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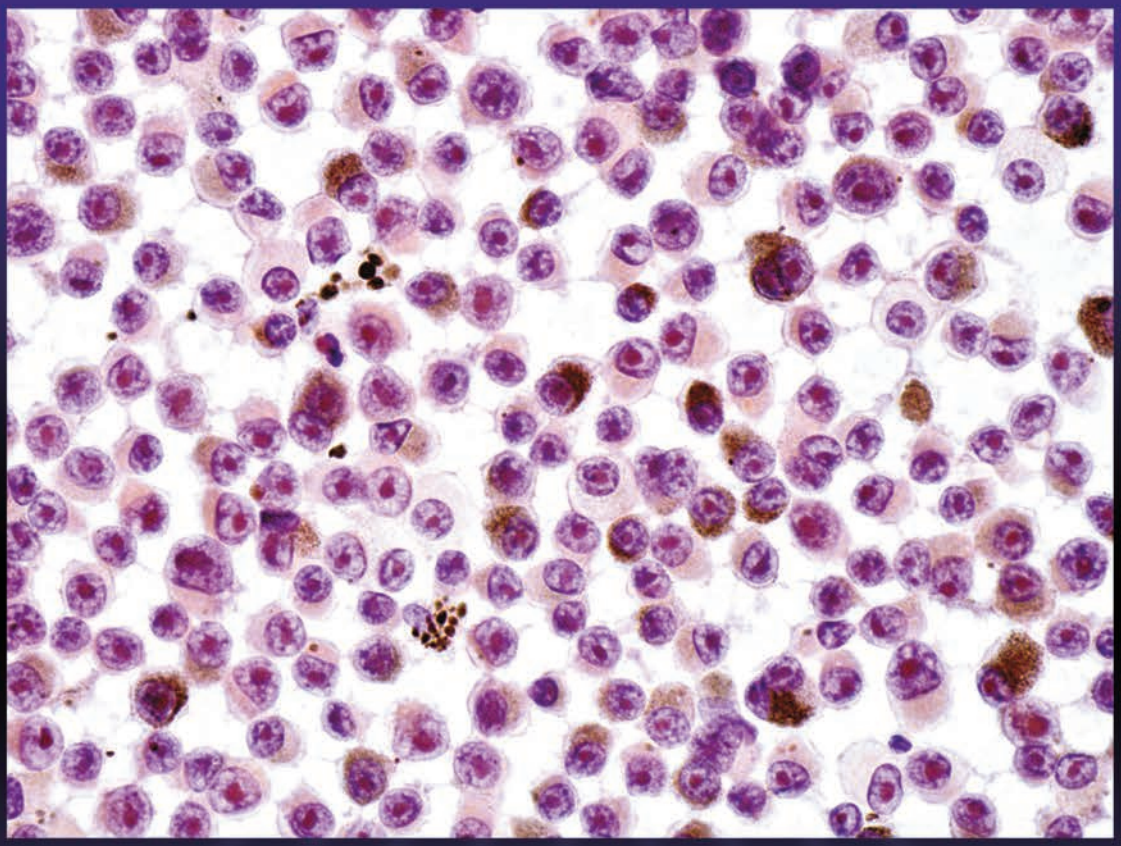

BAC British Association for Cytopathology

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Editorial

Andrew Evered

SCAN has been published twice yearly since 1990. During this time, cytology has been through changes that could hardly have been imagined 23 years ago, at least in the UK. The publication has recorded this roller coaster ride in ways that other publications perhaps cannot. Its editors aim to offer a careful balance of education, information and entertainment. Some articles are written with great seriousness, others with tongue placed firmly in cheek, but all must contain the essential ingredients of honesty and integrity, and must be written with the best interests of BAC members in mind. *SCAN* continues to evolve under the watchful eye of its editors, the BAC Executive and members of the Association.

Unlike biological evolution, which involves slow and gradual adaptation driven by random events, the direction and speed with which *SCAN* continues to develop is under the direct control of BAC members. What do you think about *SCAN?* Do you look forward to reading it? If not, why not? How would you like to see it develop? Why not submit an article, or write a letter to the editor with a burning issue you want to get off your chest, or perhaps send in a quiz or a few photos of an interesting case. We need engagement from BAC members to keep *SCAN* alive and kicking.

I hope that I have achieved the right balance of sobriety and lightheartedness in this issue. The open letter to the BAC Executive co-written by me and the indubitable Mr Behdad Shambayati stems from a deep concern we have about scientist training and career pathways in cytopathology. We sense a chasm opening up between cytopathology and sister disciplines unless action is taken. That's the serious offering. As for 'tongue in cheek', I offer a completely fictional exchange of letters between a perplexed Dr George Papanicolaou and his local research committee. For those who like a bit of hard science, Stephen Potter (a colleague at Cardiff Metropolitan University) describes his ongoing investigations of the effects of aspirin on the growth of cervical cancer cells. The preliminary results are very interesting, but we are a long way from recommending aspirin for the chemoprevention of this terrible disease.

Inside you will also find updates from BAC committee members as well as invited articles from John Crossley and Mike Rowell, both of whom are prominent members of our profession and will be known to many of you. I thank them all for helping to make this issue of *SCAN* vibrant, interesting and fun to read. I can't speak for my co-editor but despite the extra hours I must find to turn out the finished product I feel immensely honoured to be a cog in *SCAN's* machinery.

Andrew

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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

BAC British Association for Cytopathology

Chairman's Report

Allan Wilson
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September 2012 seems a distant memory but I hope those of you who attended the first BAC Scientific Meeting at Keele enjoyed a very positive meeting which was interactive and delivered a high quality scientific programme.

There was a real positive "buzz"about the meeting and the feedback has been excellent. I must pay particular thanks to Alison Cropper and the meetings subcommittee for all their hard work to deliver the meeting at a very challenging time. It was extremely gratifying to note that Austin Marshall, one of the overseas speakers decided to join the BAC after attending our meeting. It is also heartening to observe a steady trickle of new members applying to join our Association.

As mentioned in the previous issue of SCAN, we have decided not to hold a three day scientific meeting this year but we have arranged three short meetings through the year which I hope many of you will be able to attend. The programme of meeting is designed to be attractive to all of our members, deliver microscopy workshops and forge partnerships with other professional bodies. Full details are in Alison's report in this issue.

This issue of SCAN focuses on Modernising Scientific Careers (MSC) and its impact on Cytology. My suspicion is that most cytology professionals know little about this national project that is now delivering training programmes through the newly formed Academy and School of Healthcare Science. It is unlikely that the proposals from MSC will impact greatly on staff currently employed in cytology. However, we must look at the opportunities that MSC offer, particularly to existing staff. The days of ONC and HNC or day release BSc have long gone, the options now are undoubtedly more complex but offer clear opportunities for those willing and able to work hard and move between the "MSC boxes" as described elsewhere in SCAN.

The School of Healthcare Science has established a Scientist Training Programmes (STP) mirroring the programmes delivered for medical students with the expressed objective of producing scientists who will be recognised as equivalent to Medical Consultants. There are currently three candidates on the Cytopathology STP. On completion of this programme these candidates will register as clinical scientists but it is far from clear what their role will be in a Cytopathology laboratory. Elsewhere in SCAN you will find a few questions on MSC. I would urge all members to respond to these questions via our website. This will allow us to clearly represent member's views as the new training programmes become established

The BAC proposal for an Advanced Specialist Diploma (ASD) in non-gynae cytology will be discussed at the IBMS/RCPath conjoint board meeting on 15th February. Tom Giles is leading this for the BAC and the next step will be to develop a curriculum and an examination format. If this proposal is accepted, this represents an opportunity for holders of the Diploma in Expert Practice in non-gynae to attain a qualification that will be the non-gynae equivalent of the gynae ASD and allow holders to report abnormal fluids, urines and respiratory specimens. An announcement will be made on our website when further information is available.

The Gynae Code of Practice group chaired by Louise Smart met last month in Manchester and made excellent progress. A slimmer, more focussed document will emerge this year and will reflect changes in practice such as HPV testing. A work plan has been agreed and sections of the document divided among the group. The group has already identified areas where there is a lack of evidence and we plan to use the website to gather information on current professional practice, as stated before we are reliant on our members to ensure the guidance the BAC gives is reflective of current practice.

The proposal to introduce a national EQA scheme for non-gynae as part of the Cellular Pathology Technique NEQAS scheme is gathering pace. Paul Cross has been working hard on the proposal and the BAC executive has agreed to fund the pilot study to get this important initiative off the ground. Given the support for the introduction of such a scheme, we hope all cytology labs will join this scheme when it is launched later in 2013.

It is almost two years now since the first BAC executive met and we are now planning for our first call for nominations to sit on the executive. The nomination process will be discussed at the executive meeting at the end of March and information will be sent to all members. I would ask all members to consider standing for election to our executive. If you wish to discuss the commitment required please contact any member of the executive.

Finally, I must congratulate Nick Dudding on his recent award. Nick was a member of the NAC Executive and BSCC Council for many years and his support of both organisations over the years has been invaluable. I am well aware of the long hours and hard work that Nick puts into the East Pennines Training Centre and into professional issues in general. He is willing source of advice, teaching material and counsel and this award recognises his years of dedication to our profession. Well done!

Do you know your ABC?

Dr Karin Denton
Southmead Hospital, Bristol

Achievable standards, Benchmarks for reporting and Criteria for evaluating cervical Cytopathology (third edition) was published recently and contains information which will be critical to everyone reporting cytology in the cervical screening programme in England.[1]

The main thrusts of the document are to revise the terminology used for reporting cervical cytology, to revise the performance indicators, and to include the now standard management protocols involving HPV testing.

It had been hoped that the definition of sample adequacy could also be updated, but unfortunately the outcome of a large study investigating this question is not yet known. However, unlike previous NHS CSP publications the intention with this one is to publish refinements as they are agreed, without having to wait for a full new edition.

Terminology

The changes are summarised in table 1.

Previous terminology (BSCC 1986)	New terminology
Borderline change	Borderline change in squamous cells
	Borderline change in endocervical cells
Mild dyskaryosis Borderline change with Koilocytosis	Low grade dyskaryosis
Moderate dyskaryosis	High grade dyskaryosis (moderate)
Severe dyskaryosis	High grade dyskaryosis (severe)
Severe dyskaryosis ?Invasive	High grade dyskaryosis ?invasive squamous carcinoma
?glandular neoplasia	?glandular neoplasia of endocervical type
	?glandular neoplasia (non-cervical)

The document does not contain photographs but it is referenced back to the original BSCC proposed terminology publication, which does, and could usefully be read in conjunction with this section.[2]

As in its predecessor, ABC2, there are sections on pitfalls and areas of difficulty, especially focussing on distinguishing the new categories.

This is the document which lays out the details of when to perform HPV triage and test of cure. Common situations will be familiar from the NHS CSP HPV implementation guidance, but most people will occasionally need to check the rarer scenarios (for example CGIN is excluded from Test of Cure).

Performance indicators

This section has been completely revised and rewritten. It contains a fundamental concept, missing until now from the CSP; a mission statement.

'The objective of cervical screening is to reduce cervical cancer incidence and mortality by screening with a high sensitivity for the detection of CIN2 or worse, whilst maintaining a high specificity.'

This is really critical and the new performance indicators are all aimed at maximising performance at detecting CIN2 or worse lesion.

The concept of defining the range and then identifying outliers which need further investigation is maintained. The most familiar survivors are Positive Predictive Value (PPV) and rate of inadequate samples, whose ranges have now been extended to the 5th -95th percentiles.

A new addition is Referral Value (RV) – defined as the number of women referred to colposcopy to detect one case of CIN2 or worse. Fascinating data from the KC61 returns show that there is a surprising range, with up to 4.5 women being referred to detect 1 case of CIN2 (or worse) in some screening services. It is important to think of RV and PPV as screening service rather than laboratory measures, because they can be impacted by histology and colposcopy issues. Again, any service outside the 5th -95th percentile will be investigated to look for an explanation.

This section also includes several other measures which may be helpful but are not mandatory – these include the Abnormal Predictive Value (APV) which is especially useful when combined with PPV.

Others included are the Mean CIN score, and the HPV positive rate in borderline/low grade samples.

The intention of this section is clearly to give the programme the tools to make outcomes more uniform for women regardless of where they are screened, and this is very welcome.

The publication finishes with useful appendices on coding and endometrial cells, and there are hyperlinks throughout to other useful related guidance documents.

