

CME Article

The pivotal role of the pathology laboratory in the context of a Singapore cervical cancer screening programme

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ABSTRACT

Singapore is poised to implement a national cervical screening programme and pathology laboratories have a pivotal role to play. This review describes the laboratory examination of Pap smears and the importance of providing a first class service. This will require sufficient experienced cyto-technologists and pathologists. There also needs to be a mechanism in place to monitor all stages of the Pap smear, from the time it is taken until it is reported. The Bethesda System for reporting Pap smears, new smear collection devices, liquid-based specimens, use of computer screening and other measures to enhance laboratory standards, are also discussed.

Keywords: cervical cancer, cervix, cytology, laboratory standards, screening

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INTRODUCTION

The Pap smear test, with minor refinements, was devised by George Papanicolaou nearly 80 years ago, after he found cancer cells in some samples collected from the vagina for investigating hormonal changes. Despite not having done controlled trials, a point often broached by detractors, the Pap test has proved to be one of the best procedures for cancer prevention^(1,2). This is because the majority of cervical cancers start from an area of dysplastic epithelium that can be detected by a well-taken Pap test and with simple treatment, cancer is prevented from developing. Some dysplasias may regress and even if malignancy develops, it may take several years. In countries that have good comprehensive Pap smear screening programmes, the cervical cancer rate is exceedingly low^(1,2). Consequently, a group of experts stated “that with the exception of stopping the population from smoking, cervical cytology screening offers the only major proved public health measure for significantly reducing the burden of cancer today”⁽³⁾.

Although the Pap smear is an excellent test, it is not totally foolproof and there is a significant false-

negative rate with resultant undetected disease. This can be due to a number of factors, including the nature and location of the area of dysplasia, faulty sampling and laboratory error. Faulty sampling accounts for over 60% of false-negative smears, and laboratory factors are mainly responsible for the remaining cases⁽⁴⁾. In the context of a Pap test programme that fails to reduce the incidence of cervical cancer, there are two additional factors that cannot be ignored. Firstly, when the clinician does not take appropriate follow-up action on patients with abnormal Pap test results and secondly, women fail to have regular Pap tests.

THE ROLE OF THE LABORATORY

Ensuring optimal Pap smears

Both pathologists and laboratory staff should be knowledgeable on all aspects of Pap smear taking and when necessary, provide instructions to clinicians on how to improve the quality of smears submitted for examination. This includes basic procedures such as ensuring the glass slide and request form have adequate patient identification, as failure to comply can result in serious medico-legal problems. Lubricants should not be used to facilitate the insertion of a speculum as the jelly can obscure cells and make microscopical examination difficult. It is better to use tepid water to both lubricate and warm the speculum, a much more patient-friendly option.

A screening Pap smear is taken from the normal-looking cervix of an asymptomatic woman, and cervical dysplasia is invisible to the unaided eyes^(5,6). Consequently, to obtain an optimal specimen, the sampling implement is firmly swept 360 degrees once around the entire ectocervix. When placing the specimen onto a slide, a rapid stroking action should be used and not a forceful and circular motion, as the latter action will crush cells and also disrupts cell groups that can aid diagnosis. A common fault with many Pap smears is air-drying cellular changes. These make microscopical interpretation very difficult, and abnormal cells may not be identified. This artifact is due to delay in placing the slide in 95% ethyl alcohol (Fig. 1), or application of the spray fixative (Fig. 2), and is easily solved by

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Fig. 1 The slide is immersed in 95% ethyl alcohol.

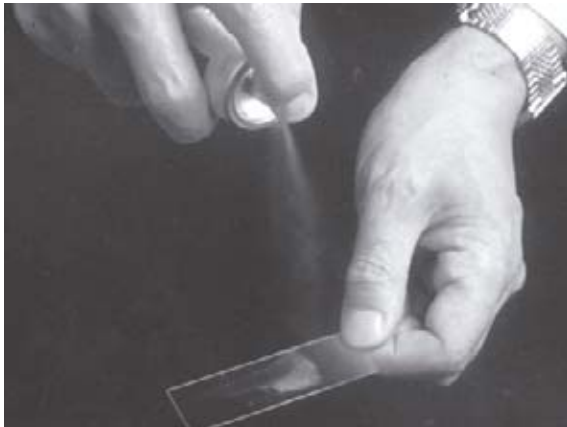


Fig. 2 An aerosol fixative is more convenient but in the author's experience, it is less effective than immersion in 95% alcohol.

more rapid fixation. A wooden tongue depressor and a cotton-wool tipped applicator stick are not suitable for taking Pap smears.

