £200

PATHOLOGISTS COURSE - NON GYNAE

This four day course covers non-gynaecological cytology.

- 14th 17th + 18th _(Optional Mock Exam) March 12th 15th + 16th _(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.

MEDIC'S 1-DAY UPDATE COURSE A refresher course for consultant pathologists/AP's

- 20th May
- 28th September

Course fee

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

Post Registration Courses

BMS/CYTOSCREENER UPDATE COURSE

- 12th 14th Januarv
- 9th 11th March
- $20^{th} 22^{nd}$ April
- 17th -19th Mav
- 6th 8th June
- 31st August 2nd September
- 22nd 24th November
- 7th 9th December

Course fee:

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

Introductory Non-Gynae Courses

RESPIRATORY CYTOLOGY COURSE

13th – 14th June .

SEROUS FLUID CYTOLOGY COURSE

22nd – 23rd September

URINE CYTOLOGY COURSE

- 29th 30th November
- Course Fees
- Contracted London regional participants: Free - Non-Contracted participants: £200

Medical Laboratory Aides (MLA's) 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.

- 25th April
- 16th 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.

NEPSEC North of England Pathology and Screening Education Centre



NEPSEC is the name for the merged NW and East Pennine Cytology Training Centres

We are excited to be able to announce a joint course programme and welcome individuals from our new merged areas and beyond...

One-Day Update Courses in ThinPrep[®] Cytology⁺

One-day updates covering areas such as HCGs glandular lesions and challenging and interesting cytological presentations from both squamous and glandular lesions

13th June, 7th Sept 2016

Course Fee*: £95

One-Day Hospital Based Programme Co-ordinators Course⁺

Aimed at Hospital Based Programme Coordinators (HBPCs) both experienced and new from any specialty. Includes an introductory session covering your role and responsibilities as wellas governance, lines of accountability, incidents, invasive cancer audit and the link between the audit and disclosure

29th June 2016

Course Fee*: £120

Breaking Bad New Workshop⁺

Designed to give delegates the opportunity to explore some of the communication challenges they face. Would be ideal for anyone involved in feedback to patients through disclosure.

30th June 2016 Course Fee*: £120

Update courses in Non-Gynae Cytology⁺

A series of three one day courses covering serous fluids, urine and respiratory cytology ideal for anyone seeking an update in these areas, particularly those intending sit the IBMS diploma. Includes an optional fourth half-day covering aspects of the IBMS exam.

26th -29th April 2016

Course Fee*: £120 per day/£395 for all 4

One-Day Introductory Non-Gynae Cytology Workshops[#]

Ideal for anyone requiring an introduction to nongynae cytology. These courses will cover specimen preparation of Head & Neck samples and understanding the morphology of urine, respiratory and effusion cytology. Very useful to anyone undertaking their Specialist Portfolio.

9th–12th May & 21st–24th November 2016 Fee*: £120 per day

Update Course specifically for Checkers & Experienced BMS staff⁺

Aimed specifically at those intending to, or already acting as Checkers. Includes a session on basic histopathology and microscopy sessions on what can be called negative and what can't!

14th & 15th July 2016 Course Fee*: £120 per day or £200 for both days

*These courses are running from the former EPCTC site

[#] These courses are running from both the East Pennine and North West Cytology Training Centre sites. Please check with our admin team for exact details

*Participants from the North West, North East, Yorkshire and East Midlands will incur £15 administration fee per day on all courses listed. All prices are subject to change.

Further information and application forms for any of our courses are available from our Administration Team:

Kathryn Hawke – 0113 246 6330 <u>kathryn.hawke@nhs.net</u> Jen Bradburn – 0161 276 8804 <u>jennifer.bradburn@cmft.nhs.uk</u>

www.cytologytraining.co.uk

Director: Dr J H F Smith BSc MBBS FRCPath MIAC Deputy Director: Dr M R Holbrook BM BS BMedSci FRCPath



NHS Lothian

Scottish Cytology Training School

Programme 2016/17

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

Training School Director

Sue Mehew Tel: 0131 242 7149 Email: <u>sue.mehew@nhslothian.scot.nhs.uk</u>

Training School Manager

Fiona McQueen Tel: 0131 242 7149 Email: <u>fiona.mcqueen@nhslothian.scot.nhs.uk</u>

Training School Administrator

Training School Administrator Pathology Department Royal Infirmary of Edinburgh 51 Little France Crescent Edinburgh EH16 4SA

Tel: 0131 242 7135 Email:<u>scts@nhslothian.scot.nhs.uk</u>

Application forms available on request from: <u>scts@nhslothian.scot.nhs.uk</u>

NHSCSP Accredited Training Centre

Courses held at The Bioquarter, Royal Infirmary of Edinburgh, 1st Floor, Building 9, Edinburgh Bioquarter, 9 Little France Road, Edinburgh. EH16 4UX

unless states (**QEUH**) Queen Elizabeth University Hospital, Glasgow.

Non-NHS Labs – price on application All courses are Liquid Based Cytology (ThinPrep) Courses are CPD accredited

Introductory Course

5 September – 30 September 2016 22 February – 18 March 2017

£1000

Introductory Course Part 2

21 November – 25 November 2016

Update Course

19 – 20 April 2016 8 – 9 June 2016 (QEUH) 8 – 9 November 2016 (QEUH) 7 – 8 December 2016 1 – 2 February 2017

£100 per day

Pre-Exam Course

22 - 24 Aug 2016 (for Oct Exam)

£250

Workshops – BMS Medical/Consultant Staff

29 November 2016 *tbc*

£100

ST1 Introduction to Cervical Cytology

5 - 9 September 2016 *tbc*

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

20 – 22 September 2016 *tbc*

£100 per day

ECC 2016 2-5 October Liverpool, UK www.cytology2016.com

Registration and Abstract Submission sites are now open for ECC 2016!

The 40th European Congress of Cytology, organised by the BAC, will be hosted in Liverpool from 2nd - 5th October 2016 at the ACC Liverpool.

www.cytology2016.com

We hope you will join us to share international experiences,

expectations and future developments at ECC 2016.

it Mannion Centre





ACC Liverpool



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Front Cover image: Small cell carcinoma pleural fluid





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