Since the document was published on line, it has been announced that all its changes will be implemented on April 1st 2013 – Highly recommended reading for all!

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What can cytologists learn from the Reverend Thomas Bayes?

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Sheffield Teaching Hospitals NHS Foundation Trust

The Royal Hallamshire Hospital in Sheffield is one of six Sentinel Sites which evaluated the feasibility of introducing high risk human papilloma virus (HR-HPV) testing for the triage of borderline changes and mild dyskaryosis, and for the 'test of cure' of women treated for cervical intraepithelial neoplasia (CIN). Sheffield is historically famous for stainless steel, the Crucible Theatre, 'The Full Monty', and Sheffield FC, the oldest football club in the world. What is probably less well known is that Sheffield is the familial origin of the mathematician and Presbyterian minister Thomas Bayes.

Bayes was born in 1701and his family moved to London soon after. At the age of 18 he enrolled at the University of Edinburgh to study logic and theology. In 1722 he returned to London to assist in his father's non-conformist chapel before moving to Tunbridge Wells to become minister of the Mount Sion chapel. He is known to have published two works in his lifetime; one theological piece entitled *"Divine Benevolence, or an Attempt to Prove That the Principal End of the Divine Providence and Government is the Happiness of His Creatures"* (1731), and one mathematical composition, *"An Introduction to the Doctrine of Fluxions, and a Defence of the Mathematicians Against the Objections of the Author of the Analyst"*(1736). However, Bayes is probably best known for a paper that was presented to the Royal Society in 1763, two years after his death, by his friend Richard Price. The paper is entitled *"An Essay towards solving a Problem in the Doctrine of Chances"* and included a statement of a special case of what has become known as Bayes' Theorem.

Bayes' Theorem relates to probability theory and statistics. At this point you may be thinking this article has been printed in the wrong publication, but probability and statistics are the foundation stones of all screening programmes. Population screening employs a particular initial test to assess the risk of the presence of a subclinical condition in an individual. A positive result will initiate further diagnostic tests for a more accurate assessment. An example of this is mammography for the detection of breast cancer followed by tissue biopsy for those women testing positive. In general, a screening test has two outcomes: positive or negative. However it is important to remember that test results can be flawed: they can detect things that aren't there (false positives) and miss things that are there (false negatives). There are a number of statistical questions we could pose regarding breast screening and positive results.

- What is the probability that a woman who does not have breast cancer will have a positive mammography?
- What is the probability that a woman with breast cancer will have a positive mammography?
- What is the probability that a woman with a positive mammography has breast cancer?

The first question relates to the specificity of the test; higher specificity produces fewer false positive results. Specificity is calculated using the equation:

$$\text{Specificity} = \frac{\text{True Negatives}}{\text{True Negatives} + \text{False Positives}} \times 100$$

The second question relates to sensitivity; higher sensitivity produces fewer false negative results. Sensitivity is calculated using the equation:

$$\text{Sensitivity} = \frac{\text{True Positives}}{\text{True Positives} + \text{False Negatives}} \times 100$$

The third, often referred to as the positive predictive value (PPV) is related to both the sensitivity and specificity of the test, but, and this is where Bayes' Theorem comes into play, it is also related to the prevalence of the disease being tested for. PPV is calculated using the equation:

$$\text{PPV} = \frac{\text{True Positives}}{\text{True Positives} + \text{False Positives}} \times 100$$

If we apply some theoretical figures to breast screening we can demonstrate the effect prevalence has on the PPV of a screening test. Suppose mammography has a sensitivity of 80%, i.e. 80 out of every 100 women with breast cancer will test positive, and a specificity of 95%, i.e. 95 out of every 100 women who do not have breast cancer will test negative (but 5 of these 100 healthy women will test positive), and the prevalence of breast cancer is 1%, i.e. one woman in 100 has breast cancer. If we screen 10,000 women, 100 will have breast cancer, 80 of which will test positive (true positives) and 20 will test negative (false negatives). 9,900 will not have breast cancer, 9,405 of which will test negative (true negatives) and 495 will test positive (false positives).

The PPV of mammography, i.e. the probability that a woman with a positive mammography has breast cancer is

$$PPV = \frac{80}{80+495} \times 100 = 13.9\%$$

This may seem a surprisingly small figure, but even if the sensitivity and specificity of the mammography test remain exactly the same and we screen the same number of women, if the prevalence of breast cancer falls to 0.2% we will now only have 20 women with cancer, 16 of which will test positive. Within the 10,000 women screened there will now be 9,980 women without breast cancer, but 499 of these will test positive. Under these lower prevalence conditions the PPV becomes:

$$PPV = \frac{16}{16+499} \times 100 = 3.1\%$$

If the first figure seemed small, this second figure is verging on the ridiculous! In this scenario 97 women are incorrectly told they may have breast cancer for every 3 women that do have the disease. Clearly, this theoretical breast screening programme would be 'probably doing more harm than good'. You may be wondering why this figure is so low when the sensitivity is 80% and the specificity is 95%. The simple answer is prevalence. When prevalence is low, the 'disease free' individuals vastly outnumber the 'diseased' individuals. As we can see with the examples above, even with a test that has a specificity of 95%, when prevalence is low the number of false positive test results far exceed the true positive results, making a positive result virtually irrelevant.

To prove the point, if, within the 10,000 women screened the prevalence were 90%, we will now have 9,000 with cancer, 7,200 of which will test positive. There will now be 1,000 women without breast cancer, but 50 of these will test positive.

Now the PPV of mammography, i.e. the probability that a woman with a positive mammography has breast cancer is

$$PPV = \frac{7200}{7200+50} \times 100 = 99.3\%$$

With a breast cancer prevalence of 90% a positive mammography result is virtually conclusive of cancer, but it is important to remember that in this scenario, even without screening, all women have a 90% chance of having the disease. You can thank Thomas Bayes for all these mind-bending facts!

2008 saw the commencement of the vaccination of 12 – 13 year old girls in the UK against the high-risk human papilloma virus (HPV) types 16 and 18. There was also a phase of 'catch-up' where young women up to the age of 18 were vaccinated. These two virus types are responsible for more than half of the cases of cervical intraepithelial neoplasia (CIN) grade 2 & 3 and cervical glandular intraepithelial neoplasia (CGIN) and for around 70% of cervical cancers. This vaccination programme means that the next 2 to 3 years will see these vaccinated women entering our cervical screening programmes, which in turn will bring about a year-on-year reduction in the baseline prevalence of CIN, CGIN and cervical cancer.

Even if we can maintain the current sensitivity and specificity of cervical cytology it is quite clear from the theoretical examples of breast screening above, that the inevitable outcome of this will be a reduction in the PPV of cytology and therefore a reduction in the benefit to women of cervical screening (as more 'disease free' women will be given a positive result). I said 'even if we can maintain the sensitivity and specificity of cervical cytology' because I believe the reduction in prevalence of CIN, CGIN and cancer will also bring about a reduction in the sensitivity of cytology screening. Allow me to use another theoretical situation to explain my reservations.

A cytologist primary screens 5,000 cervical cytology samples per annum. Within this workload there is a prevalence of high grade dyskaryosis of 1.4%, which equates to 70 samples with moderate dyskaryosis or higher. Let us assume that for every 2,500 samples screened this screener misses 1 high grade dyskaryosis. In the year the screener will detect 68 and miss 2, the screening sensitivity for high grade dyskaryosis will be

$$Sensitivity = \frac{68}{68+2} \times 100 = 97.14\%$$

This figure is well within the quality standard (≥95%) expected of primary screening. If, in a vaccinated population, the prevalence of high grade dyskaryosis falls to 0.7%, there will be only 35 samples with moderate dyskaryosis or higher, however there is no reason to believe the screener will not still miss the same number of high grades per 2,500 samples screened. The screening sensitivity for high grade dyskaryosis will now be

$$Sensitivity = \frac{33}{33+2} \times 100 = 94.29\%$$

The sensitivity of screening has fallen and is now below 95%, even though, in terms of errors made per samples screened, the performance has remained the same. This drop in sensitivity could also be exacerbated by the increased 'expectation of negative' which comes with lower prevalence, i.e. if you don't find something often enough, you begin to expect that it will not be there, which lowers your attention and makes you more likely to miss it if it is present.

Faced with an inevitable fall in PPV and probable fall in sensitivity of cytology cervical screening programmes may begin to look for alternative strategies. One possible approach would be to introduce high risk HPV testing as the primary screening tool coupled with cytology as a method of triage to determine which women require referral to

colposcopy. Various studies have demonstrated that HPV testing is more sensitive than cytology for the detection of CIN2, CIN3 and CGIN. However, it has a relatively low specificity, with many women who have no significant cervical pathology testing positive. If cytology is used to triage the HPV positive cases there are two beneficial outcomes. Firstly, only women who are HPV positive and have cytological abnormalities are referred to colposcopy rather than the entire HPV positive cohort. Secondly, the elimination from cytology screening of the HPV negative cases artificially increases the prevalence of the abnormal cases, thus the PPV of cytology (following a positive HPV test) will increase.

However, primary screening with HPV testing is not without its pitfalls. When prevalence increases, PPV increases *if* sensitivity and specificity remain the same. There is no reason to believe the sensitivity of cytology will change significantly when it is used as a method to triage HPV positive cases, but specificity may fall. The reason for this is twofold; firstly there will be an 'expectation of positive' because of the increased prevalence of abnormal cases, and secondly, the cytologist will know that all the samples screened are high risk HPV positive which by definition increases the risk of significant disease within the cervix and makes a 'diagnosis' of negative more difficult. When cytology is used as a method of triage for HPV primary screening, it is vital that strict cytological criteria are applied and adhered to when reporting samples as abnormal, in order to maintain the relatively high specificity of cervical cytology.

This brings me nicely back to where I began this article. Early in 2013 the Royal Hallamshire Hospital will, along with the other five Sentinel sites begin using high risk HPV testing as a primary screening tool for a significant proportion of its workload. It will be interesting to see if the potential benefits of HPV primary screening are realised and are translated into a more efficient and accurate screening programme.

Quality – what is it good for?

Dr Paul Cross
Queen Elizabeth Hospital, Gateshead

To paraphrase Edwin Starr "Quality — what is it good for?" If you are sitting in the DoH the answer may well be "absolutely nothing". Following the fallout from the Kings' Mill episode who can blame them? This high profile apparent failure of quality assurance at a laboratory testing for breast tumour oestrogen receptor status, resulting in 60 women not receiving the best available treatment, hit the news last year.[1] This incident has called into question the methods by which cellular pathology laboratories, and possibly pathology as whole, assure the quality of their work. An external review of the service, involvement of the CQC and letter to all Trusts has certainly indicated that this is being taken seriously.[2] The announcement that the DoH was to undertake a review of quality assurance across Pathology, led by Ian Barnes (National Clinical Director for Pathology) which "will scrutinise NHS arrangements for the oversight and safeguards of laboratory testing", and "will work to find out what more can be done to strengthen processes that exist to detect, correct and prevent problems like these in the future". Let no one be left in any doubt – this is a topic being taken very seriously!

As cytologists we are all too aware of the numerous quality standards within cervical cytology, and the use of Quality Assurance Teams (QATs) to make sure they are adhered to. But as cytologists we are also well aware of the dearth of such an approach within non-gynaecological (NG) cytology. How has this been allowed to develop? Why has this not been addressed? Why have we, as professionals, allowed this to be so?

The use of NG cytology has been around ever since the beginning of cytology as a technique. Cervical cytology, and that of cervical screening, developed much later. Organised cervical screening started in the late 1980s in England, and it did not take that long for serious failings within it to be found and publicised. The high profile problems at Kent and Canterbury in particular at the height of the then GP Fund holding system (with GPs commissioning services and Trusts far more competitive for business between each other) led directly to the quality initiatives within the NHS CSP. These major publications, starting in 1995, revolutionised how cervical cytology was performed, and led to external bodies, such as the QATs, effectively "policing" their use. Laboratories also of course had Clinical Pathology Accreditation (CPA) to comply with. CPA applied standards and guidelines as they then existed as part of their overall quality approach, which have become significantly more onerous with each passing year. However, again, whilst we all had to comply with EQA, and national guidelines etc such an approach within NG cytology was again largely conspicuous by its absence.