In women of child-bearing age, adequate samples should have endocervical and/or metaplastic squamous cells to indicate that the transformation zone (TZ), the region where the majority of cancer develop, has been sampled^(7,8). In older women with migration of the TZ into the canal, endocervical cells may be absent from the smear. A good smear should have at least 10% of the slide covered with well-preserved and well-visualised squamous cells. In the Bethesda System (TBS) for reporting Pap smears, the adequacy of the specimen forms an integral part of the report^(9,10). Laboratories thus have a duty to inform clinicians of their smear quality and this should be done on a regular basis.

Finally, all smears should be accompanied by adequate clinical data. The minimum information includes the patient's age, date of last menstrual period

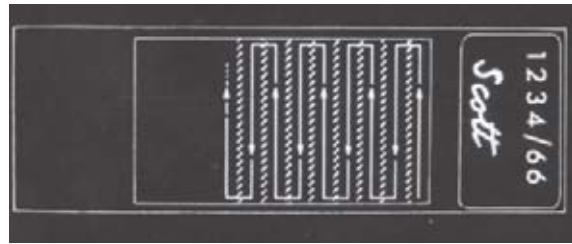


Fig. 3a Schematic diagram showing how a Pap smear is examined methodically so that no abnormal cells are missed.

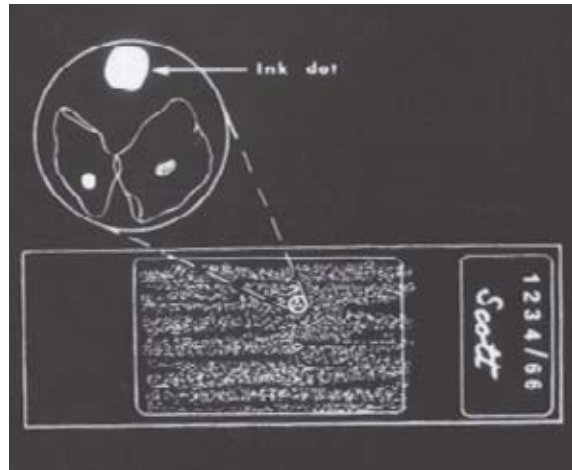


Fig. 3b The cyto-technologist marks any abnormal cells for the pathologist to check before a report is issued.

(LMP), previous obstetrical and gynaecological history, hormone therapy and a brief description of any clinical findings. This information can help increase the sensitivity and reliability of the laboratory interpretation of the Pap smear, especially in cases where the findings are of an uncertain nature.

Laboratory examination

The examination of Pap smears is a labour intensive process. It can be boring, and yet requires the full attention of the cyto-screener. In Singapore and many other countries, cyto-screeners or cyto-technologists are usually medical technologists with additional training in cytology and certification by the International Academy of Cytology or other recognised institutions. Unfortunately, there is a shortage of these skilled workers and moreover, they are part of an ageing workforce.

A conventional Pap smear can have several hundred thousand cells, and it is the exacting task of the cyto-screener to systematically examine the entire slide and identify abnormal cells that are marked and referred to the pathologist for final assessment before reporting (Figs. 3a-b). An experienced screener will take five to six minutes to examine a slide and in an hour, it may be possible to examine 12 smears and notionally, 96 slides in a day. However, fatigue can set in and a good laboratory will ensure that screeners have regular

Table I. Squamous cell abnormalities and various classifications.

Description	CIN grades	The Bethesda System (2001)	Papanicolaou classes (closest equivalent)
Normal	Normal	Negative for intra-epithelial lesion or malignancy	Class I
Atypical (Reactive or neoplastic)	Atypia	ASC-US (ASC-H)*	Class II
HPV	HPV	LSIL	Class II
Mild dysplasia	CIN I	LSIL	Class II
Moderate dysplasia	CIN II	HSIL	Class III
Severe dysplasia	CIN III	HSIL	Class III
Carcinoma in-situ	CIS	HSIL	Class IV
Invasive carcinoma	Invasive carcinoma	Invasive carcinoma	Class V

*ASC-H: Atypical squamous cells cannot exclude HSIL. This category has no real equivalent terminology in the Papanicolaou Classification.

breaks and a realistic number of smears to examine. Otherwise, abnormal cells may not be detected, with disastrous consequences. This was graphically demonstrated in the accounts of substandard laboratories in the USA that paid screeners by the number of cases examined. This resulted in unacceptably high false-negative rates.

