

## Common specific cervical infection in cytologic diagnosis

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การติดเชื้อชนิดจำเพาะของปากมดลูกที่พบบ่อยในการตรวจวินิจฉัยทางเซลล์วิทยา

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### บทคัดย่อ

ได้ทำการศึกษาสเมียร์จากปากมดลูกจำนวน 53,526 ราย เพื่อตรวจวินิจฉัยทางเซลล์วิทยา หาการติดเชื้อชนิดจำเพาะของปากมดลูก ในห้องปฏิบัติการเซลล์วิทยา ภาควิชาพยาธิวิทยา คณะแพทยศาสตร์ มหาวิทยาลัยขอนแก่น

ผลการศึกษาพบการติดเชื้อรา เชื้อพยาธิทริโคโมแนส เชื้อแบคทีเรียแลปโตทริก เชื้อไวรัสเริมและเชื้อไวรัสแปปิโลมา เป็นอัตราร้อยละ 17.9, 2.7, 0.1 และ 0.5 ตามลำดับ ในกลุ่มสเมียร์ที่มีเซลล์ผิดปกติทั้งหมด 3,414 ราย พบการติดเชื้อรา เชื้อพยาธิทริโคโมแนส เชื้อแบคทีเรียแลปโตทริก เชื้อไวรัสเริม และเชื้อไวรัสแปปิโลมา เป็นจำนวนร้อยละ 10.2, 3.5, 0.1, 0.7 และ 7.5 ตามลำดับ

อนึ่ง เป็นที่น่าสังเกตว่าการติดเชื้อจำเพาะเหล่านี้ พบการติดเชื้ออย่างเดียวกว่ากว่าการติดเชื้อร่วมกับเซลล์ปากมดลูกผิดปกติ ยกเว้นเชื้อไวรัสแปปิโลมาทุกรายพบการติดเชื้อร่วมกับเซลล์ผิดปกติ และเชื้อไวรัสเริมพบการติดเชื้ออย่างเดีย্বর้อยละ 55.8 และมีการติดเชื้อร่วมกับเซลล์ผิดปกติร้อยละ 44.2 ซึ่งเมื่อเปรียบเทียบแล้ว เป็นจำนวนที่ใกล้เคียงกันมาก

การวินิจฉัยการติดเชื้อจำเพาะของปากมดลูกในการตรวจวินิจฉัยทางเซลล์วิทยานี้ มีประโยชน์ในการตรวจค้นหาความผิดปกติต่างๆ ในกลุ่มประชากรจำนวนมาก และยังช่วยให้แพทย์เกิดความสนใจที่จะตรวจติดตามผู้ป่วย ที่มี การติดเชื้อไวรัสแปปิโลมาและไวรัสเริม ซึ่งเป็นกลุ่มที่มีความเสี่ยงต่อการเกิดมะเร็งปากมดลูก เพื่อจะได้ตรวจค้นหาในระยะเริ่มแรก ซึ่งจะให้การรักษาได้ดีขึ้น

## Abstract

From January 1989 to December 1993, 53,526 cervical smears were studied to detect common specific infection including fungus, Trichomonas, Leptothrix, HSV and HPV infection in Cytology Laboratory, Department of Pathology, Faculty of Medicine, Khon Kaen University.

The prevalence of fungus, Trichomonas, Leptothrix, HSV and HPV infection were 17.9%, 2.7%, 0.1%, 0.1% and 0.5% respectively. In the 3,414 abnormal Pap smear, the coexisted infection of fungus, Trichomonas, Leptothrix, HSV and HPV infection were 10.2%, 3.5%, 0.1%, 0.7% and 7.5% respectively.

It is noted that, most of these infection could be detected alone much more than coexisting with abnormal Pap smear, except HPV infection where all cases coexisted with abnormal Pap smear. And HSV infection that occurred alone was 55.8% comparing to infection associated with abnormal Pap smear was 44.2%, which is about the same proportion.

The diagnosis of these micro-organism in Pap smear is useful for routine screening examination in the large population study. It is useful in convincing the clinician to pay special attention to the patients, who had HPV and HSV infection. They were considered to be a high risk patients for cervical cancer who should be closely followed in order to detect precancerous lesion which can be satisfactory treated.

## Introduction

Cervicitis is the most common gynecologic disease and most common cause of leukorrhea. It may result from many different causes, such as infection, mechanical irritation, alteration in hormone and malignancy. Infection is the most common factor that may be present alone or in combination with other factors. Infective organism<sup>1,2</sup> may be bacteria, parasite, fungus, virus and other microorganisms. Bacterial infection is the most common cause of inflammation which produces a common inflammatory process called "nonspecific cervicitis". Parasitic and fungal infection usually present an infective organism, that can be easily identified in cytology smear. Viral infection<sup>1,2</sup> produces specific characteristic cell change that can be easily recognised. These organisms were also categorized in the group of sexually transmitted diseases, especially HPV infection are considered an important etiological factors in the process of cervical carcinogenesis.