The implementation of the Breast Screening Programme (BSP) in the 1980s relied heavily on the use of breast fine needle aspiration (FNA) cytology for diagnosis. Whilst all pathologists reporting histology from breast screening derived cases had to take part in national breast histology EQA (and still do), there was no such requirement or system for breast FNA cytology. Monitoring of outcomes for cytology was a requirement, but this was effectively a cyto-histological correlation audit. With the demise of cytology within the BSP, the need and opportunity for such a scheme has gone.

Apart from andrology, there is no other national UK NG cytology scheme in existence. There are some regional interpretative schemes,[4] which can act to educate and raise standards, but there is a complete contrast with the world of gynaecological cytology. The BSCC did produce guidelines for both gynaecological and in particular NG cytology, but these are not mandatory, only good practice.[5]

Why is this? As stated above, the cervical screening programme learned from high profile errors. The world of NG cytology, however, has not really had such a high profile publically or professionally. Egan undertook a telephone survey of cytology laboratories in England and Wales in 1999.[6] Of those that replied (146 out of 212) they showed enormous variation in the approach used to monitor quality in NG cytology. As Egan stated, this "study suggested that an integrated approach to quality had not been adopted in English and Welsh cytology laboratories and that there may be a need for a more strategic approach with greater availability of EQA, guidelines on quality tools, closer linkage of accreditation and quality procedures and the production of minimum and ideal standards." That was over a decade ago. Why has this not occurred?

We can speculate about these apparent failings. I am sure we can all quote good local initiatives and practice, but that is what they are – local. In this current climate we need, and the public expects, a better nationally co-ordinated approach. Quality has always been taken for granted – events such as the King's Mill episode has eroded the quality glow of pathology. It has raised doubts in the minds of the public, commissioners and of politicians. We must, as a discipline fighting to exist and develop in the world of modern medicine, ensure we are as good as we can be. Can we honestly say that this is so? It is up to all of us who believe in cytology as a valuable clinical, diagnostic and effective tool to ensure we can demonstrate this. If not, we may wither on the vine. The changes within the NHS and the development of Clinical Commissioning Groups and GPs' with direct budgetary control for services smacks those of us with long enough memories of the times of GP fundholding and how quality was lost in the pursuit of business. We must not allow this to happen again.

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Non-Gynaecological Cytology technical EQA scheme pilot

As members will be aware, the BAC is working with the UK NEQAS CPT to help develop a technical EQA scheme for non-gynae cytology. The BAC survey from last year identified a need for this, and the BAC is keen to help promote any moves to promote quality in cytology as a whole. The pilot phase is intended to operate as two rounds, over the Spring and Summer of 2013, and will help develop the necessary SOPs etc for it. After this the plan is for UK NEQAS CPT to incorporate the scheme into its repertoire. The initial first phase pilot was heavily oversubscribed, which augers well for the scheme! Further news and developments about the scheme will be posted on the BAC and UK NEQAS websites (www.ukneqascpt.org.uk).

Effects of aspirin on the growth of cervical cancer cells: A mini review

Stephen Potter,
Cardiff Metropolitan University

Background

Cervical cancer is currently the most common form of cancer in women under 35 in the UK and is the second most common cancer in women worldwide, affecting around 1 in 10 women diagnosed with cancer.[1] The greatest causal factor of cervical cancer is infection with high risk human papillomavirus (HPV), and two types in particular are implicated in at least 70% of cervical cancers worldwide.[2,3] High risk HPV oncoproteins enhance cervical carcinogenesis by causing abnormal functioning of the genes and proteins that normally regulate cell homeostasis. One way that it achieves this is through the upregulation of prostaglandin synthesis via cyclooxygenase (COX)-dependent pathways.[4] Cyclooxygenases are key enzymes that catalyse the first stage of prostaglandin synthesis. There are two forms of this enzyme, COX-1 and COX-2. COX-1 is expressed in low levels in all cells but plays a role in COX-2 and prostaglandin regulation in cervical neoplasia. COX-2 expression is virtually undetectable in most normal tissues and is absent or weakly expressed in the cervix except during pregnancy, labour, parturition and at certain stages of the menstrual cycle.[5] However it is over-expressed in a substantial proportion of cervical cancers at all stages of development, including precancerous lesions.[6,7] Both forms of COX promote chronic inflammation but their involvement in tumour biology is far more sinister. In neoplasia, COX enzymes may enhance cell growth, blood vessel formation (angiogenesis) and tumour invasiveness, and may inhibit immune recognition and programmed cell death (apoptosis).[4,8,9,10] Pharmacological inhibition of COX-1 or COX-2 reduces tumourigenesis.[11] This, combined with the fact that COX-2 overexpression in these tumours is associated with poor patient prognosis,[12] makes COX a useful target for both therapeutic intervention and chemoprevention of cervical neoplasia.

Can aspirin be used to treat cervical cancer?

Aspirin (acetyl-salicylic acid) is one of the most widely used drugs in the world and has been used for a number of conditions for over 100 years. Aspirin was originally developed as an analgesic, anti-pyretic and anti-inflammatory drug. Over the last 25 years numerous studies have shown that aspirin use significantly reduces the incidence of epithelial cell cancers, particularly colorectal cancer.[8,13,14,15] Long term aspirin use may also reduce the incidence of various other cancers, such as bladder, gastric and breast cancer, by 40-50%.16 Its effect on cervical cancer is less well known.

The molecular mechanisms involved in aspirin's actions on cancer have been well researched. However, these mechanisms are less clear in the context of cervical cancer but are known to be highly complex and involve multiple signaling pathways. Broadly, aspirins effects can be classified according to the schematic in figure 1.

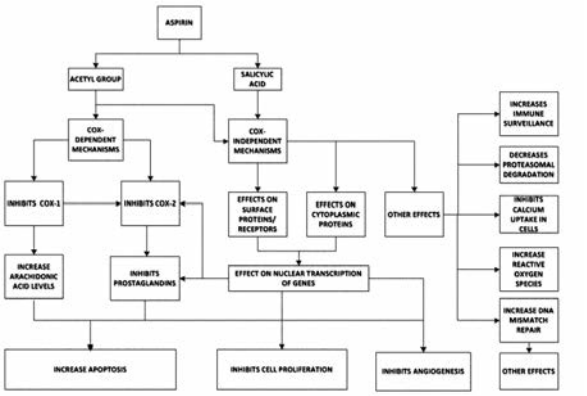

Figure 1 Schematic diagram to show various anti-cancerous effects of aspirin in cervical cancer

Aspirin is a COX inhibitor

The physiological effects of aspirin are due mainly to its ability to inhibit COX-2 enzymes.[9] The inhibition of COX-2 in cancer cells leads to a reduction in prostaglandin synthesis, which ultimately leads to reduced cell growth, increased apoptosis and improved immune surveillance.[17] Aspirin differs from other non-steroidal anti-inflammatory drugs (NSAIDS) in its ability to irreversibly inhibit both COX-1 and COX-2, but with a greater selectivity towards COX-1.[8] Given that COX-1 is also over-expressed in cervical cancer cells, it is likely that aspirin's actions are through dual-COX inhibition.

Aspirin can acetylate key proteins associated with cancer

Inhibition of COX and therefore prostaglandins cannot solely be responsible for aspirin's chemopreventive effects, since similar effects are have been noted in COX-deficient cell models and prostaglandin-deficient animal model

studies.[18] Aspirin consists of an acetyl and salicylate group and both groups are known to have very different molecular targets. Aspirin's acetylation properties are thought to be the one reason why it differs from other NSAIDS. Recent studies have shown that aspirin is able to bind and modulate multiple cellular proteins in cancer cells through acetylation of lysine and serine residues.[19] For instance, aspirin's role as a COX inhibitor is due to the binding of its acetyl group with serine residues on cyclooxygenases, causing irreversible inhibition of function.[20] Furthermore, aspirin at physiological concentrations is able to acetylate several cellular components relevant to cervical cancer, such as the tumour suppressor p53, causing induction of growth arrest or cell death.[21]

Aspirins metabolite, salicylic acid, acts through COX-independent pathways

It has been suggested that aspirin's main metabolite, salicylic acid (SA), plays a larger role in COX-2 inhibition than acetylation, since acetylation of serine on COX-2 does not necessarily lead to inactivation.[18] One study has suggested that SA may instead be a weak competitor for COX with its target arachidonic acid.[22] SA is a poor inhibitor of COX directly, yet is still seen to reduce levels of COX's metabolites, prostaglandins.[23] It is far more likely that SA indirectly modulates COX through nuclear transcription factors, which mediate the balance between cell life and death. Suppression of Nuclear factor Kappa Beta (NFKB) transcriptional activation is thought to be the main target of SA, since NFKB plays a major role in regulating COX expression.[24,25] SA can also degrade NFKB's inhibitory cofactor genes in cervical cancer models.[26,27] The mechanism by which SA achieves this is thought to be independent of COX.[28] Other nuclear transcription factors associated with COX in cervical cancers may also be pharmacological targets of aspirin, such as AP-1 and PPAR receptors.[5,23,29]

Aspirin induces cancer cell death through multiple pathways

Apoptosis is programmed cell death in response to a stress signal, cell damage, inflammation or mutations. The central regulators of apoptosis are caspases, which can respond to extracellular inducers such as TNF or Fas, or to intracellular inducers, such as mitogen activated kinases. This process also crucially involves the tumour suppressor p53 and the mitochondria. Cervical cancer cells are known to inhibit apoptosis through the inhibition of various pro-apoptotic proteins (e.g. p53) and upregulation of anti-apoptotic proteins.[17,30] Numerous studies have reported that aspirin can induce caspase – dependent apoptosis in cancerous cells, mainly through upregulation of p53.[31] However, there is no shortage of other proposed mechanisms. For example, Lee et al suggested that aspirin modulates calpain gene expression leading to activation of caspase-3.[32] Also, inhibition of COX by aspirin leads to accumulation of ceramide which also induces caspase-dependent apoptosis through cellular stress signaling.[18]

The role of the mitochondria is important for apoptosis since execution of apoptosis can only occur following involvement of its BCL2 proteins and its release of cytochrome c.[33] Aspirin and salicylic acid are able to modulate these proteins. For example, SA has been shown to down-regulate the anti-apoptotic BCL2 family member MCL-1.[34] Aspirin can induce apoptosis through mitochondrial cytochrome c release through inhibition of the ubiquitin-proteasome pathway, thereby preventing protein signalling of key transcription factors.[35] Mitochondrial calcium uptake inhibition is another mechanism by which aspirin causes cell death.[36]

An extrinsic pathway of apoptosis is through the TRAIL (Tumour necrosis factor-Related Apoptosis Inducing Ligand) receptor, a cell membrane-bound protein which triggers tumour-specific apoptosis. Activation of the TRAIL receptor pathway is a promising therapeutic strategy to selectively eradicate cancer cells, but unfortunately many cancers are known to be resistant to TRAIL therapy. Combination therapy involving TNF and aspirin treatment has shown an enhanced ability to cause caspase-induced cell death in tumor cells compared to TRAIL therapy alone.[37] Aspirin also reduces levels of the protein survivin and sensitizes cancer cells to TNF/TRAIL-induced cell death.[38] The mechanisms for this sensitizing property of aspirin are unknown but suggest a promising future for its use in cancer chemoprevention.

Aspirin inhibits angiogenesis

An important aspect in tumour progression and growth is its ability to induce the formation of new blood vessels around them (angiogenesis) to ensure the cells are provided with nutrients and oxygen. Cycloxygenases have been shown to regulate angiogenesis in colon cancer by promoting endothelial activity.[39] Aspirin has been shown to inhibit vascular remodeling and to inhibit pro-angiogenic factors such as metalloproteinases (MMP's) or vascular endothelial growth factor (VEGF).[40] In cervical cancer, COX-1 expression plays a role in enhancing and maintaining angiogenesis.[41] As Aspirin is a potent inhibitor of COX-1, it is likely that aspirin also inhibits angiogenesis through COX-1 dependent pathways.