The revelations created a public uproar and resulted in Congressional hearings and enactment of the Clinical Laboratories Improvement Amendments of 1988⁽¹¹⁾. The regulations laid down guidelines on the maximum number of slides that could be screened daily by technologists. Furthermore, all abnormal smears must be examined by a pathologist before reports were issued, and laboratories were mandated to re-screen 10% of their negative Pap smears. In addition, cyto-pathologists and cyto-technologists are monitored by the Centre for Disease Control. These stringent regulations resulted in the closure of many second-rate laboratories⁽¹¹⁾.

Reporting Pap smears

In Singapore, most laboratories use TBS, with or without modification, for reporting Pap smears. The nomenclature was the outcome of three workshops sponsored by the National Cancer Institute in Bethesda, Maryland, USA, held in 1988, 1991 and 2001. The third workshop evaluated changes in the practice of cytopathology since the 1991 revision, including the use of new processing methods, ancillary techniques and tests, and automation⁽¹⁰⁾. TBS has largely replaced the Papanicolaou Classification in which cytological findings were designated Class I (normal) through to Class V (conclusive for malignancy), and which no longer reflected the present-day understanding of cervical and vaginal neoplasia (Table I). In addition, the Papanicolaou Classification did not correlate well with the diagnosis in biopsy material, and abnormal but benign entities were not adequately catered for.

Moreover, as a result of modifications, the various classes had a different meaning when used by different laboratories. TBS also lends itself to the computer entry of results.

In brief, TBS covers specimen quality and adequacy, general categorisation of cytological findings, and a descriptive diagnosis of any abnormality. The lesions that are designated low-grade squamous intraepithelial lesion (LSIL) encompass cervical intraepithelial neoplasia grade one (CIN I) and human papillomavirus (HPV) lesions while high-grade squamous intraepithelial lesion (HSIL) includes CIN II, CIN III and carcinoma in-situ (CIS) lesions. Tables II and III list the major elements of the TBS, including the 2001 modifications.

In the atypical squamous cells of undetermined significance (ASC-US) category, the squamous cells have changes that are intermediate between those seen in benign reactive changes and those seen in a squamous intraepithelial lesion. The microscopist therefore cannot be certain whether the changes are reactive or due to squamous intraepithelial lesion. In the 2001 revision, a new category of atypical squamous cells was introduced, namely: atypical squamous cells of undetermined and cannot exclude high-grade squamous intraepithelial lesion ASC-H. The term ASC-H is used when a smear has a majority of abnormal cells showing ASC-US changes but in addition, there are a small number of cells that have the cytological features of a high-grade lesion. The changes could be the result of human papilloma virus (HPV), inflammation, or atrophy and inflammation. About 5% to 10% of all ASC-US are in the ASC-H category.

The ASC-US rate for a low-risk population should be less than 5% of results and for high-risk populations, around two to three times the SIL rate. If a laboratory has a squamous intraepithelial lesion rate of 2%, then the frequency of ASC-US should not exceed 6%⁽⁹⁾. The diagnosis of ASC-US should be based on rigid criteria and it should not be used to “lump” all

Table II. Classification of specimen adequacy.

TBS 1991	TBS 2001	Change
Satisfactory	Satisfactory for evaluation (Describe presence or absence of endocervical transformation zone component and any other quality indicators, e.g., partially obscuring blood, inflammation, etc.)	For liquid-based cytology, an adequate sample would have a minimum of 5,000 epithelial cells to be satisfactory. However, professional judgement may be needed when applying numerical criteria in certain cases, e.g. atrophy. The presence of an epithelial cell abnormality automatically makes a specimen satisfactory-regardless of the number of epithelial cells.
Satisfactory but limited by (specify reason) • Lack of endocervical cells • Obscuring blood • Obscuring inflammation • Air-drying artefact.		The category SBLB has been eliminated. The descriptors are to be used in a comment section, but not to determine adequacy.
Unsatisfactory (specify reason) • Obscuring blood • Obscuring inflammation • Air-drying artefact	Unsatisfactory for evaluation (specify reason) • Specimen rejected/not processed (specify reason) • Specimen processed and examined, but unsatisfactory for evaluation (specify reason) – Too few squamous cells – Poor preservation – Totally obscured by blood	The reasons to refer to a specimen as unsatisfactory have been reduced to the reasons noted (left).

Table III. General categorisation of TBS.

