Weekly Rescreening of 10% of the Total Cervical Papanicolaou Smears: A Worthwhile Quality Assurance Scheme

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Background : *In awareness of possible false negative cervical Papanicolaou tests in routine service, the authors developed and tested a new scheme that would be a practical adjunct in quality assurance.*
Objective : *To evaluate the value of a weekly rescreen of 10% of the total cervical Papanicolaou smears as a quality assurance scheme.*
Design : *A prospective descriptive study.*
Results : *Of 31,914 slides in the 9-month study period, a total of 3,097 slides (9.7%) were picked up in the rescreen scheme. There were 29 discordant cases (0.9%) consisting of 7 cases (0.2%) of errors from the initial reporting, 2 cases of errors from the rescreening and 20 other cases from disagreements on designating atypical squamous cells of undetermined significance. The errors of the initial reports could be further classified into 6 cases due to screening errors and one case because of interpretation error. The proper diagnoses had been revised and resent to the attending gynecologists.*
Conclusion : *A weekly rescreening 10% of total cervical Papanicolaou smears scheme was worthwhile for quality assurance. It could be used for evaluating screener performance and create internal quality improvement. The detected false diagnoses were manageable.*

Keywords : *Cervical Pap smear, Pap test, Quality assurance, 10% rescreen*

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Cervical Papanicolaou test (Pap test) is a substantial part of pathology serviced laboratories nowadays. It challenges the laboratory management to minimize false diagnosis cases. Usually cytopathologists (CP_s) and cytotechnologists (CT_s) work side by side. The CTs do the primary screening and the CPs review the slides and sign out reports. For a day-to-day working scheme, the CP's review is required for every abnormal Pap smear including 'reactive and reparative changes' that have been labeled by the CTs. In addition, those Pap smears from symptomatic patients and those for diagnostic purpose need the expertise of the CPs. Because hundreds of smears emerge every day and most of the screened slides are negative, therefore, the CTs' role to release some of the negative Pap smears is rewarding. A mandate of prospective rescreening of at least 10% of negative Pap smears has been practiced since the Clinical Laboratory Improvement Act (CLIA 67) passed in the 1960s [1]. The means is recommended for the process of quality control that is performed before a report is issued. However, there are still some false negative slides that have been missed. The published false negative rates range from 1.6 to nearly 28% [2]. Some events caused lawsuits in the United States [1]. As a consequence, two more quality control/assurance means - 5-year lookback of negative Pap smears for every newly found high-grade squamous intraepithelial lesion (HSIL) and cytologic-histologic correlation of all relevant cases - and other stringent measures such as workload limits have been added to the revised Act under the Clinical Laboratory Improvement Amendment of 1988 (CLIA 88). Since the means will discover mistakes only when surgery took place (after-event means), there should be some measures operating before the event period and that mistakes are manageable. The authors

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speculated that a scheme of weekly 10% rescreen of total Pap smears could be a routine adjunct in the quality assurance. This is to report the authors' 9-month study scheme on its feasibility and values.

Material and Method

A prospective study was carried out. The cervical Pap smears from a large-volume serviced pathology laboratory (Hitech Lab Center, Bangkok) during the period of 1 December 2002 to 6 September 2003 (a 9-month period) have been determined as the studied population. This laboratory had the annual Pap workload in the past year around the figure of 40,000. All of the Pap smears were collected with conventional smearing method and prepared with wet-fixation in 95% ethanol. They were stained according to the modified Papanicolaou protocol. For laboratory personnel, there were three in-charge CPs and six CTs. The reports were rendered within the average of 3 days after reception. The reporting system employed the 1991 Bethesda System.

On every Monday of the studied period, a secretary would draw one digit out of ten (0-9) to denote the selected slides for rescreening. The selected slides were slides in the past week that had the rear figure corresponding to the drawn digit. All previous dots or pen-marks on the slides were erased and the results were blinded to the rescreeners who were comprised of one CP and four CTs of the laboratory personnel. The rescreener can be the same or another person from the first report screener. The same Bethesda System was applied.

The secretary collected and compared the two times reports. Discordant cases between the two reads were set threshold at atypical squamous cells of undetermined significance (ASC-US) and neoplastic categories. These case slides were scrutinized to reach a consensus by the panel. The causes of errors were classified into 3 categories as follows. (1) Screening errors were those slides that contained a few abnormal cells of neoplastic categories being missed either at the first or the second reading. (2) An interpretation error was designated when the identified atypical cells were interpreted differently except for the discordant pairs of ASCUS and benign cellular change (BCC). (3) ASCUS/BCC disagreements were separated. On the review, the panel followed the definition of ASC-US according to the latest 2001 Bethesda System of reporting.