Summary

For the most part, it appears that aspirin might be a valuable weapon against cervical neoplasia due to the multitude of mechanisms by which it exerts its effects. Aspirin inhibits COX enzymes, prostaglandins, cell proliferation and angiogenesis. It also prevents cell invasiveness and promotes immune surveillance. It achieves this through through COX-dependent and COX-independent pathways, using the dual properties of its acetyl group and its salicylate group. There are certain limitations however, when considering aspirin as a potential chemopreventive drug in the context of cervical cancer. Firstly many of the observations drawn from previous research have used supra-physiological concentrations when making their observations. Secondly, what might be observed in one epithelial

cancer may not necessarily correspond to others. Most research in this area has focused on colorectal cancer. One must exercise caution when comparing these results to cervical cancer as different mutations and different genes are implicated in this disease. Other considerations are the adverse side effects associated with aspirin use such as gastrointestinal bleeding, ulceration, hypersensitivity reactions,[42] renal damage and more recently macular degenerative disease.[43] Attempts to improve aspirin's safety record, such as the development of pills with a protective coating or the development of intravenous lithium salicylates, still have yet to prove their worth but are a good indication that this drug is worth investing in. It is clear that improvements to patient management and risk to benefit ratio are of paramount importance when considering aspirin as a long term preventive aid. However, aspirin's role in combination therapy may help to improve its reputation for short term use; its ability to cause acetylation of key proteins involved in cervical tumourigenesis gives the drug a distinct advantage over other NSAIDS. Despite the apparent detail provided in this article, we are still some way from a complete understanding of the complex mechanisms by which aspirin might exert its effect in cervical cancer.

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Case study:

Dr Diane Hemming, Consultant Cellular Pathologist

Queen Elizabeth Hospital, Gateshead

Clinical Details: The patient was a 57 year old woman known to have left ventricular failure presenting with a unilateral pleural effusion. This was aspirated for cytology, below is an image from the Papanicalaou- stained spread. What is the diagnosis? How would you confirm your diagnosis?

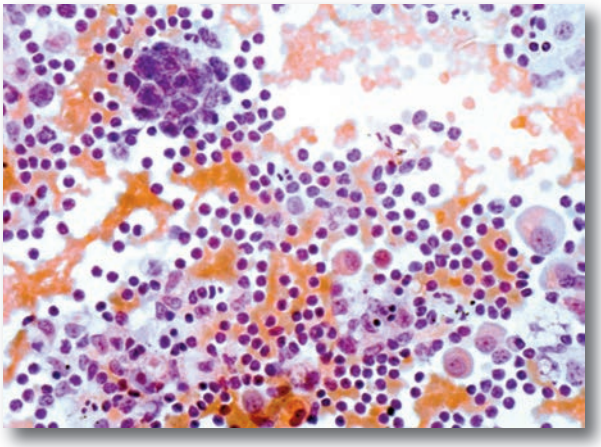

Figure 1

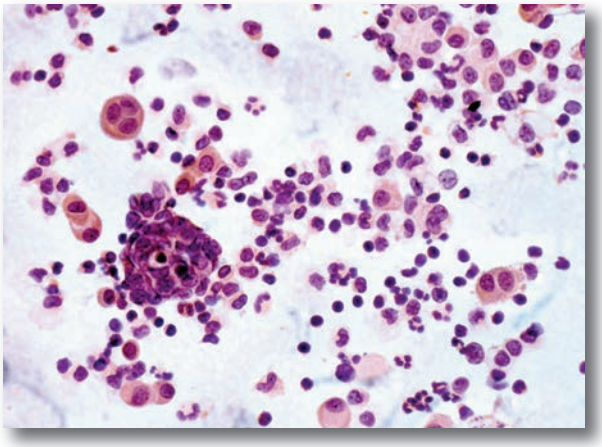

Figure 2

Answers on page 29

BAC Conference 2012 — Keele University 13–15th Sept

Alison Cropper, Chair, Meetings Sub Committee

The inaugural conference of the BAC was held at Keele University, Staffordshire, in September 2012. The conference began on Thursday afternoon with two very successful and well attended microscopy workshops in gynaecological and non-gynaecological cytology.

The opening of the Trade Show on Thursday evening by Mr Richard Winder, Deputy Director of the NHSCSP, was accompanied by a drinks reception and a 'pink' theme. Dr Mina Desai kindly brought along the torch she very proudly carried in the Olympic torch relay, and raised money by asking for donations in exchange for photographs taken with the torch. The proceeds were donated to Jo's Cervical Cancer Trust.

As always we are indebted to our Trade sponsors, and thanks go to David Carter (CellPath) our Trade Liaison Officer who did a fantastic job securing support from nine companies, without which we would be unable to run our meetings and conferences.

The two-day scientific programme contained a wide variety of topics, including presentations on synovial fluid, thyroid, andrology, biliary tract malignancy, FISH, QA in non-gynae, type 2 cervical carcinomas, ABC 3 and histopathology reporting in cervical screening. We were honoured to have two eminent speakers from the USA, Dr Amy Clayton and Professor Marshall Austin, who gave very thought provoking presentations about utilising the skills of cytoscreeners and adjunctive HPV testing in cervical screening, respectively. Two highly topical and (some would say) controversial symposia were held on 'Cytologists – an endangered species?' and 'The Only Way Is HPV – or is it?', both of which stimulated a great number of questions and audience participation.

The conference gala dinner was held on Friday night in the beautiful surroundings of Keele Hall, with after-dinner entertainment by Drew McAdam, who amazed the audience with his 'Mindplay' show.

The BAC inaugural AGM was held during the Saturday scientific programme and enjoyed better attendance than either the BSCC or NAC in the latter years of their existence, so many thanks to everyone who attended.

Minutes of the AGM can be found on our website **www.britishcytology.org.uk**

This year our AGM will be held during our one-day scientific meeting in Manchester on October 24th – it would be fantastic to see as many there as last year, giving BAC members an opportunity to hear from the BAC Executive on its activities and plans and also to pose questions to the Exec.

The BAC will not be holding a conference every year, but we intend to hold a bi-annual scientific meeting, alternating with the IBMS Congress meetings. However, this does not mean the BAC will not be holding any scientific meetings in 2013. Far from it – three are already planned for this year – see details elsewhere in this edition of SCAN and also on the website.

Planning for the next BAC conference has already begun and the Meetings Sub-Committee is busy searching for suitable venues. Whilst the facilities at Keele have been excellent and served our needs well in recent years, we have responded to feedback and are looking for a new venue for 2014.

It is hoped that this will be held in October 2014, as this was the month that was most favoured in recent feedback from both attendees and non-attendees of Keele 2012.


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Open letter to BAC Executive and BAC members (via SCAN)

27th December 2012

Dear colleagues,

Concerns about higher specialist scientific training in cytopathology

In 2012 the Academy of Medical Royal Colleges announced its intention to support the development of Higher Specialist Scientific Training (HSST) curricula for non-medical scientists working in the NHS. HSST programmes are just one innovative component of the Modernising Scientific Careers (MSC) agenda. Successful candidates from the 10 new HSST programmes will enjoy much deserved medical consultant equivalence for the important clinical roles they will be trained to undertake. Sadly, and for uncertain reasons, it appears that cytopathology is not among the disciplines for which higher specialist training or medical consultant equivalence is deemed necessary or desirable. We were deeply disappointed and feel that the profession will suffer as a result.

"The absence of higher specialist training in cytopathology will leave a vacuum at the top of the career framework, discontent in the middle ranks, and poor recruitment at the bottom."

Changes at the upper end of the career pathway may not seem such a high priority for those embroiled in the daily challenges of working in a rapidly changing laboratory environment, but as the dust settles and cytology services reach a new equilibrium, we believe that many will look back on MSC as a missed opportunity for cytopathology. As professionals who are proud to be involved in the delivery of the Practitioner (PTP) and Scientist Training Programmes (STP), we say this with a heavy heart.

Our frustration is perhaps best understood by examining some of the overriding principles of MSC, which is intended to "encompass all professions across every career band", allow "progression from one level to the next", facilitate "equity of opportunity", "equip staff with the right set of skills for the 21st century" and "improve workforce planning". We could go on. One of the intentions of MSC is to provide "transparent career pathways for those thinking of entering healthcare science in the NHS". As experienced NHS scientists, we are often required to provide undergraduates with the facts they need to make informed career choices. It would be very wrong of us to mislead. We must tell them that for the blood sciences, infection sciences and genetics there is the opportunity for higher specialist training leading to consultant scientist status. For those with an interest in cellular science there is an HSST in histopathology. The absence of higher specialist training in cytopathology will leave a vacuum at the top of the career framework, discontent in the middle ranks, and poor recruitment at the bottom. The damaging effects will be felt at all levels.

We would welcome a position statement from the BAC Executive.

Yours sincerely,

Andrew Evered
Principal Lecturer in Biomedical Science

Behdad Shambayati
Consultant Clinical Cytologist
IBMS Chief Examiner for Cytopathology

Position statement from the BAC Executive on the impact of Modernising Scientific Careers on cytopathology

There is no doubt that Modernising Scientific Careers (MSC) has radically changed training for all non-medical staff working in clinical laboratories. The introduction of a five year training programme known as Higher Specialist Scientific Training (HSST) has raised the possibility of Biomedical Scientists accessing this qualification. In the generic MSC structure, candidates who successfully complete the HSST can apply for membership of the Royal College of Pathologists and attain equivalence to a Medical Consultant. The feasibility of this in cellular pathology is currently being explored.

Cytopathology is currently included in a broad curriculum within the College training and examination structure and is not available as a stand-alone qualification for medical staff. A pilot study began last year to assess the suitability of Biomedical Scientists to train in specific areas of Histopathology. This pilot will be reviewed at the end of 2013 after the first round of assessments are complete. The group managing this project has representation from the IBMS. Until the outcome of the first year of this pilot is fully reviewed it is difficult to predict what mechanisms will be available for access to HSST. The fact that advanced practice in cervical cytology has already proved successful provides good evidence that competence at HSST year 1 level can be acquired in cytology hence there is not considered to be a need to include cytology in this pilot.

The BAC fully supports advanced roles for Biomedical Scientists and the support of the BSCC and NAC was critical in the establishment of the current Advanced Practitioner role. The BAC will also support any additional proposals to advance the role of BMS staff providing this can be achieved without risk to the quality of the service currently delivered.

Equivalence offers an alternative route to HSST and this is currently being explored by the Academy of Healthcare Science, which has strong Cytopathology representation within it. Criteria will be determined to assess equivalence to outcomes from the Scientist Training Programme (STP) and Consultant Biomedical Scientists can submit a portfolio of evidence for assessment. Successful candidates can be registered as Clinical Scientists and this provides a route to HSST. As outlined above, the exact routes to HSST are not yet clear. The situation will improve as the Academy and School of Healthcare Science become established and the results of the College pilot study are known. Until we have clarity on these issues, the BAC Executive is of the opinion that the equivalence pathway offers a potential path to HSST. Whatever the future for cytology, it must involve trained staff, irrespective of their backgrounds, working together to offer a high quality service.

Members are asked to consider the following questions about this important topic and send their replies to mail@britishcytology.org.uk

- ***Do you perceive a role in Cytopathology for the Clinical Scientists who will emerge from the Scientist Training Programme?***
- ***If you do see a role for Clinical Scientists please outline briefly what this role could be?***
- ***Do you agree that further qualifications should be available for the Biomedical Scientist and the role should be further advanced to achieve medical consultant equivalence?***
- ***If an HSST in cytology, or an equivalent qualification was developed, would you be interested in attaining this qualification?***
- ***The training programmes under development by the School of HCS offers the opportunity for staff to move between "the boxes" to the Scientist Training Programme (STP). Would you be interested in undertaking further study to apply for STP?***

CEC Local Officers
(Spring 2013)

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LONDON
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VOLUNTEERS REQUESTED

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

CEC News – Spring 2013

Jenny Davies

The scheme continues to tick along nicely, with book submissions and JBLs being sent in on a regular basis, thankyou.

Since the last edition of CEC news, stickers have been designed and printed, so all books that are sent from now on will have the correct logo on the front! I have also met with Christian Burt to see how the two databases (CEC and membership) can be streamlined. There is still work to be done here and any changes that affect current administration will be communicated through the website.

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 – **15 questions – 15 credits.** I have chosen this JBL as it relates to the eagerly awaited ABC3, which is very pertinent to all of us. 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 JBL's as they come up in each issue of SCAN. JBL's 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

ABC 3, Part 1 — a review of the guidelines

Cytopathology 2012, **23**, 353 – 359

Dr J.H.F. Smith

1. Why has it been considered that the UK has one of the most successful screening programmes in the world?

2. List 3 changes in the last decade that have had a major impact on the cervical screening programme.

3. The revised ABC guidance applies to England, Scotland, Wales and Ireland. True/False

4. Why has it been decided not to publish ABC3 in a peer reviewed journal?

5. Two reports have been published indicating a minimum number of squamous cells that may increase the detection of high grade dyskaryosis. What is this figure?