TBS 1991	TBS 2001	Change
Within normal limits (WNL)	Negative for intraepithelial lesion or malignancy • Organisms • Other non-neoplastic findings	WNL is now named negative for intraepithelial lesions or malignancy and includes the previous category of BCC as a descriptor only.
Benign cellular changes (BCC) • Infection • Repair		BCC was eliminated as a diagnostic category (see above).
	Other • Endometrial cells in a woman \geq 40 years (specify if negative for SIL)	This category is new.
Epithelial cell abnormality <u>Squamous cells</u> • ASCUS [atypical glandular cells of undetermined significance) – Favour reactive – Favour neoplasia – Not otherwise specified (NOS) • LSIL • HSIL • Squamous cell carcinoma	Epithelial cell abnormality <u>Squamous cells</u> • Atypical squamous cells of – undetermined significance (ASC-US) – cannot exclude HSIL (ASC-H) • LSIL • HSIL • Squamous cell carcinoma	The multiple subcategories of ASCUS have been reduced to just two: (ASC-US, ASC-H), with no other modifying statements.
Epithelial cell abnormality <u>Glandular cells</u> • AGUS (atypical squamous cells of undetermined significance) • Favour reactive • Favour dysplasia • NOS • Adenocarcinoma	Epithelial cell abnormality <u>Glandular cells</u> • Atypical (NOS) – Endocervical cells – Endometrial cells – Glandular cells • Atypical (favour neoplastic) – Endocervical cells – Glandular cells • Endocervical adenocarcinoma in situ (AIS) • Adenocarcinoma – Endocervical – Endometrial – Extrauterine – Not otherwise specified [NOS]	The subcategories of AGUS have been expanded to allow for a more descriptive diagnosis of glandular abnormalities. AIS is now a distinct entity.
	Other malignant neoplasms (specify)	This category is new

cases with minimal cellular abnormalities. It has been shown that women with ASC-US are at risk of harbouring a more advanced lesion. In one study, 28% of 2,765 women with ASC-US had biopsy-proven SIL, and 10% had a CIN II or higher grade lesion⁽¹²⁻¹⁴⁾. Thus women with persistent ASC-US need to be further investigated, such as with colposcopy. Glandular and other abnormalities are also covered in TBS (Table III). Reports from good laboratories will include recommendations such as repeating a smear or referral for other investigations. Clinicians and pathologists should have good lines of communication so that reports are clearly understood.

THE NEED FOR OPTIMAL LABORATORY STANDARDS

Cyto-technologists

Cyto-technologists are skilled healthcare professionals who can be considered to be the back-bone of a cervical screening programme. Cyto-technologists also evaluate other specimens that include sputum, urine, body cavity fluids, and fine-needle biopsy specimens. Unfortunately, there is a shortage of qualified cyto-technologists in Singapore. This makes it difficult to implement a first-rate comprehensive cervical screening programme, unless women are willing to wait weeks for their results. An even more serious outcome is false-negative results resulting from cyto-technologists having to cope with a heavy workload. This would discredit a screening programme and deter women from participating.

Recruiting cyto-technologists from overseas is a quick solution but this may be difficult as there is a world-wide shortage of qualified people. A better strategy is to establish a Singapore cyto-technology training centre and although this will take time to implement, it will be worthwhile. The disadvantages will be offset by long-term benefits, especially if high-calibre persons can be attracted to train and remain in the specialty. This can be facilitated by having a career structure in place, and implementing mandatory registration for medical laboratory staff to give these skilled paramedical personnel appropriate professional recognition.

It is interesting to note that medical laboratory technologists (MLTs) or scientists, despite having a tertiary education and further professional qualification, are not required to be registered in Singapore. In contrast, pharmacists and nurses, two vocational groups with comparable educational requirements and professional responsibility, are required to be registered. Laboratory test results are pivotal in the treatment of patients, thus the work undertaken by technologists must be of the highest possible standard and the mandatory licensing of this group of workers would

further help in maintaining standards and professionalism. In many countries, MLTs are required by legislation to be registered and to undertake continuing professional education to enable them to keep abreast with the latest developments in their field. Registration also provides the general public with greater protection as their laboratory tests are undertaken by licensed technologists and if there are problems, disciplinary action can be undertaken by the licensing authority.

Quality assurance programmes

Internal quality assurance programmes include the monitoring of all aspects of specimen processing within a particular laboratory. This encompasses continuing education, training, review of procedures and their implementation, re-screening of a proportion of normal smears and various auditing procedures. Additional activities are case reviews, clinical meetings, histological-cytological correlation, and the review of individual staff performance. External programmes entail the evaluation of slides sent from an external agency, and the collective diagnosis is returned within a specified time. Slides can also be submitted for various staining procedures to evaluate technical competence. The results are analysed, laboratories are informed of their performance, and the information is disseminated to all staff. In addition, a laboratory's performance can be compared with that of the other participating laboratories, and this competitive element is a valuable tool for enhancing standards.