Results

Of 31,914 slides in the study period, a total of 3,097 slides (9.7%) were picked up in the re-screen scheme. There were 29 discordant cases accounting for 0.9% (Tables 1-3). Table 1 illustrates the discordant cases due to screening errors. Six cases were errors occurring at the first read; five of them were missed for focal LSIL and the other one was missed for focal HSIL (Fig. 1). Two cases of screening error occurred at the second (rescreener) read (Fig. 1). Interpretation error was found in one case (Table 2). The smear of severe inflammation with regenerative atypia was misinterpreted as HSIL (Fig. 2). Table 3 lists the 20 ASCUS/BCC discordant cases. Some of them are depicted (Fig. 3). The distribution of the original result categories of the total population in the study period is summarized in Table 4.

Discussion

Cervical Pap test is one of a few fruitfully mankind programs to prevent cancer [3,4]. Though it has brought success by reducing the mortality rate, it has never eradicated cervical cancer. False diagnoses do exist and usually are divided according to the etiologies into sampling and laboratory errors. The latter incorporates screening and interpretation errors [1]. The mean sensitivity of the Pap test is 47% (range 30-80%), and the mean specificity is 95% (range 86-100%) [5]. The retrospective rescreening of a prior

Table 1. Discordant cases due to screening errors

Case No.	First read	Second read	Consensus
1	BCC	LSIL	LSIL
2	BCC	LSIL	LSIL
3	BCC	LSIL	LSIL
4	BCC	LSIL	LSIL
5	BCC	LSIL	LSIL
6	BCC	HSIL	HSIL
7	HSIL	BCC	HSIL
8	HSIL	BCC	HSIL

(BCC = Benign cellular changes,
LSIL = Low-grade squamous intraepithelial lesion,
HSIL = High-grade squamous intraepithelial lesion)

Table 2. Discordant case due to interpretation error

Case No.	First read	Second read	Consensus
9	LSIL	BCC	BCC

(LSIL= Low-grade squamous intraepithelial lesion,
BCC= Benign cellular changes)

Table 3. Discordant cases due to ASCUS/BCC

Case No.	First read	Second read	Consensus
10	BCC	ASCUS	BCC
11	BCC	ASCUS	BCC
12	BCC	ASCUS	BCC
13	BCC	ASCUS	BCC
14	BCC	ASCUS	BCC
15	BCC	ASCUS	BCC
16	BCC	ASCUS	BCC
17	BCC	ASCUS	ASC-US
18	ASCUS	BCC	ASC-US
19	ASCUS	BCC	ASC-US
20	ASCUS	BCC	ASC-US
21	ASCUS	BCC	ASC-US
22	ASCUS	BCC	BCC
23	ASCUS	BCC	BCC
24	ASCUS	BCC	BCC
25	ASCUS	BCC	BCC
26	ASCUS	BCC	BCC
27	ASCUS	BCC	BCC
28	ASCUS	BCC	BCC
29	ASCUS	BCC	BCC

Note the ASCUS in the first and second reads followed the 1991 version and the consensus, ASC-US, followed the 2001 version of the Bethesda System of reporting.
(BCC= Benign cellular changes, ASCUS, ASC-US= Atypical squamous cell of undetermined significance)

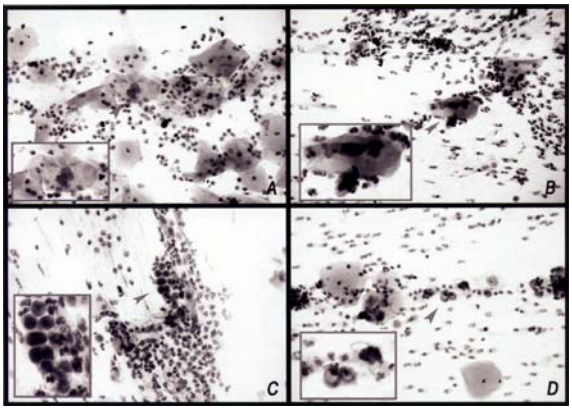

Fig. 1 Discordant cases due to screening errors
- A. Case No.1 showing a LSIL cell with bi-nucleation and basophilic cytoplasm that was overlooked in the first read.
- B. Case No.2 showing a LSIL cell with multi-nucleation and acidophilic dense cytoplasm that was missed in the first read.
- C. Case No.6 illustrating a group of HSIL cells hiding themselves amongst leukocytes.
- D. Case No.8 illustrating a few atypical cells with increased nuclear cytoplasmic ratio being missed by the second screener.

