CHAPTER IX

RESULT OF THE STUDY

Of the 161 patients that had abnormal Pap smear, forty were excluded due to pap smear from other sources rather than cervix, for example, peritoneal washing from cancer of the ovary, tracheal larvage, or thyroid aspiration (table 1)

Total of 121 cases of abnormal pap smear from cervix, 18 were excluded because of old case followed up after treatment and 10 were excluded because they had frank carcinoma of cervix (typical fungating mass on the cervix seen in the pelvic examination). This type of lesion did not need colposcopy because the physician could easily diagnose and biopsy. Eight were excluded because there were referred cases from other hospitals for further management.

The remaining eighty five cases were the new cases and were eligible for the study.

These 85 patients were contacted by mail appointment to attend the colposcope clinic.

Five patients lost follow-up, eventhough the researcher used many methods in attempting to communicate. Eighty patients who responded to medical invoice were

TABLE 1 Summarization of abnormal pap smear patients during January 1991 to December 1991

Abnormal pap smear patients	number
Total cases	161
Old cases	18
Pap from other sources (ovary,breast,thyroid trachal larvage)	40
Frank carcinoma	10
Referred cases	8
New cases	85

TABLE 2 Summrization of investigation of the new cases

The New Cases	85	
Refuse to Colposcopy Clinic	5	
Refuse to Further Diagnostic Procedure	6	
Final Results not complete	5	
Cases Available to Analyse	69	
Final Tissue Diagnosis Preformed		49
Conization Alone		25
Conization and Hysterectomy		15
Hysterectomy Alone		2
Invasive Detected by Colposcopy		7
Final Diagnosis from Colposcopy and Follow up		20

described about their abnormal finding and possible diseases that could occurred. The physicians or the nurses or staff of the research team also described the diagnostic modalities that they would receive. The complications and the benefits were explained in details. All of the respondents were agreed to undergo colposcopic examination by the staff of the research team. There were 80 patients who underwent colposcope, the range of age was between 20 to 63. The mean age was 36.28 (SEM. = 1.302) and standard deviation is 10.89.

Figure 1 show the proportion of the result of the classes of pap smear diagnosed in these patients.

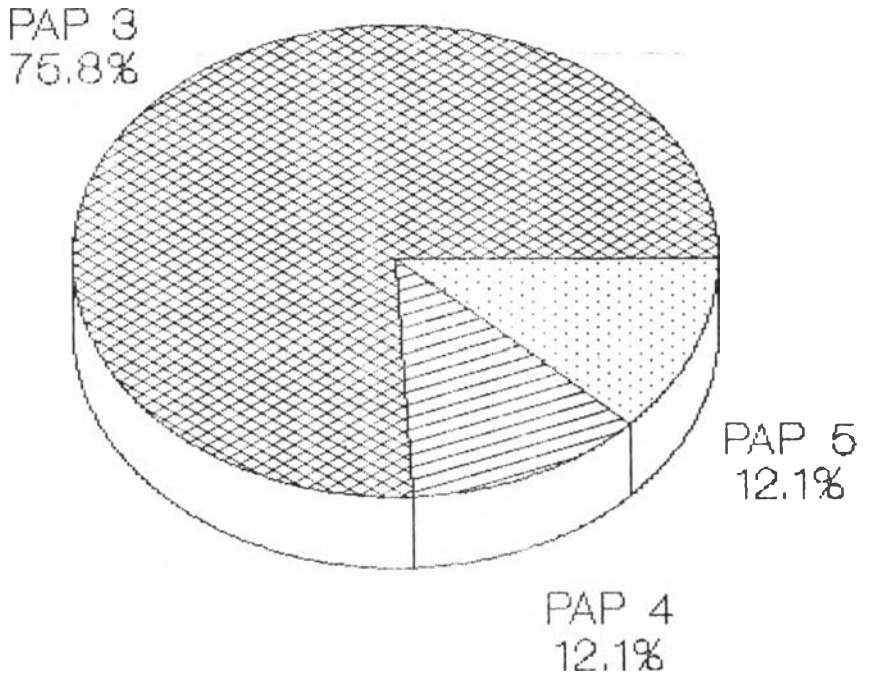
Colposcopic examinations were performed and the cervical tissues were pickup at the point of the most serious lesions seen under colposcopy (called "colposcopic directed biopsy") and examined by the pathologists. After that the physician would make the appointment with the patients for further diagnostic procedure depended on the result of the colposcopic directed biopsy.

All of the patients were suggested for diagnostic conization except for some conditions listed in table 3

These exceptions were made by the committee of the oncologic staff of the team in order to give the patients a chance to enter follow - up program of colposcopy to eliminate the unnecessary diagnostic conization in some patients.

If the patients conditions could fulfill these regimens, the sequential follow - up program was scheduled. The program included 4 visits in the 1^{st} month, 3^{nd} month, 6^{th} month and 12^{th} month after initial colposcopic examination.

FIGURE 1. *CLASSIFICATION OF PAP SMEAR*



The follow-up examination included history taking, physical examination, pelvic examination, repeating pap smear, colposcopic examination, colposcopic directed biopsy. If there were some evidences of disease progression listed in table 4 (Remains abnormal pap smear equal or higher than the 1st abnormal Pap smear, colposcopic lesion persist or progressed, histopathology of their lesion progressed), the conization was performed without any exception.

From eighty patients, five patients are still in the process of investigation. They came in the later months of the year, and have appointment for conization. But operating rooms in Bhumipol Hospital are crowded with the operative cases. They must wait for one or two months. Then their final results are not concluded during the analysis.