Laboratory accreditation

At the time of writing, several pathology laboratories in Singapore have been accredited by a dedicated medical laboratory assessment agency. Modern medical treatment requires an accurate diagnosis. Thus, laboratories must be able to produce results that are accurate, and within an acceptable turn-around time. When a laboratory has been accredited, it means it has a system in place that allows high quality laboratory work to proceed and additionally, the work-place is safe for staff. A process of formal evaluation of a laboratory by an unbiased external testing agency, such as College of American Pathologists (CAP) or the National Association of Testing Authorities Australia (NATA), is an essential step to ensure Pap smears are evaluated to the highest possible standard.

During an accreditation inspection, all aspects of laboratory operation are scrutinised; not just how tests are performed but also the qualification and experience and supervision of staff, methodology, reporting practice, record keeping, and quality control programmes (internal and external), staff training, continuing education and safety⁽¹⁵⁻¹⁷⁾. In the inspection



Fig. 4 Several Pap smear sampling devices. From the left to right, these are the original Ayre spatula, cotton-tipped applicator (not recommended), Cervex[®] brush, Cytobrush[®], modified Ayre spatula (most commonly used), Accellon Combi biosampler, and three others for obtaining endocervical and ectocervical samples.



Fig. 5a The Cervex[®] brush is inserted into the cervical os and turned five times in a clockwise direction.

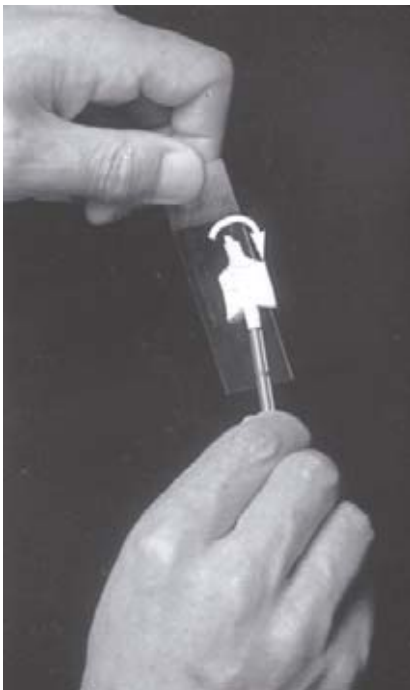


Fig. 5b The sample is placed on the slide by "wiping" the bristles on one side on the slide and then the other side.

of a laboratory for accreditation, a peer review system is used, and a team of outside expert pathologists and technologists carry out the evaluation. In some countries, accreditation is mandatory if a laboratory is to receive insurance and government funding⁽¹⁶⁾.

Histological-cytological correlation

In order to improve cytology standards, an important and regular exercise is to correlate the cytology diagnosis with relevant histology. The close interplay of histopathology and cytology is well-illustrated in the contemporary management of any woman with a significantly-abnormal Pap smear. The cervix will have a normal appearance when examined with the unaided eye and in addition, the patient usually has no symptoms such as pain, discharge or bleeding. A colposcopic examination will allow the lesion to be identified and during this procedure, directed biopsies are taken for histological verification. The biopsies are important because if the pathologist can exclude invasion, simple ablative therapy is usually sufficient for satisfactory treatment.

A Cone biopsy is seldom used to treat the precursor lesions of cervical cancer, especially in younger women. Excessive removal of normal tissues can result in either cervical stenosis or incompetence and both are undesirable, especially if future pregnancy is contemplated. In contrast, if invasion is detected, more extensive surgery will be needed, with or without more biopsies being taken to allow histological confirmation of the clinical diagnosis⁽⁶⁾. Pathologists also have a pivotal role to play in the management of patients with more advanced disease and who need major surgery. The meticulous examination of the radical hysterectomy specimen and associated lymph nodes is crucial for optimal patient management.

IMPROVING THE PAP SMEAR SPECIMEN

A major problem with the conventional Pap smear is that only 20% to 30% of cells are transferred onto the slide, while the rest are discarded with the sampling device⁽¹⁸⁾. Consequently, there is ample scope for a false-negative smear result.

New samplers

The wooden sampler that is widely-used is a modified version of the one invented in 1947 by Ernest Ayre, a Canadian gynaecologist⁽¹⁹⁾. To improve cell collection, other devices have been developed, including the Cytobrush[®] and Cervex[®] brush (Fig. 4). An adequate Pap smear can be obtained by using the modified Ayre's spatula to collect an ectocervical sample, and a Cytobrush[®] to obtain an endocervical component. This is particularly useful in older women, when the endocervix is less accessible. The Cytobrush[®] usually causes some bleeding so it should be used after the



Fig. 6 The sample obtained with a Cervex[®] brush placed into a preservative solution by detaching the "broom" part.