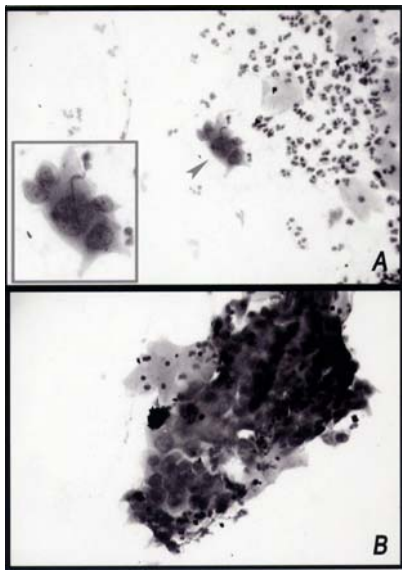

Fig. 2 Discordant cases due to interpretation error. Case No. 9 showing two overread clusters for LSIL (A.&B.). These are interpreted as benign cellular change on consensus.

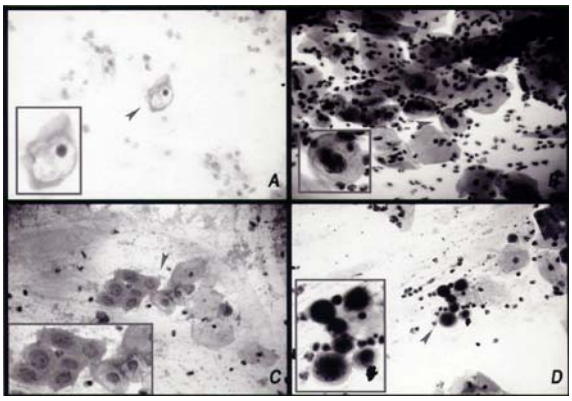

Fig. 3 Discordant cases due to ASCUS/BCC
- A. Case No.10 revealing a koilocyte-like but lacking characteristic nucleus. It is non ASC-US.
- B. Case No. 17 demonstrating a cell with slightly enlarged and irregular nucleus. The cell is called ASC-US according to consensus.
- C. Case No. 22 illustrating some parabasal cells with perinuclear halo. They are not called ASC-US by the consensus.
- D. Case No.18 exhibiting some basal-like cells having enlarged nuclei with some coarsely granular chromatin. They are called ASC-US by the panel.

normal cervical Pap smear in women with a high grade squamous intraepithelial lesion could find atypical cells in 20-94% [6-9]. In routine practice, a lot of quality control measures are emphasized in the pre-issued period. These include educating and assessing personnel performances, specimen control, staining control and

Table 4. The distribution of the original results of the total Pap test during the studied period

Categories	Number of cases	Percentage
Within normal limits	25,381	79.53
Benign cellular change	6,023	18.87
ASCUS	215	0.67
LSIL	201	0.63
HSIL	62	0.19
SCC	24	0.075
Atypical glandular cells/ADC	8	0.025
Total	31,914	100

Note the categories based on 1991 Bethesda System of Reporting (ASCUS= Atypical squamous cell of undetermined significance, LSIL= Low-grade squamous intraepithelial lesion, HSIL= High-grade squamous intraepithelial lesion, SCC= Squamous cell carcinoma, ADC= Adenocarcinoma)

even workload limits. Quality assurance aims at assuring the issued results. In the United States, Clinical Laboratory Improvement Amendment (CLIA88) has been reinforced [1]. The required measures include the 5-year lookback and cytologic histologic correlation in addition to the 10% rescreen means from the previous CLIA. In Thailand as well as in Singapore [10] and in Hong Kong [11], no such formal Act regarding quality control/assurance of the cervical Pap test is endorsed. The Society of Cytology in Thailand, formally settled in 2001 has focused on the issue. However, the shortage of CTs in the country is a big problem.

For quality assurance, the authors have usually performed a lookback into available Pap smears when a newly diagnosed HSIL or other abnormalities are made in the surgical specimens. However, the measures are regarded as an after-event assurance means of which detection of false diagnosis is not manageable. The authors, therefore, proposed a new scheme of weekly 10% rescreen of the total Pap smears in the speculation that when a false diagnosis is detected, the revised diagnosis can be rendered. Accordingly, a prospective study on its feasibility and value was carried out.

Rationally, the rescreening of 10% of the total Pap smears is more accurate than the rescreening of 10% of the negative Pap smears, because it can avoid bias from the rescreener on one hand and can evaluate the false negative cases by the rescreener on the other hand [12]. From Table 1, two of the eight cases were screening errors made by rescreeners while six were actually "undercalled" or "false negative" at the initial reports. The missed abnormal cells are scarce (Fig. 1). Such an error is not pure sampling or pure screening error but a so-called relative screening error [13]. Because of the scarcity of these abnormal cells, they had passed undetected in a normal screening procedure. With a more careful screening procedure and sufficient time in this scheme, most of them would be recognized.

Interpretation errors occur when abnormal cells have been observed but have been misclassified. There was only one case in the present study (Table 2). It was a smear that comprised atypical cells distinguishing between squamous intraepithelial lesion (SIL) and reparatory atypia. On the consensus review, the latter was rendered because the cells aggregated in a cluster and showed pale staining (Fig. 2).