6. List 3 changes that will bring the NHSCSP closer to Bethesda and European reporting guidelines.

7. Why has there been an adoption of a free text distinction between high grade (moderate) and high grade (severe) dyskaryosis?

8. Why is it advocated that koilocytosis and other features of HR-HPV should not be included in the cervical cytology report?

9. What guidance is given to help grade cells with dyskaryotic nuclei that are not circular?

10. Why has the ABC 3 working party chosen to re-emphasise the potential causes of false positive and false negative reports?

11. In the reporting of glandular neoplasia, what new report code has been introduced and what is it for?

12. To help differentiate between squamous dyskaryosis and glandular neoplasia, particularly when they are in the same sample , what particular feature has been highlighted in the guidance?

13. What is the modified definition of borderline nuclear change?

14. Why is it considered safe to return cytology positive, HR-HPV negative women to routine recall?

15. What is the advantage of the test of cure protocol in the follow-up of treatment for CIN?

Note:

15 credits available rather than the usual 10

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

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 support they have loyally 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.

Leica Microsystems (UK) Ltd Lisa Howard Tel: 01908 246246 e-mail: lisa.howard@leica-microsystems.com website: www.leica.com 2011/12	**Nikon UK Ltd** Chay Keogh Tel: 0181 541 4440 e-mail: Chay.Keogh@nikon.co.uk website: www.nikon.co.uk 2011/12
Thermo Fisher Scientific Helen Tucker Tel: +44 (0) 800 0189396 e-mail: helen.tucker@thermofisher.com website: www.thermo.com 2011/12	**Pioneer Research Chemicals Ltd** Julie Jarman Tel: 01206 791781 e-mail: sales@pioneerresearch.co.uk website: www.pioneerresearch.co.uk 2012/13
Source BioScience Healthcare Emily Shaw Tel: 0115 973 9012 e-mail: Emily.Shaw@sourcebioscience.com website: www.sourcebioscience.com 2012/13	**Olympus Medical** Sarah Sankey Tel: 01702 616333 Ext: 3565 e-mail: Sarah.Sankey@olympus.co.uk website: www.olympus.co.uk 2012/13
Hologic (UK) Deborah Purvis Tel: 01293 522080 e-mail: ukreception@hologic.com website: www.hologic.com 2012/13	**Carl Zeiss Ltd (Rene Hessler)** 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 2012/13

This list will be regularly reviewed for each issue of SCAN, and on the BAC 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.

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Impact of Modernising Scientific Careers on Cytopathology in the UK

Allan Wilson
Monklands Hospital, Scotland

Background

Modernising Scientific Careers was led by the Chief Scientific Officer at the Department of Health. It is analogous to the Modernising Medical Careers scheme for medical staff training.

The Modernising Scientific Careers project has been the subject of much debate; however, despite the fact that it is now in the process of implementation, misunderstanding and conjecture continues to surround degrees, registration and career paths for biomedical scientists.

The announcement at the BAC meeting in September that only three candidates had been selected for the Cytopathology Scientist Training Programme (STP) took many by surprise. This requires an assessment of the impact of MSC on Cytopathology in the UK.

Key elements

There are four main elements to Modernising Scientific careers:

- Introduction of a new healthcare science career pathway.
- New training and education programmes, incorporating both academic and workplace-based training. This includes qualifications and awards and arrangements for assessment of previous 'equivalent' education and skills.
- Identification of regulatory implications for changing education and training.
- Supporting delivery of the changes. This includes improving communication strategies, workforce planning, and education commissioning together with ensuring sustainable funding arrangements.

Modernising Scientific Careers career structure

Figure 1 indicates the four HCS roles. It is theoretically possible to move between the "boxes" from HCS assistant to Consultant HCS.

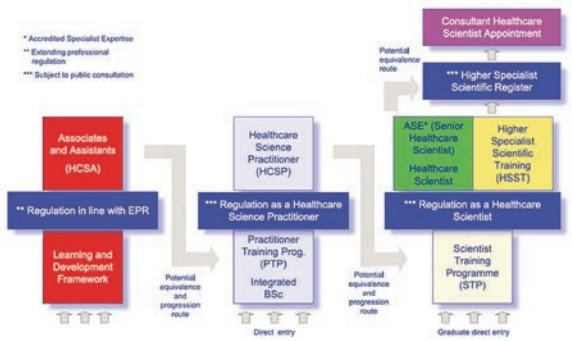

Figure 1. MSC career structure

New academic courses/training programmes

- A modular vocational training programme for Associate and Assistant Healthcare Scientists has been developed by the IBMS and is currently being piloted in London.
- 3-year Practitioner Training Programme (PTP) including a BSc degree in Healthcare Science (HCS) integrated with workplace learning. Many are not approved for HCPC registration.
- 3-year Scientist Training Programme (STP) underpinned by a part time Masters degree in Clinical Science. Graduates are eligible to register as a Clinical Scientist
- 5 - year Higher Specialist Scientific Training (HSST) programmes similar in standard to specialist medical training are currently being developed for Clinical Scientists by joint medical and scientist curriculum working groups, facilitated by the Medical Royal Colleges.

Healthcare Scientist roles in Cytology

Role	Education & training	Cytology roles
Healthcare science assistant and associate	Further and higher education programmes. IBMS modular vocational training integrating work based training	MLAs Cytology screeners Associate practitioners (levels 3 and 4)
Healthcare science practitioner	BSc (Hons) programme which integrates work based training	Band 5 Biomedical Scientists
Healthcare scientist	MSC programme and linked work based training	Specialist Biomedical Scientists and senior Biomedical Scientists (levels 6 and 7)
Consultant healthcare scientist	Doctorate level award and linked work based training	Consultant Biomedical Scientists (Advanced practitioners) (levels 8 and 9)

Impact on staff in existing cytology screener and BMS posts in cytology

Staff in existing posts will remain on the same AfC bands and their current job descriptions should not be affected by MSC and the changes to training. The introduction of new training programmes offers an opportunity to existing staff to either apply for the new programmes or apply for equivalence based on qualifications and experience and potentially advance through the "boxes" illustrated in figure 1. Staff currently in training and part way through a degree course approved by the IBMS for registration with HCPC can continue their studies.

Access to the Scientist Training Programme (STP)

It is likely that the majority of entrants to the STP training course will be new graduates. The selection process for these places is rigorous. The three candidates currently on the Cytopathology STP were selected from ninety applicants. There is also a 'home grown' route for biomedical scientists currently in employment who, with the support of their employer, wish to enter the STP selection process. Some existing biomedical scientists may apply for exemption from some elements of the course through the equivalence route.

Academy for Healthcare Science (AHCS)

The Academy's functions are to:

- Act as the overarching body for issues related to education, training and development in the UK health system and beyond, including standards of education and training and the delivery of equivalence processes for individuals.
- The Academy has now been established as an independent Limited Liability Company and is now recognised as an Education Provider by the HCPC, thus enabling graduates from STP programmes to be registered Clinical Scientists (CS).
- Professional groups advise the Academy Council and management board on specialised professional areas.

The National School of Healthcare Science (NSHCS)

Function	Rationale
Provides oversight and co-ordination • rotational & specialist placements • supervisors & training managers • assessments & trainee performance and On-line Assessment Tool [OLAT] • integration of academic & workplace learning **Manages national recruitment** **Quality assessment management** • workplace training/ environment • monitoring of training outcomes and maintenance of standards	• equity of access and delivery of curriculum • standardises delivery • enables delivery of full curriculum across work and academic interface • fair recruitment/ recruits the best • standardises high quality training • identifies training/outcomes and ensures they are equivalent • equity in assessments/ supervision

NSHCS Themed Boards

The Themed Boards have been established by the National School of Healthcare Science (NSHCS) to support delivery of healthcare science education and training within specialist areas. The Themed Boards provide a forum for all professional bodies, employers and Higher Education Institutions (HEIs) to work closely together to ensure successful implementation of all of the modernised training programmes in healthcare science.

The themed boards review performance of individual candidates and board members may contact candidates directly and offer support if they are not on target to complete the required number of competencies and assessments.

The STP's have been heavily based on the current medical and dental training programmes and will have an exit exam based on those used in Medical Schools. Best practice from within the UK and internationally has been used to develop the STP.

BAC input to NSHCS and AHCS

Allan Wilson is a member of the Academy for Healthcare Science Cellular Sciences Professional Group. This group will meet for the first time on 13th February. This is an IBMS nominated position. Behdad Shambayati is also on this group. Allan Wilson is a member of the NSHCS Cellular Science Themed Board. This group has met on three occasions. Behdad Shambayati is also on this group.

Jenny Davies is a corresponding member of the Academy for Healthcare Science Cellular Sciences Professional Group and will receive all papers for comment.

Equivalence

Equivalence assessment is a way to allow individuals who have relevant qualifications, skills and experience to gain exemption from parts of training or even be judged equivalent to someone who has been through the whole training programme. Equivalence assessments are unlikely to begin for Consultant healthcare scientists until mid-2013. Equivalence is a potential route for Consultant Biomedical Scientists (Advanced Practitioners) to gain Clinical Scientist status. One of the first tasks of the AHCS professional groups will be to implement a system to assess equivalence with the outcome of the MSC programmes. The AHCS already has approval from HCPC for equivalence assessment at the Scientist level. Candidates completing this assessment process successfully will be eligible to register with HCPC as a Clinical Scientist.

Cytology qualifications for STP candidates

It is currently unclear if candidates on the cytology STP will be required to attain the City & Guilds Diploma. Without this qualification it is difficult to see how they can participate in the cervical screening programme. At a meeting of the National Cervical Cytology Education and Training Committee (NCCETC) in November 2012, it was agreed that candidates in the cytology STP should obtain the C&G Diploma. This issue was discussed at a NSHCS, which is now seeking a meeting with the NHSCSP.

There has since been some discussion about an "equivalent" qualification for STP candidates but it is currently unclear what this qualification would look like and who would deliver it. It has been proposed that after STP candidates complete the three year MSc and become registered as clinical scientist they will not be required to primary screen cervical samples and therefore do not require the C&G Diploma. However, every other non-medical member of staff involved in reporting cervical cytology samples holds the diploma or its predecessor.

The programme has never trained staff to "check" samples who are not already experienced in primary screening and many programme professionals feel strongly that this should not change. Current NHSCSP regulations indicate that Clinical Scientists will not be permitted to report abnormal samples as they will not hold the ASD in cervical cytology. The STP is a full curriculum and it is impossible to screen substantial numbers of slides and to gain sufficient experience of cervical cytology samples during the programme.

Given the lack of clarity around cytology training qualifications and training, it is difficult to envisage what the role of clinical scientists will be in cytology. It could be argued that this role is already filled in cervical cytology by Consultant Biomedical Scientists & Advanced Practitioners. Non-gynae cytology is a possibility and training could be delivered in house and at training schools. The Non-gynae diploma and the proposed Advanced Specialist Diploma in non-gynae cytology could be options but these are IBMS exams and are only open to IBMS members.

At a recent meeting of the NSHCS cellular sciences themed board, the possibility of STP candidates not being trained in cervical cytology was raised. The focus would then be on non-gynae cytology. It was agreed at this meeting to discuss further with NHSCSP.

Future of the Association of Clinical Scientists (ACS)
Since April 2003, the only routes for registration as a Clinical Scientist with the Health and Care Professions Council (HCPC) was through the award of the Association of Clinical Scientists' (ACS) Certificate of Attainment or the "grandparenting" rules of HCPC. However, since the recent decision that the AHCS can award certificates of equivalence and attainment which are accepted by HCPC for registration as clinical scientists, the future role of the ACS is unclear.

Pilot study for extended roles of scientists in Histopathology
Modernising Scientific Careers proposes the creation of Consultant Healthcare Scientists in pathology. Consultant-level scientists are an accepted facet of clinical provision in some pathology disciplines. However, traditionally clinical work in Histopathology involving reporting and clinical diagnosis has been performed by medically-qualified Consultants and doctors in specialist training.

No curriculum currently exists to support the training of Healthcare Scientists in Histopathology. The Royal College of Pathologists has been tasked with production of these on behalf of Modernising Scientific Careers and a feasibility study has been established to advise the development of the histopathology curriculum. This study commenced in 2012 and several Consultant Biomedical Scientists in cervical cytology are involved in this study.