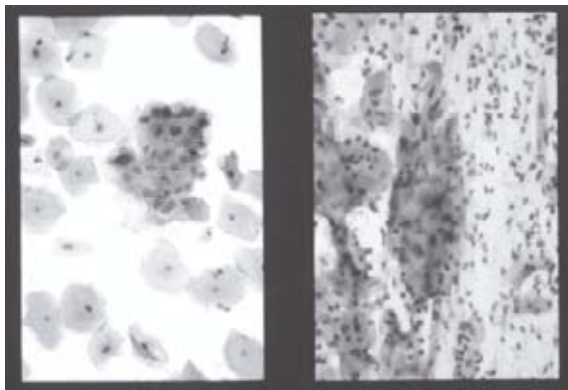


Fig. 7 This composite picture shows a liquid-based smear with a clean background (left panel) contrasted with a conventional Pap smear (right panel) which contains more cells, often overlapping along with mucus and neutrophils (right panel).

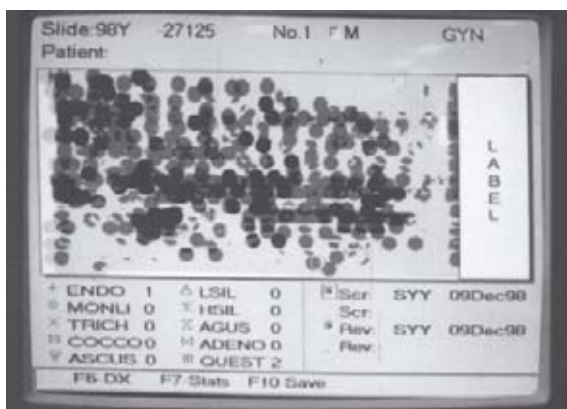


Fig. 8 The monitor displays the screening "map". Each dot represents a field that was examined.

spatula sample has been obtained. Otherwise, the ectocervical specimen is contaminated with blood and this makes examination more difficult. A Cytobrush[®] sample alone constitutes an inadequate examination

as few ectocervical cells are available for examination. The newer Cervex[®] brush (Figs. 5a-b) can collect a comparable sample to that obtained by using both a wooden scraper and Cytobrush[®](5,20).

Liquid-based Pap smears

Previously, liquid-based cytology (LBC) preparations had been successfully used for fine-needle aspiration specimens, sputum samples and body cavity fluids. The specimen is collected in the similar way to a conventional Pap smear but instead of being smeared onto a glass slide, the sample is placed in an alcohol-based preservative solution (Fig. 6). This solves the problem of drying artefact in cells, which is often present in poorly-fixed conventional smears. The sample is sent to the laboratory where it is processed to remove obscuring material, such as mucus or inflammatory cells, and a random sample of the remaining cells is taken. A thin layer of the cells is deposited onto a slide (Fig. 7). The slide is examined in the usual way under a microscope by a cyto-technologist⁽²¹⁾. Studies have shown that liquid-based samples have sufficient cells to allow a diagnosis, and the detection rate is as good as or better than conventional smears⁽²²⁾.

The examination of smears is faster because all the cells are located within a 13-20mm diameter circle, and obscuring material is removed during processing⁽²¹⁻²⁴⁾. Any unused material can be used for ancillary investigations, such as human papilloma virus (HPV) testing. The main disadvantage of the liquid-based Pap smear is the higher cost. Smears have to be obtained with a more expensive sampler, such as the Cervex[®] brush, because cells adhere to the wooden Ayre's spatula and are difficult to transfer into the fixative fluid. Other costs include the laboratory processor, liquid preservative, special slide and single-use filter. However, costs should decrease with wider use.

COMPUTER TECHNOLOGY HELPS IMPROVE PAP SMEAR SCREENING

The examination of Pap smears is very labour intensive, and computer-based devices are available to help improve human screening. One system, i.e. the PathFinder[®], consists of a computer and a small monitor that are attached to the microscope (Fig. 8). When the screener examines a smear, a "map" is produced and if the screener has a tendency to overlook areas on the slide, this can be observed and corrective action can be taken. The "map" can be recorded and retrieved for later review. Additionally, the system also allows the electronic marking and labelling of any abnormal cells identified, and these can be retrieved for examination at a later date. As these instruments can also record the work undertaken by each screener, workload statistics are easily generated without the need for additional paper work. Quality assurance functions, such as the correlation



Fig. 9 The trays of Pap smears are loaded into the FocalPoint® instrument. It takes approximately 8 minutes to scan one slide.

of previous smear and biopsy results, can also be undertaken and screening efficiency can be improved by up to 15% by the use of these computer-linked devices⁽²⁶⁾.