According to the 2001 version of the Bethesda System, the term atypical cell of undetermined significance has newly been defined and its abbreviation is ASC-US. At present, it denotes a neoplastic category but falls short of morphologic criteria for low-grade SIL [14]. In the early versions of the Bethesda System, - the abbreviation ASCUS, it had a broad meaning that encompassed cell changes equivocal for SIL [15]. Since the initial and rescreening reports of the present study were based on the 1991 version which defied reproducible definition, there were a relatively high number of discordant cases as shown in Table 3. On the panel discussion, 5 cases fulfilled the new definition. The cell changes of ASC-US and non ASC-US are illustrated in Fig. 3. The ASCUS/BCC category was regarded as an internal quality improvement but no significant implications for evaluating a laboratory [15]. There was no need to re-issue the revised diagnosis.

For treatment purposes, the false negative cases that required revision of diagnoses consisted of six cases of the screening error group and one case of the interpretation error accounting for 7 cases out of the 3,097 reviews or 0.2%. When the total population in the period of nine months was considered, the estimated false diagnosis cases may make 0.2% of 31,914 slides equal to 70 cases in a nine-month period or 9-10 cases per month.

In conclusion, a weekly rescreening 10% of total cervical Pap smears scheme was worthwhile for quality assurance. It could detect 0.2% of meaningful cases to revise the proper diagnosis to the attending gynecologist. Furthermore, the scheme facilitated the laboratory performance assessment and improvement.

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การตรวจกรองซ้ำร้อยละ 10 ของแป๊ปสเมียร์ปากมดลูกทั้งหมดเป็นรายสัปดาห์ได้ประโยชน์ในงานประกันคุณภาพ

พิเชฐ สัมปทานุกุล, พงษ์ศักดิ์ วรรรณไกรโรจน์, อุษณีย์ พรหมประกอบ, สิริสรรพางค์ ยอดอาวุธ, ชัยยุทธ อนันต์ศิริประภา

ที่มา *: ด้วยตระหนักว่าอาจมีการรายงานผลแป๊ปสเมียร์ปากมดลูกที่มีผลลบลวง ทางคณะนักวิจัยจึงวางแผนและทำการศึกษาวิธีการประกันคุณภาพของผลที่อ่านโดยการตรวจกรองซ้ำร้อยละ 10 ของแป๊ปสเมียร์ปากมดลูกทั้งหมดเป็นรายสัปดาห์*

วัตถุประสงค์ *: เพื่อประเมินคุณค่าของการตรวจกรองซ้ำร้อยละ 10 ของแป๊ปสเมียร์ปากมดลูกทั้งหมดเป็นรายสัปดาห์ในการประกันคุณภาพการอ่านผล*

รูปแบบ *: เป็นการศึกษาเชิงพรรณนา แบบดำเนินงานไปข้างหน้า*

ผลการศึกษา *: จากสไลด์จำนวน 31,914 แผ่นในระยะเวลาวิจัย 9 เดือน มีสไลด์ที่เข้าหลักเกณฑ์การสุ่มซึ่งต้องตรวจกรองซ้ำจำนวน 3,097 แผ่น คิดเป็นร้อยละ 9.7 พบว่า มีสไลด์ที่เห็นไม่ตรงกัน 29 ราย (ร้อยละ 0.9) ประกอบด้วยความผิดพลาดเกิดในการรายงานครั้งแรก จำนวน 7 ราย (ร้อยละ 0.2) ความผิดพลาดเกิดในการตรวจซ้ำครั้งหลัง จำนวน 2 ราย และความเห็นต่างกันในการเรียกเซลล์ที่ผิดปกติเป็นเซลล์ผิดปกติที่ไม่ทราบความสำคัญ จำนวน 20 ราย ในการจำแนกสาเหตุของการรายงานครั้งแรกผิดพลาด สามารถจำแนกออกเป็นตรวจกรองพลาด 6 ราย และแปลผลผิด 1 ราย ซึ่งได้มีการแก้ไขรายงาน ส่งให้สูติ-นรีเวชแพทย์ ที่ดูแล*

สรุป *: การตรวจกรองซ้ำร้อยละ 10 ของแป๊ปสเมียร์ปากมดลูกทั้งหมดเป็นรายสัปดาห์ให้ประโยชน์ในงานประกันคุณภาพการรายงานผลและสามารถดำเนินการได้จริง วิธีการนี้ยังให้ประโยชน์ในการช่วยประเมินการอ่านผลของเจ้าหน้าที่และพัฒนาวิชาการ นอกจากนี้ผลที่ผิดพลาดสามารถดำเนินการแก้ไขได้ทัน*