The purpose of this report is to study various kinds of specific cervical infection that can be identified in Pap smear diagnosis.

## Materials and methods

From January 1989 to December 1993, 53,526 cervical smears were collected from women who visited the outpatient clinics of the obstetrics and gynecology department in Srinagarind hospital. The smears were immediately fixed with 95 % ethanol and send to the Cytology laboratory, Department of Pathology, Faculty of Medicine, Khon Kaen University. The smear were stained by the standard Papanicolaou method, screened and diagnosed.

## Results

### 1. Results of Pap smear diagnosis (Table 1)

In the total 53,526 specimens, there were 49,976 smears (93.4%) which were negative for malignancy, 1,660 smears (3.1%) were inflammation. The abnormal Pap smear 1,376 (2.6%) and 378 (0.6%) were cervical intraepithelial neoplasia (CIN) and carcinoma respectively.

### 2. Comparison between specific infections (Table 2)

The specific causes of cervical infection are fungus, Trichomonas, Leptothrix, HSV and human papilloma virus infection. The corresponding numbers were 9,574, 1,470, 62, 52 and 253 with the prevalence of infection 17.9%, 2.7%, 0.1% and 0.5% respectively.

It was found that fungus and Trichomonas infection occurred in all age group. Leptothrix, HSV and HPV infection were present from the age group <20 to 60-69.

### 3. Specific infection coexisted with abnormal Pap smear (Table 3)

Among the total number, (3,414) of abnormal Pap smears, the fungus, Trichomonas, Leptothrix, HSV and HPV infections were detected in 349(10.2%), 119(3.5%), 5(0.1%), 23(0.7%) and 253(7.5%)

### 4. Comparing between the detection of infection alone and the infection coexisted with abnormal Pap smear (Table 4)

**Table 1 Results of Pap smear diagnosis**

Age	Unsatisfy	Negative for malignancy	Inflammation with atypia	Abnormal Pap Smear		Total No. of specimen
				CIN	carcinoma	
<20	2	1,461	36	50	1	1,550
20-29	22	13,235	356	381	7	14,001
30-39	25	13,298	424	349	72	14,168
40-49	29	7,145	304	179	103	7,760
50-59	22	3,080	144	100	62	3,408
60-69	6	1,039	37	16	36	1,134
>70	2	254	8	5	13	282
Unknown	28	10,464	351	296	84	11,223
Total	136	49,976	1,660	1,376	378	53,526
%	0.3	93.4	3.1	2.6	0.6	100

**Table 2 Comparison between specific infections**

Age	Total No. of specimen	Infection					Total No. of infection
		Fungus	Trichomonas	Leptothrix	HSV	HPV	
<20	1,550	209	34	1	2	23	478
20-29	14,001	2,461	271	12	18	100	2,862
30-39	14,168	3,038	392	17	19	56	3,552
40-49	7,760	1,435	332	14	3	12	1,796
50-59	3,408	358	124	2	4	5	493
60-69	1,134	77	20	1	1	3	102
>70	282	27	3	-	-	-	30
Unknown	11,223	1,969	294	14	5	54	2,336
Total	53,526	9,574	1,470	62	52	253	11,649
%	100	17.9	2.7	0.1	0.1	0.5	21.3

**Table 3 Specific infection coexisted with abnormal Pap smear**

Age	Total No. of abnormal Pap smear without infection	Specific infection coexisted with abnormal Pap smear					Total No of abnormal Pap smear
		Fungus	Trichomonas	Leptothrix	HSV	HPV	
<20	52	9	1	-	1	23	87
20-29	525	84	25	-	10	100	744
30-39	645	103	32	2	7	56	845
40-49	494	55	23	1	1	12	586
50-59	273	13	11	1	3	5	306
60-69	83	1	2	-	-	3	89
>70	23	3	-	-	-	-	26
Unknown	569	81	25	1	1	54	731
Total	2,664	349	119	5	23	253	3,414
%	78	10.2	3.5	0.1	0.7	7.5	100

**Table 4 Comparing between infection alone and infection with abnormal Pap smear in various type of infection**

Infective organism	Infection alone	Infection coexisted with abnormal Pap smear	Total
Fungus	9,225 (96.4%)	349 (3.6%)	9,574 (100%)
Trichomonas	1,351 (91.9%)	119 (8.1%)	1,470 (100%)
Leptothrix	56 (91.8%)	5 (8.2%)	61 (100%)
HSV	29 (55.8%)	23 (44.2%)	52 (100%)
HPV		253 (100%)	253 (100%)

In total number of 9,574 fungus infections, 9,225(96.4%) were infections alone and 349(3.6%) were infections coexisted with abnormal Pap smear.