Recruiting more women to have Pap tests may overburden existing laboratories and employing an automated cervical smear screening instrument, such as the FocalPoint® primary screening system (Fig. 9), can alleviate problems. Studies have shown that the use of this instrument may increase the overall accuracy of the cervical screening process, as well as improving laboratory productivity^(24,25,30). Any automated primary screening system must have high sensitivity in order that cancers and precursor lesions are detected. In addition, high specificity is important if laboratory and clinical productivity is to be optimised. Other important requirements are the ability to identify inadequate samples, accurately mark abnormal cells for subsequent human examination, and increased throughput of cases (compared to manual screening) at a reasonable cost.

The FocalPoint® uses a high-resolution scanner and a high-speed video microscope to obtain cell images from conventional Pap smears. The images are digitised and the data processed with image interpretation software. Specially-designed algorithms are used to recognise, analyse and identify cases that have the highest probability of containing abnormal cells. Slides having the lowest probability of being abnormal can be safely reported as normal, and need no further manual review by a cyto-technologist. Slides having a higher probability of abnormality require manual cyto-technologist screening, with an additional quality control rescreening on the highest probability slides deemed normal on initial manual screening.

Currently, the FocalPoint® is the only instrument approved by the United States Federal Drug Administration (FDA) for primary screening. Outside of the USA, up to 50% of Pap smears are being archived with good performance⁽³⁰⁾. In addition to overall slide classification, the instrument produces a printed map of the slide (PAPMAP®) that contains up to 15 circles. One such circle is referred to as a field-of-view (FOV). In abnormal cases, the FOVs are highly likely to contain individual abnormal cells.

Accompanying each slide map is information on specimen adequacy, the presence of endocervical cells, the degree of obscuration by inflammatory cells, and the overall ranking of the case.

The screening time could be substantially shortened if an accurate cytological diagnosis was obtainable by looking only at the FOVs that the instrument identified as containing abnormal cells, without the need to screen the entire slide. Studies have showed that the screening time for Pap smears can be halved by using the FocalPoint® system⁽³⁰⁾. A recent development interfaces the FocalPoint® to the screener's microscope which is equipped with an automated stage so that the screener is taken directly to the location of the abnormal cells identified without having to use the slide map, thus further speeding up the examination process. The instrument is also able to examine liquid-based Pap smears.

CONCLUSION

Pathology laboratories have a pivotal role in ensuring a cervical cancer screening programme is successful. This is because the ultimate diagnosis, and hence the management of any patient, is dependent on the all important Pap smear result. The examination of Pap smears must be first class, or false-negative results will eventuate and the consequences of this can be tragic. This has been graphically shown in some well-publicised Pap smear blunders in other countries^(11,31-33). Accreditation by a specialised external agency is the simplest way of ensuring laboratories are up to standard. During the thorough evaluation for successful accreditation, all facets of work are scrutinised – ranging from staffing through specimen accession, reporting, quality systems and continuing professional training and education. The rigorous preparation and scrutiny ensures laboratory attain an international level of operation. To achieve this, laboratories that are not presently accredited will need time to bring their operations up to standard. If compliance could be achieved voluntarily, this would be most desirable. However, in other jurisdictions, government intervention has been necessary as voluntary schemes did not produce the desired result^(11,16). Hopefully, in Singapore where a cooperative mind-set prevails, as evidenced by the recent SARS crisis, self-regulation may be sufficient and all laboratories will soon be accredited.

Other requirements to ensure Singapore has an optimal cervical cancer screening programme includes: establishing a national agency to monitor the performance of laboratories examining Pap smears, and a slide proficiency testing programme that requires cyto-technologists and pathologists to regularly evaluate unknown cases and return their diagnosis to a central registry. As previously

alluded to, the registration and certification of cyto-technologists is another issue that needs to be addressed in Singapore. These measures along with attractive working conditions will help attract motivated people into becoming cyto-technologists, and also help solve a manpower problem.

Of the new technologies described, LBC is worthy of adoption in Singapore. LBC would reduce the number of "inadequate" tests and hence the number of women who would be recalled for a repeat Pap test. Additionally, it would decrease pressure on a skilled workforce. Cyto-technologists and pathologists would have fewer inadequate smears to examine and the current workforce would be able to examine a larger volume of Pap smears as the time to examine a LBC Pap smear is significantly shorter. After critical evaluation, the National Health Service in England and Wales has decided to replace the conventional Pap smear with LBC as the benefits of having less unsatisfactory specimens offsets the additional cost of using this technique⁽³⁴⁾.