Non-gynae Advanced Practitioner exam
A detailed proposal to introduce an Advanced Specialist Diploma in non-gynae cytology will be discussed at the IBMS/RCPath conjoint board in February 2013. An outline proposal has already been approved by the board. If approved, candidates who attain this qualification will be permitted to "sign out" abnormal serous fluids, urines and respiratory cytology samples.

Future vacancies
Employers can still choose to recruit to BMS posts through traditional routes and as stated above the IBMS is working with academic providers of the new degree courses to assess their suitability for registration with HCPC. When the new courses are well established, it is likely that the traditional route to registration may "wither on the vine" although there may be some regional and national allegiances to the existing routes.

Higher Specialist Scientific Training (HSST)
The college has previously stated that it is firmly of the view that expertise in cervical cytology, no matter how detailed, is simply too narrow to constitute grounds for college membership:

"Cytology comprises cervical and diagnostic (non-gynae) cytology and the role of BMSs in the latter is limited, because full medical training is required to appreciate the breadth of clinico-pathological management". However, it is unclear if this position has moved over the last year and with the developments described above it is also not clear when multiple "narrow" specialties such as dissection, focussed histology reporting, gynae and non-gynae reporting are considered as consultant equivalent.

Department of Health/MSC statement on HSST: *"Scientists who successfully complete Higher Specialist Scientist Training (HSST) equivalent to medical Higher Specialist Training, with 4 to 5 years of specialty-specific training, should be considered competent to provide consultant-level clinical scientific expertise, advice and leadership."*

The Department of Health vision for HSST is to achieve training and learning outcomes to develop Consultant Clinical Scientists who provide:

- clinical and scientific expertise and leadership
- consultant level scientific and clinical advice within the context of direct patient care
- strategic direction, innovation and highly developed and specialised skills supporting service development and new ways of working

BAC and HSST – how do we respond?
There is absolutely no doubt that the BAC and its predecessor bodies, NAC and BSCC have strongly supported advance roles for senior, experienced Biomedical Scientists. The creation and further development of the role of Consultant Biomedical Scientists has undoubtedly added extra value to the UK cervical screening programmes over the last ten years. Consultant Biomedical Scientists are already acting at the level of Consultant Cytopathologist in cervical cytology.

The MSC project offers the possibility of Consultant Biomedical Scientists formally achieving academic parity with medical consultants by accessing HSST. However, the recruitment of candidates to the Cytopathology STP has introduced an alternative route for medical consultant equivalence but one which would provide candidates with considerably less experience in cervical cytology and knowledge of the UK Cervical Screening Programmes.

The MSC programme clearly states the intention of introducing HSST in Histopathology. Currently, the RCPath HSST in Histopathology includes cytology (gynae and non-gynae) as a core element. There are no separate Histopathology and Cytopathology training programmes and the RCPath has no plans to develop this HSST.

What do we need in a modern health service to deliver the service that patients need/expect?
The service will need trained cytologists irrespective of their background as long as they are competent, appropriately trained and supported in post. Whichever route is agreed it will not be a "quick fix". Currently it would appear that an HSST in Cytopathology will not be developed. How then do we support the further development of non-medical roles in cytology? Is the answer to offer a route to medical consultant equivalent to existing Consultant Biomedical Scientists, possibly through the equivalence route described above? This will not be an easy option and successful applicants will have to complete a five year HSST to achieve medical consultant equivalence and this will involve training in histopathology. The criteria used to assess equivalence have yet to be developed but will be discussed at the first AHCS cellular sciences professional group meeting next month.

Nick Dudding receives international award!

Most of us in UK cytology will know Nick Dudding through his cytology achievements and especially his training and educational work over the years. However, what many may not know is that Nick has won the highly coveted International Cytotechnologist of the Year award for 2012! The International Cytotechnologist of the Year Award is given yearly to a Cytotechnologist of exceptional merit honouring a lifelong dedication to teaching, research and service in cytology. Recipients receive a gold medal and an honorarium. The Award has been given since 1975 to 32 recipients from 14 countries, but this is only the second time since its inception that a UK based cytologist has won the award.

Nick Dudding is an Advanced Practitioner at Sheffield Teaching Hospitals and Assistant Director for the East Pennine Cytology Training Centre. He has been working in cervical cytology since 1987 and has been involved in training since 1989. He was also a former council member of the BSCC and served on the NAC Executive for several years. He has sat on numerous national committees and groups, and has had a hand in many of the major developments within the NHSCSP especially over the last 20 years. He has taught all over the world, and this award recognises his unique skills as an educator and promoter of cytology.

Perhaps surprisingly for Nick he was left speechless when he heard of the award, but no doubt he will find his voice in time for his acceptance speech at the IAC meeting in Paris in May, when he will receive it. Our congratulations go to Nick for this international recognition and much merited award!

Technical EQA – Past, Present & Future

Mike Rowell, South West Regional Cervical Screening Quality Assurance Reference Centre

It was 1990 and I had recently returned to Bristol after a 3-year stint running the Welsh Cytology Training School. The quality of the staining had deteriorated noticeably, at least to me, in the intervening period and I found myself having to convince the laboratory manager of the validity of my perceptions. After much coercion he finally capitulated in the face of my persistent protestations and allowed me free range to alter the departmental staining.

Having never been much of a chemist I resorted to scouring textbooks on the subject, in particular the works of Mathilda Boone (Holland) and obviously the original works of Dr George Papanicolaou, including his now famous litho-prints, copies of which still adorn many a training school.

Enlisting the help of my erstwhile colleague Mr. David Proe (Taunton) I set about producing routine staining which I felt more appropriate for use in a Regional Cytology Training Centre and for some two or three years gave the question of Papanicolaou staining little or no more thought.

However, I knew something was amiss when a trainee cytoscreener, on an introductory course at the Cytology Training Centre, observed, somewhat loudly, ***"Dyskaryosis is so much easier to recognize here in Bristol than in my own lab!"*** I could have dismissed this comment but it intrigued me. Now in my experience dyskaryosis doesn't look any different whether it originated in Bristol, Birmingham or Timbuktu! However, given the deterioration in staining quality I had initially encountered upon my return to Bristol, I quickly realized that what the student was actually saying was ***"the staining here is better than in my own laboratory!"*** This incident coupled with the fact that during the same period, whilst engaged on my Regional Gynae EQA assessments, I was often confronted by disgruntled scheme participants either asking me for sunglasses or complaining ***"this doesn't look like our slides!",*** led me to believe that standardization of staining could only be a good thing and certainly worth pursuing.

Recruiting some likeminded individuals I initiated a Regional Technical EQA scheme, inviting participation from all the cytology laboratories and the rest, as they say, is history!

Several years later, and after the successful introduction of the scheme within the South West Region, I was approached by Julietta Patnik, National Coordinator of the NHSCSP, to join a working group, to produce some national guidance on staining. Julietta related stories of rescreening exercises where reviewing laboratories had stated, ***"I'm not surprised they are missing things their staining is awful!"*** She cited these occurrences as of some concern and as a primary reason for forming a working group to review the issue. NHSCSP Publication No. 19. Technical EQA of Papanicolaou staining was the outcome and this document was published in February 2004. Participation became mandatory in all cervical screening laboratories.

As is the case with most NHSCSP publications, authors are generally drawn from appropriate arms of the programme. Publication No.19 was no exception, having input at the time from the IBMS, NAC and BSCC as well as valuable statistical advice from the DoH. Writing this article enables me to recognize the input and assistance afforded me by two unsung individuals, coincidentally the co-editors of this publication, Mr. Andrew Evered (Cardiff) and Mrs. Sharon Roberts-Gant. Both Andrew and Sharon helped me considerably in drawing up meaningful criteria and in allotting scores to the same and although they are not attributed in NHSCSP No.19 they were very much instrumental in formulating the scoring scheme.

The content of the publication took several years to finalise before becoming a mandatory requirement of the programme. The final stumbling block to the publication was the impending rollout of liquid based cytology (LBC) and although the document originally incorporated mention of this it was removed prior to publication so as not to pre-empt a still to be taken decision on national LBC implementation. Once published the document polarized camps into Thin prep vs. Surepath user and the subsequent Orange vs. No Orange debated raged loudly across the UK. Despite standardization of assessor training and the implementation of National SOPs and protocols the scheme served to highlight regional variations that continue to this day! With the advent of automation, the debate became even more heated. The Focalpoint system designed to evaluate Surepath preparations was rivaled by the Cytyc Imager, which also required its own modification of the established Papanicolaou technique. This culminated in one English region outlawing the use of the Imager stain on the basis that it failed the TEQA evaluation. However, it must be noted that this was an exclusively 'Thinprep' region and had the same assessors been evaluating Surepath stained material the outcome would, I surmise, been identical. It is also of note that the imager stain is still in use in some UK laboratories and that this has NOT failed recent TEQA assessment.

Whilst I still strongly fall into the ***"Give me Orange!"*** camp, I also feel like King Canute trying to resist the tide. Automation remains the Holy Grail of cytology and clinging blindly to idea that staining should be suited to the human eye rather than a machine's algorithms appears to be futile.

Implementation of a National TEQA Scheme has produced significant improvement and its value should not be underestimated in making the screener's life a lot easier and evaluation of abnormality more accurate. Results Nationally are collated and reviewed on a regular basis by a sub group of the National Laboratory QA Group. A special mention is in order to Sue Melling (East Midlands) who is tasked with the somewhat onerous number-crunching and analysis of regional performance for consideration by the group.

Whilst overall staining quality continues to improve nationally, it is clearly of concern that the regional variation of scheme assessment is still evident. With this in mind proposals are in place to take the scheme to the next level. The use of pooled samples for both LBC technologies to promote further standardization would be a welcomed step, along with the introduction of National rather than Regional assessments. Both these moves would further promote standardization and hopefully ultimately eradicate regional variation – watch this space!

Further Reading

Papanicolaou GN. *Atlas of Exfoliative Cytology.* Harvard University Press, 1960, ISBN 0 674 05150 5.

Boon ME, Driver JS. *Routine Cytological Staining Techniques.* Macmillan, 1986, ISBN 0 333 38316 8.

Boon ME, Suurmeijmer AJH. *The Pap Smear.* Coulomb Press, 1991, ISBN 90 7142117 1.

Proe D. Variability in Papanicolaou staining. *Biomedical Scientist,* 1997, June: 328–330.

External Quality Assessment Scheme for the Evaluation Of Papanicolaou Staining In Cervical Cytology. Protocol and Standard Operating Procedure. NHSCSP Publication No 19, February 2004

George Papanicolaou goes head to head with local R&D committee

Andrew Evered, Principal Lecturer in Biomedical Science Cardiff Metropolitan University

Imagine what might have happened if George Papanicolaou had the problems of modern day biomedical scientists…

23rd April 1923

Dr Pap: I have asked my wife to donate a cervical sample for my research. She is more than happy to comply and this could lead to a new screening test that will save millions of lives. Can I proceed please?

R&D: Dear Dr Pap, Thank you for sending us your interesting proposal. Please complete the enclosed forms so that we may consider your research in further detail. In addition, you must register your research at www.r&d_red_tape.com . You should be aware that it may take up to 60 days to process your application.

Two months later

Dr Pap: Sir, I submitted an application for research approval two months ago and was promised a response within 60 days.

R&D: Dear Dr Pap, the application will take up to 60 working days.

One month later

Dr Pap: Sir, I eagerly await your response to my application sent to you three months ago.

R&D: Dear Dr Pap, Since your proposed research involves human participants you will need to complete additional forms. We have streamlined the application process and the forms can now be completed entirely online. Your application will take up to 60 days to process.

Dr Pap: Sir, My original application made it clear that I require human participants. Why has it taken three months for you to realise this?

(No reply)

Three months later

R&D: Dear Dr Pap, Thank you for your application. The committee considers your proposal as potentially worthy of support. However, before we can grant approval we require further information relating to participant recruitment, study rationale, experimental design, outcome measures, power calculations, costs, intellectual property rights and the clinical, financial and reputational risks to your employer. Please complete the enclosed forms in triplicate, as we are currently experiencing problems with the online system.

Dr Pap: Sir, with the greatest respect, why didn't you send me these forms originally?

R&D: Dear Dr Pap, You need to understand that due process is far more important than research output.

Three months later

R&D: Dear Dr Pap, Thank you for providing further details about your research proposal. The response of the committee is summarised below. If you could provide the additional information indicated we would be pleased to consider a revised application.