In 1,470 cases of Trichomonas infection, the inflammation alone and inflammation coexisted with abnormal Pap smear were detected in 1,351(91.9%) and 119(8.1%) specimens.

In 61 cases of Leptothrix infection, 56(91.8%) were infection alone and 5(8.2%) were infection coexisted with abnormal Pap smear.

In 52 cases of HSV infection, the infection alone and infection coexisted with abnormal Pap smear were 29(55.8%) and 23 (44.2%) respectively.

All total 253 cases of HPV infection were infection coexisted with abnormal Pap smear.

## Discussion

Female lower genital tract is the organ that is predisposed to various kinds of infection. Many organisms may spread from person to person by this route and causing various degrees of cervicovaginitis. These infections have been reported in many previous studies as shown in the following data.

### Fungal infection

According to Kearns and Gray<sup>3</sup> 80 percent of mycotic infection are due to *Candida albicans*. In this study, all of fungal infection in yeast form and pseudohyphae were *Candida albicans* (Monilia). The prevalence of Monilial infection was 17.9 percent, but it can be detected only 10.2 percent of abnormal Pap smear. Among the total number (9,574) of fungal infection, the number of infection alone and infection coexisted with abnormal Pap smear were 96.4 percent and 3.6% respectively.

### Trichomonas infection

The well known organism causing acute cervicitis is *Trichomonas vaginalis*. Bibbo<sup>2</sup> reported the prevalence of this infection to be 14.4 percent. In the past, there were some reports mentioned about the association between cervical cancer and trichomoniasis.<sup>4, 5</sup> In this study, the prevalence of *Trichomonas* infection was 2.7 percent, whereas it can be detected in 3.5 percent of abnormal Pap smear.

### Leptothrix infection

Leptothrix is the most commonly observed in conjunction with vaginal trichomoniasis. Bibbo et al.<sup>2</sup> observed this association in 95% of 1003 consecutive genital smears with Leptothrix. Occasionally, association with fungi and other infections agents was noted. In this study, the prevalence of Leptothrix infection was only 0.1 percent and it can be detected only 0.1 percent of abnormal Pap smear.

### Herpes simplex virus infection

The significance of Herpes virus infection is venereal transmission usually associated with gonorrhea, risk of neonatal infection and associated with carcinoma of cervix. About 20-30 percent of herpetic lesion appear on the vulva and the vagina. Bibbo and Weid<sup>2</sup> report that the prevalence rate was 2.2 percent of their study. Anderson et al.<sup>6</sup> reported detection rate 307/512,000 Pap smear (0.06%). In North America<sup>7</sup> reported range from 87 to 217 per 100,000 smears (0.09-0.2%).

In this study, the prevalence of HSV infection was 0.1 percent, whereas the detection of coexisted with abnormal Pap smear was 0.7 percent. In the total number (52 cases) of HSV infection, 29(55.8%) and 23(44.2%) were infection alone and infection with abnormal Pap smear respectively.

Anderson et al.<sup>6</sup> mentioned that the detection of diagnostic cell change in a routine Papanicolaou smear is a finding with a high degree of sensitivity (91%) and specificity (95%) of HSV infection. The immunoperoxidase staining technique for HSV can be particularly of value in confirming the presence of Herpetic infection in the patients, in which the cytologic findings on the Papanicolaou stained smear are thought to be equivocal.<sup>6, 8</sup>

### Human papilloma virus infection

Many reports<sup>9</sup> from various laboratories showed the prevalence of HPV infection varying from 0.5 to 0.3 percent in women attending routine screening examination. Meisel and Morin<sup>10</sup> found that HPV infection was associated with dysplasia and neoplastic lesion in 25.6 percent of the cases. In this study, the prevalence of HPV infection was 0.5%, whereas its detection rate with abnormal Pap smear was 7.5 percent (253 out of 3,414). In all of the 253 cases

the infection coexisted with abnormal Pap smear. Crum and co-workers<sup>11</sup> mentioned that the coexistence of HPV infection and dysplasia is not a statically random occurrence and reported that the coexisting HPV infection may hasten the transit time between the various grades of dysplasia.

Although detection of microorganisms in Pap smear cannot replace the other specific methods for a definite identification of the virus and for other organism. The Pap smear is useful for routine screening in a large population study. Besides, the detection of HPV and HSV infection will alert the gynecologist to pay special attention to their patients, who are considered to have a high risk for cervical carcinogenesis, and who should be closely followed to detect early cervical neoplastic change.

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