Computer-screening devices could help alleviate some of the problems due to a shortage of cyto-technologists but such instruments are expensive and there are also ongoing maintenance costs. Even though new technologies may improve the test, when healthcare resources are limited, it is important to ensure their adoption does not mean money allocated for screening is diverted to pay for their implementation and thereby deprive those who have never been tested the chance of having a Pap smear. Despite the emergence of new techniques, the conventional Pap smear, when well taken and evaluated by a competent laboratory, is still an excellent and "most cost-effective" test for cervical cancer prevention⁽³⁵⁾. An important qualification is the need for women to have regular follow-up tests. Finally, the message for Singapore physicians who take Pap smears is simple, namely: you have a critical role to play in cervical cancer prevention. Your role is to encourage your patients to have regular tests, obtain optimal smears and lastly, ensure they are screened by laboratories that are committed to providing a first class service.

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SINGAPORE MEDICAL COUNCIL CATEGORY 3B CME PROGRAMME

Multiple Choice Questions (Code SMJ 200406A)

	True	False
Question 1. The main objective of Pap smear screening is to:		
(a) Detect the precursor lesions of cervical cancer.	<input type="checkbox"/>	<input type="checkbox"/>
(b) Assess hormonal status.	<input type="checkbox"/>	<input type="checkbox"/>
(c) Diagnose cervical cancer.	<input type="checkbox"/>	<input type="checkbox"/>
(d) Diagnose endometrial disease.	<input type="checkbox"/>	<input type="checkbox"/>
Question 2. A laboratory request form accompanying a Pap smear should have the following information:		
(a) Date of last menstrual period.	<input type="checkbox"/>	<input type="checkbox"/>
(b) Information on hormone intake (e.g., oral contraceptive, hormone replacement).	<input type="checkbox"/>	<input type="checkbox"/>
(c) Previous history of any cervical abnormality and treatment.	<input type="checkbox"/>	<input type="checkbox"/>
(d) Clinical appearance of the cervix at the time of taking the smear.	<input type="checkbox"/>	<input type="checkbox"/>
Question 3. The following devices can be used to obtain a good Pap smear:		
(a) A wood Ayre's spatula.	<input type="checkbox"/>	<input type="checkbox"/>
(b) A cotton tipped applicator stick.	<input type="checkbox"/>	<input type="checkbox"/>
(c) A Cytobrush® alone.	<input type="checkbox"/>	<input type="checkbox"/>
(d) A wood tongue depressor.	<input type="checkbox"/>	<input type="checkbox"/>
Question 4. A false- negative Pap smear result can be due to:		
(a) A poorly-visualised cervix during sampling.	<input type="checkbox"/>	<input type="checkbox"/>
(b) Use of an aerosol fixative.	<input type="checkbox"/>	<input type="checkbox"/>
(c) An excessively bloody smear.	<input type="checkbox"/>	<input type="checkbox"/>
(d) Substandard laboratory practice.	<input type="checkbox"/>	<input type="checkbox"/>
Question 5. To avoid problems, including medicolegal ones, the following procedures are important:		
(a) The patient's name and identification (preferably the NRIC) number should be clearly written on the Pap smear glass slide.	<input type="checkbox"/>	<input type="checkbox"/>
(b) Laboratory accreditation ensures a high standard of operation.	<input type="checkbox"/>	<input type="checkbox"/>
(c) A patient with two consecutive Pap smears with ASC-US changes does not need further investigation.	<input type="checkbox"/>	<input type="checkbox"/>
(d) Cyto-technologists can safely examine over 100 smears per day.	<input type="checkbox"/>	<input type="checkbox"/>

Doctor's particulars:

Name in full: _____

MCR number: _____ Specialty: _____

Email address: _____

Submission instructions:

A. Using this answer form

1. Photocopy this answer form.
2. Indicate your responses by marking the "True" or "False" box
3. Fill in your professional particulars.
4. Either post the answer form to the SMJ at 2 College Road, Singapore 169850 or fax to SMJ at (65) 6224 7827.

B. Electronic submission

1. Log on at the SMJ website: URL <http://www.sma.org.sg/cme/smj>
2. Either download the answer form and submit to smj.cme@sma.org.sg or download and print out the answer form for this article and follow steps A. 2-4 (above) or complete and submit the answer form online.

Deadline for submission: (June 2004 SMJ 3B CME programme): 25 July 2004

Results:

1. Answers will be published in the SMJ August 2004 issue.
2. Successful candidates will be notified by email in August 2004.
3. Passing mark is 60%. No mark will be deducted for incorrect answers.
4. The SMJ editorial office will submit the list of successful candidates to the Singapore Medical Council.