Scientific reviewer 1: I am concerned about the design of this study. My own research in this field indicates that a double blind randomised control trial would be more appropriate.

Scientific reviewer 2: The benefit of such research is dubious and the idea seems far-fetched.

Statistician: My power calculations are at odds with those of Dr Pap. It would appear that at least 10,000 participants are required to detect the expected effect size.

Finance manager: There is an error in the costings and the source of funding is unclear. Dr Pap intends to produce six stained slides at a cost of nine pence per slide. The estimated cost of 54 pence does not take into account laboratory overheads and staff time.

Risk officer: There is an unacceptable risk to the reputation of the organisation and the intellectual property rights require clarification.

Dr Pap: Sir, I am disappointed with your responses and beg you to reconsider. First, in reply to the scientific and statistical review, I would like to point out that this is a preliminary feasibility study and as such does not require a statistically robust randomised trial, which would come at a huge cost to the Greek taxpayer. Second, I apologise for miscalculating the cost of the study, which will in fact be 59 pence rather than 54 pence. I will pay for this out of my own salary. Finally, I will gladly hand over all intellectual property rights and commercial benefits to my employer.

R&D: Dear Dr Pap, In that case we are happy to approve your study. You may now proceed to an application for ethical approval.

Dr Pap: Sir, isn't that what I have just done?

R&D: No, the research ethical approval is a separate process and may take up to 20 years to complete.

18th October 1941

R&D: Dear Dr Pap, We are pleased to inform you that your study has been approved. Please note that approval lapses within 12 months of the date of this letter, after which time you will need to reapply. We wish you good luck with your research.

Dr Pap: Sir, I have already conducted my research. Realising that I cannot now publish in a peer reviewed journal I will publish my research as a book, probably in Greek!

This article is loosely based on a similar paper written by an equally exasperated scientist who wrote of the experiences of Isaac Newton (who, incidentally, published his findings as a book, … in Latin).

Report from BAC Publication and Website Sub-Committee

Dr Paul Cross

Queen Elizabeth Hospital, Gateshead

The BAC website has undergone some significant changes over the winter. The introduction of the members login facility (using your BAC membership number and BAC registered email address) now allows you direct access to material not available to non-BAC members. This includes some of the talks form last year's ASM meeting in Keele, and also previous editions of SCAN on line. We are also developing the educational role of the website, with some self-learning cases being added. These will be added to in the coming weeks, so keep an eye out for new ones. The website also has regular updates on developments within the world of cytology. We are also moving to a system of email newsletters/alerts to BAC members of developments, news, etc using the email address we have for you. If you have any problems logging onto the BAC website, or are not getting emails from us, then email us **(mail@britishcytology.org.uk)** to make sure we have the correct contact details for you.

This edition of SCAN contains a range of articles, which we hope you find stimulating and provocative. We are always on the lookout for articles from BAC members, so feel free to submit articles that you feel would be of interest. Cytopathology goes from strength to strength as the only European peer reviewed cytology journal. BAC members receive both SCAN and Cytopathology as part of their membership. If you are not receiving them (published twice and six times a year, respectively) then do contact us to make sure we have the correct mailing address for you, using the usual contact email address.

BAC educational events in 2013

Alison Cropper, Chair, Meetings Sub Committee

22nd March 2013, joint meeting with RCPath, London
This one day meeting, run jointly with the Royal College of Pathologists, will appeal to all those involved in the reporting of gynaecological and non-gynaecological cytology and histology related in this area. Details can be found on the BAC website and also at

http://www.rcpath.org/meetings/college-conferences

6th -7th June 2013, joint meeting with ACP, at the Royal Institute for British Architects, London
This meeting, jointly organised with the Association of Clinical Pathologists, will cover varying aspects of screening and how it relates to Pathology, and cytology in particular. Posters are encouraged for this meeting. Full details on the BAC website, along with booking instructions, and also at

http://www.pathologists.org.uk/all-page-stuff/meetings_frameset2.htm

24th October 2013, BAC Autumn Tutorial & AGM University of Manchester Innovation Centre
This one day course will deal with aspects of both gynaecological and non-gynaecological cytology. It will involve both lectures and workshops.

The BAC will also be holding its Annual General Meeting during this meeting. Full details will be posted on the website once the full programme is finalised, but put the date in your diary!

www.britishcytology.org.uk

Case study answer

Dr Diane Hemming, Consultant Cellular Pathologist

Queen Elizabeth Hospital, Gateshead

Metastatic small cell carcinoma of bronchogenic origin.

Examination of the pleural fluid showed a mixed population of benign mesothelial cells, numerous small lymphocytes and scattered collections of atypical cells. The atypical cells showed high nuclear/cytoplasmic ratios with little or no visible cytoplasm. The nuclei showed a 'salt and pepper' granular chromatin pattern with no nucleoli evident. There was moulding of nuclei in the groups. Elsewhere the atypical cells formed Indian files. The nature of the malignancy was confirmed on immunocytochemistry performed on the formalin fixed, paraffin embedded clot, the tumour cells being CD56 and CK7 positive. Subsequent imaging confirmed malignancy. The patient was commenced on appropriate chemotherapy.

Metastatic small cell carcinoma is not uncommon in serous effusions. When the cells are scanty the diagnosis can be missed, and misinterpreted as representing benign lymphoid cells. The differential diagnosis may include metastatic lobular carcinoma of the breast or lymphoma. Metastatic lobular carcinoma of the breast can present as small malignant cells forming Indian files in serous fluids, but careful examination often reveals magenta bodies and oestrogen receptor status will be positive. Lymphoma is usually suspected from the history, but can be confirmed by an appropriate immunocytochemistry panel including LCA, B and T cell markers.

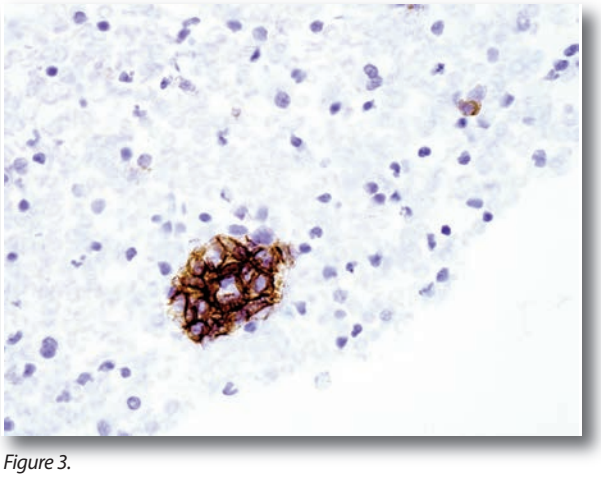

Figure 3.

Cytological Curiosities

Andrew Evered
Manager, Welsh Screening Training Centre
Principal Lecturer in Biomedical Science,
Cardiff Metropolitan University

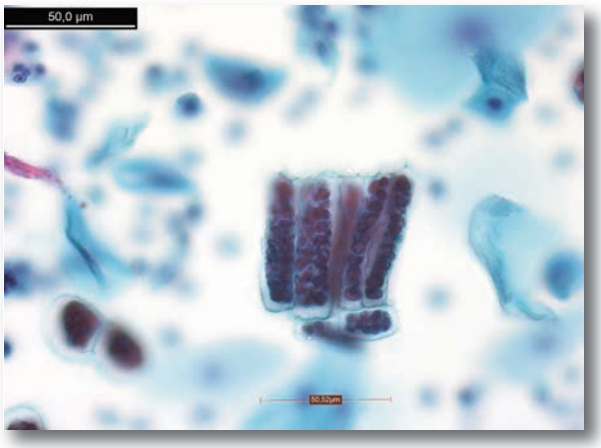

Figure 1. Cervical smear from Greenland. Any ideas?

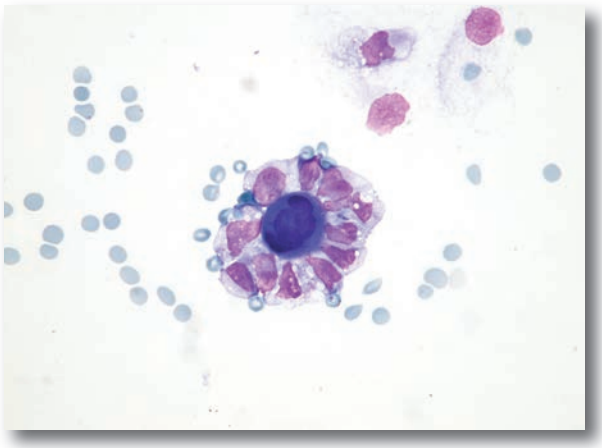

Figure 2. Ganging up.

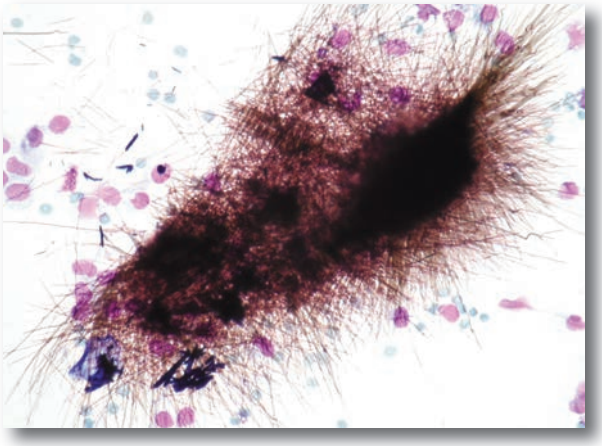

Figure 3. Ouch!

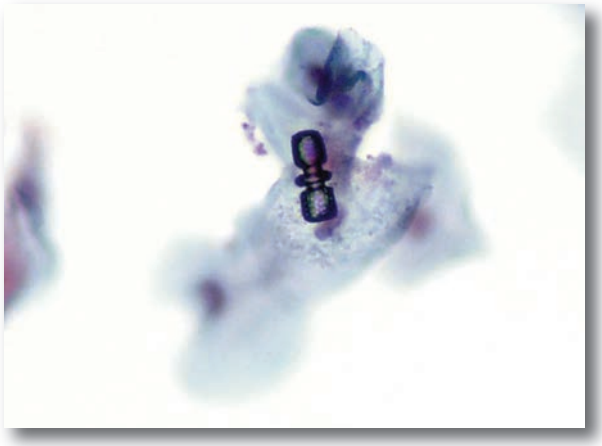

Figure 4. Alien species.

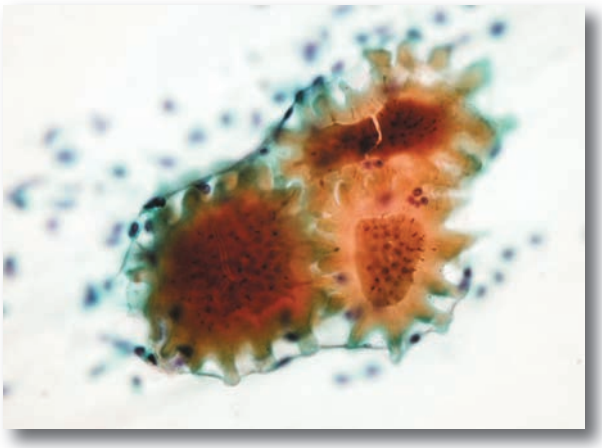

Figure 5.Piece of fruit anyone?

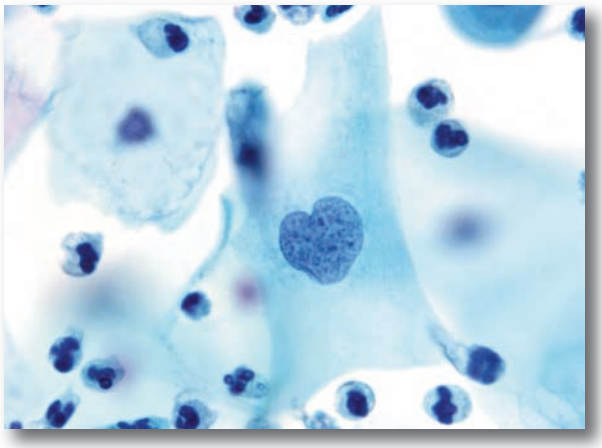

Figure 6. Must be love.

Birmingham Women's NHS
NHS Foundation Trust

BIRMINGHAM CYTOLOGY TRAINING CENTRE

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

INTRODUCTORY COURSES FOR CITY & GUILDS DIPLOMA IN CERVICAL CYTOLOGY

Dates for 2013 to be arranged as required

We will be pleased to offer this training if required—please contact BCTC for further information

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

14-18 October 2013

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

13-15 May 2013; 16-18 September 2013

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

UPDATE COURSES IN GYNAECOLOGICAL CYTOLOGY (ThinPrep & SurePath)

1 May 2013 (Checkers' Update); 11, 12 & 13 September 2013

September update days can be booked separately or as a 3-day update. Topics covered will be:
Iatrogenic changes and hormonal effects; Aspects of Squamous Cell Carcinoma;
Metaplasia & false negative/positive reporting

NON-GYNAECOLOGICAL CYTOLOGY FOR TECHNICAL STAFF

25-26 April 2013

Ideal for those completing their portfolio for the Specialist Diploma

WEST MIDLANDS AUTOPSY PATHOLOGY COURSE

22-23 May 2013

For trainees in preparation for the FRCPath and as a refresher for consultant pathologists involved in coronial work

BIRMINGHAM HISTOPATHOLOGY COURSE

10-21 June 2013

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.
NEW for 2013—optional Saturday morning for personal review of workshop slides

GYNAECOLOGICAL CYTOLOGY FOR TRAINEE PATHOLOGISTS (StRS)

2-3 September 2013

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)

4-7 September 2013

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
NEW for 2013— optional Saturday morning for personal review of workshop slides

INTRODUCTORY COURSE FOR ST1s

2-6 December 2013

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
EC IBMS RCPath CPD accredited courses

London Regional Cytology Training Centre

The North West London Hospitals NHS NHS Trust

2013 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®)

- *25th February – 22nd March*
- *30th September – 25th October*

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

FOLLOW UP COURSE (Thinprep®)

- *7th – 11th January*
- *29th July – 2nd August*

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

PRE – EXAM COURSE (Thinprep®)

- *13th – 17th May*
- *2nd – 6th December*

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

Medical Practitioners Courses

PATHOLOGISTS COURSE – GYNAE

This two day course covers gynaecological cytology.

- *18th – 19th + 20th (Optional Mock Exam) February*

Course fee: - £200 Mock exam - +£50

PATHOLOGISTS COURSE – NON GYNAE

This four day course covers non-gynaecological cytology.

- *4th – 7th + 8th (Optional Mock Exam) February*
- *9th – 12th + 13th (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

- *21st May*
- *26th September*
- *21st November*

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

Post Registration Courses

BMS/CYTOSCREENER UPDATE COURSE

- *14th – 16th January*
- *11th – 13th February*
- *17th – 19th April*
- *22nd – 24th May*
- *10th – 12th June*
- *18th – 20th September*
- *13th – 15th November*
- *25th – 27th November*
- *11th – 13th December*

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

Introductory Non-Gynae Courses

RESPIRATORY CYTOLOGY COURSE

- *17th – 18th June*

SEROUS FLUID CYTOLOGY COURSE

- *5th – 6th September*

URINE CYTOLOGY COURSE

- *19th – 20th 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.

- *24th May*
- *1st 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.

East Pennine Cytology Training Centre

EPCTC NHS

Overall Winner 2010
Achieving Excellence in Learning, Teaching & Development

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 Masterclasses

Challenging masterclasss aimed at practicing consultants or trainees wishing to refresh or extend their knowledge.

"Cytology of the Salivary Gland and Lymph Node"

Date: 7th May 2013

Course Fee: * £120 each

A One-Day Course for Hospital Based Programme Coordinators

Venue: Westbrook House, Newmarket

This one day course is aimed at all HBPCs and would be particularly suitable to anyone new to post (from any specialty). We will cover the role of the HBPC and touch upon other issues such as your role in the NHSCSP cancer audit

16th September 2013

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, the use (or not) of BNC HG and a whole session on the NHSCSP cancer audit. Suitable for Thinprep® or Surepath™ users

20th – 22nd November 2013
Course Fee* : £15 / £230

Mock Exam Course for the Advanced Specialist Diploma in Cervical Cytopathology

A two-day course ideal for anyone intending to sit the Advanced Diploma exam. Practice at both written and practical elements and a full mock exam.

29th & 30th April 2013
Course Fee*: £200

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 and microscopy sessions on what can be called negative and what cant!

17th July 2013

Course Fee*: £15 / £120 per day

****Participants from the North East, Yorkshire and East Midlands will incur £15 administration fee only 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***

East Pennine Cytology Training Centre

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Training Centre Manager:

Mr N Dudding
0114 2712538
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 ThinPrep® Cytology

A one/two day course covering Borderline High-Grade Lesions and the use of HPV Triage and Test of Cure

These two days cover the difficult areas of borderline changes, high grade dyskaryosis cannot be excluded and how HPV triage links to the management of such women. The first day will cover the use of the category of borderline high grade, the second day will cover basic aetiology and the benefits and limitations of including HPV in the screening programme.

19th & 20th June 2013
Venue: Westbrook House, Newmarket
Course Fee: * £120 each

HPV. Its role in cervical carcinogenesis and how to Detect it

A one day course that aims to give anyone involved in HPV testing an overview of basic cell biology, the role that HPV plays and the different techniques that can be used to detect it.

17th June 2013
Course Fee*: £95

One-Day Non-Gynaecological Cytology Courses

Aimed at anyone undertaking their Specialist Portfolio, but also suitable for anyone requiring an introduction to non-gynae cytology. These courses will cover specimen preparation, urine, respiratory and effusion cytology.

17th & 18th September 2013
Course Fee*: £95 per day

One-Day Update Course for Medics Pitfalls & Problems in Cervical Cytology – Glandular Lesions

This workshop covers the many challenging and interesting cytological presentations associated with glandular lesions in particular endocervical abnormalities. The day includes discussions on current issues in cervical screening including automation, HPV testing and new technologies and recent developments with the NHSCSP invasive cancer audits and other issues relevant to the NHSCSP.

14th May 2013
Course Fee: * £95

Participants from the North East, Yorkshire and Trent Regions will incur £15 administration fee only 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

South West Regional

CYTOLOGY training centre

2013 Course Schedule

Date	Gynae Courses	Fee*
25 Feb-22 March 30 Sept-25 October	**Introductory in Gynae Cytology**	NHS £1000 Other £1200
22-24 April 9-11 September 25-27 November	**Prep for C&G Diploma in Cervical Cytology**	NHS £250 Other £300
16-18 April 11-13 June 3-5 September 3-5 December	**Update in Cervical Cytology for Technical Staff**	NHS £300 Other £350
24 September	**Update for Cytology Checkers**	£100
21 May 12 November	**Update in Cervical Cytology for Pathologists & Consultant BMS's & Holders of the Advanced Specialist Diploma in Cervical Cytology**	£100
6 June	**Gynae Histology for Technical Staff**	£100
22-24 January 25-27 June	**Gynae for Trainee Pathologists**	£300
30 April-1 May	**Gynae Pathology for Trainee Colposcopists**	£200
18-19 February 17-18 June 16-17 September	**Cervical Sample Taker Training**	£250

Date	Non-Gynae Courses	Fee*
16 May	**Serous Fluid Cytology**	£100
20 June	**Respiratory Cytology**	£100
7 November	**FNA Cytology**	£100
21 November	**Urinary Tract Cytology**	£100
5-8 February 2-5 July	**Non-Gynae for Trainee Pathologists**	£400

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

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

Depart of Cellular Pathology
Lime Walk Building
Southmead Hospital
BRISTOL BS10 5NB
Phone: 0117 323 5649
Fax: 0117 323 5640
E-mail: SWRCTC@nbt.nhs.uk

Dr K Denton
Director
Mr M Rowell
Deputy Director

Mrs Helen Burrell
Manager
Mrs Helen Hoskins
Deputy Manager

Lisa Holder
Course Administrator

North Bristol NHS
NHS Trust

Central Manchester University Hospitals NHS
NHS Foundation Trust
Directorate of Laboratory Medicine

THE NORTH WEST CYTOLOGY TRAINING CENTRE COURSES 2013

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

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

£100 per day

20 – 22 February 2013 (Last round of topics from previous year)

23rd April (A)
21st May (B)
12th June (C)
3rd July (A)
28th August (B)
17th September (C)
22nd October (A)
19th November (B)
10th December (C)

Introductory Course in Cervical Cytology for BMS/Cytoscreeners*

£1000

8th July – 2nd August

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

£250

30th April – 2nd May
3rd – 5th September

FRCPath COURSE NON- GYNAECOLOGICAL CYTOLOGY

£500

4th – 8th March
12th – 16th August

FRCPath Pre – Exam course

£400

11th – 15th March
19th – 23rd August

20% discount for regional trainees

Gynae Master Classes

Topics to be confirmed
16th April
10th October

Non Gynae Beginners Guides (BMS/Screeners)

£80 per day
(£25 admin fee only for NW Staff per day)
15th – 17th January
Respiratory
Serous Fluids
Urine
5th February
Breast

Non Gynae Master Classes for Medical Staff

Thyroid
14th October
Course fee: £100 / £80 for NW regional staff

Non Gynae Master Classes for Medical Staff

EBUS
27th November
Course fee to be agreed

Theoretical Cytology Course for Novice Sample takers

£100

26th – 27th February
25th – 26th June
12th – 13th November

Primary Care ½ day Update

£5 admin fee

7th February
9th May
8th August
17th October
5th December

£80 per day
(£25 admin fee per day only for NW)

Cytology for Virologists

18th June

Histology for Cytologists

New Date to be confirmed

Virology for Cytologists

Date to be confirmed

Head and Neck Adequacy Assessment for BMS staff

17th June
Course fee: £100 / £80 for NW regional staff

*Mandatory Courses Are Free Of Charge to North West Region Technical Staff.
Please note that all gynae courses are based on SurePath morphology

Director
Dr Mina Desai CBE
Consultant Cytopathologist/Director
Email: mina.desai@cmft.nhs.uk

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

For information, please contact:
Administrator:
Miss Jen Bradburn
0161 276 8804
Email: jennifer.bradburn@cmft.nhs.uk

Association of Clinical Pathologists in conjunction with British Association for Cytopathology

Histopathology, Cytopathology & Forensic Pathology Scientific Meeting

RIBA, 66 Portland Place, London, W1B 1AD

6 & 7 June 2013

Thursday 6 June - Start 9.55 - Finish 17.00

Histopathology, Cytopathology

Quality assurance of screening programmes	Dr K Denton
Molecular Tools in screening of Tumours	Dr S Diaz-Cano
Prostate Screening	Mr J Hines
Screening for Cholesterol and Diabetes	Dr W Simpson
Colorectal Screening	Dr V Sheshappanavar
Anal Screening	Professor R McMahon
Challenging Cases from the Female Genital Tract	Dr N Singh & Dr A Faruqi

Presidential Address

Dr M J Galloway

Poster Presentations

Full details available on ACP website

Friday 7 June - Start 10.00 - Finish 15.45

Histopathology, Cytopathology

Cytology screening in at risk populations	Dr K Denton
HPV primary screening	Mrs K Ellis
Breast Screening	Dr D Ryan
Identification of high risk patients for skin cancer	Professor R Cerio

Forensic Pathology

Will post mortem imaging kill the autopsy?	Professor I S D Roberts
Post Mortem imaging and Forensic Pathology	Dr N Hunt

Pathologists in Training session

Friday 7 June at 13.30 to 16.00

An approach to medical liver biopsies	Professor S Hubscher
Slide Seminar – common patterns of liver disease and the diagnostic approach	Dr R Brown

For further information and a registration form please visit our website: www.pathologists.org.uk

Telephone: 01273 775700

E-mail: info@pathologists.org.uk

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BAC British Association for Cytopathology

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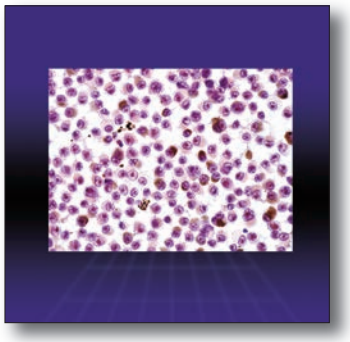
Material for publication should be sent direct to the Editor; all other correspondence with the Association should be addressed to the Secretary.

Cover Image: courtesy of Dr Diane Hemming, Gateshead. This is a malignant melanoma from a fine needle aspirate of a skin lump.



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