From 75 patients, 6 patients refused to have further diagnostic procedures. Twenty patients were in the follow up program. Final diagnoses of this group depended on the colposcopy results combined with follow up results. The final tissue diagnoses were performed in 49 patients. In 49 patients, histopathology of colposcopic directed biopsy of 8 patients were invasive. Seven of the invasive were admitted in Radiation Therapy Clinic. One was performed definitive surgery by Wirthiem's operation. In this invasive group, the diagnostic conization is not necessary because the invasive stage is the most advance stage. The physician could proceed directly to definitive treatments. All of the final tissue diagnoses were the results from colposcopic directed biopsy.

Data are summarized in table 2.

Table 5. shows the result of histopathology of the cervical tissue gained from colposcopic directed biopsy compared with final histopathology result from conization, hysterectomy and colposcopy plus follow up in 69 patients.

From this table, 20 patients diagnosed as CIN 0 by colposcopy, 3 patients were wrong diagnosis. One patients was invasive adenocarcinoma of uterus invading cervix. One patients was severe dysplasia. Although colposcopy is not designed to detect the abnormalities upper in the cervical canal, it must be kept in mind that this error can occur. The abnormal Pap smear can produce from the diseases in the higher genital tract. Uterine cancer or cancer of the Uterine tube can also produce abnormal cytology (DiSaia, 1989). Colposcopy is not enough in managing the patients suspected to have uterine diseases. The percentage of wrong diagnoses in this group was 15 % (3 from 20).

In the moderate dysplasia (CIN II) group, 7 patients were wrong diagnosis. Percentage of wrong diagnosis is 50 %. This was very dangerous because missing rate of potentially invasive stage was too high to apply in the clinical application.

In the severe dysplasia and CIS (carcinoma in situe) group (CIN III), one invasive case was miss diagnosed by colposcopy. Although it was in the range of plus or minus 1 stage, this error can not be accepted. Because missing invasive disease is very dangerous to the patients. The diagnostic performance of colposcopy in this situation can not be accepted.

Sensitivity of colposcopy in diagnosis of Cervical Neoplasia in abnormal Pap smear women is 94.3 %. Although

Table 3 Exceptional criteria for some patients to be followed up rather than performed diagnostic conization at first diagnosis (Disaia,1989)

- Satisfactory colposcopic examination (total lesion and transformation zone seen)
- Histopathology of colposcopic directed biopsy of cervix not more than moderate dysplasia (CIN II)
- Young age group (less than 35)
- Available to attend close follow up program
- Single (unmarried) or had no children
- Wanted to have another child (not complete family life)
- Pap smear class III only

Table 4 Data collected at the follow up Examination of patients

history taking ,
physical examination
pelvic examination
repeating pap smear
colposcopic examination
colposcopic directed biopsy.

Colposcopy has high sensitivity, the clinical application is limited because 2 missed diagnosis cases were in serious stage.

From 75 patients, 42 patients had further tissue diagnoses. Twenty five patients had conization alone. Fifteen patients had conization followed by hysterectomy. Two patients had hysterectomy alone, one patient was performed hysterectomy because of myoma uteri, and one patients was performed due to invasive carcinoma detected. Seven patients were detected invasive stage by colposcopy, the further tissue diagnosis was not performed. Colposcopy results could be the final tissue diagnoses because invasive stage was the most advance stage.

In the 49 patients who had final tissue diagnoses, the comparison of colposcopy results with final tissue results was shown in table 6.

From this table, 7 patients diagnosed as CIN 0 by colposcopy, 2 patients were wrong diagnosis. One patients was invasive adenocarcinoma of uterus invading cervix. One patients was severe dysplasia. The percentage of wrong diagnoses in this group was 28.5 % (2 from 7). Diagnostic performance of colposcopy in this group cannot be accepted.

In the moderate dysplasia (CIN II) group, 7 patients were wrong diagnosis. Percentage of wrong diagnosis is 70 %.

In the severe dysplasia and CIS (carcinoma in situe) group (CIN III), one invasive case was miss diagnosed by colposcopy. Although it was in the range of plus or minus 1 stage, this error can not be accepted, because missing invasive disease is very dangerous to the patients. The diagnostic performance of colposcopy in this situation can not be accepted.

TABLE 5. shows the result of histopathology of the cervical tissue gained from colposcopic directed biopsy compared with final histopathology result from conization, hysterectomy and colposcopy plus follow up in 69 patients.

	FINAL HISTOPATHOLOGY					
COLPOSCOPY	CIN 0	CIN 1	CIN 2	CIN 3	CIV	TOTAL
CIN 0	**17**	1	0	1	1	20
CIN 1	0	**4**	0	0	0	4
CIN 2	0	0	**7**	7	0	14
CIN 3	0	0	0	**21**	1	22
CIV	0	0	0	0	**9**	9
TOTAL	17	5	7	29	11	69
TOTAL %	24.6	7.2	10.1	42.0	15.9	100.0

The correct agreement between colposcopy and final histopathology is the number in the diagonal line (bold letter). The correct agreement rate is 84 % (58 from 69).

If we use the agreement in the acceptable range of plus and minus 1 stage, the agreement rate is 97.1 % (within the dark line space).

There were 4 patients (8%) whose colposcopy were more severe than final histopathology from conization or hysterectomy. This result was compatible with Benedet et Al (1976).

The agreement rate between colposcopy and final tissue diagnosis from conization and hysterectomy was low. Wrong diagnosis of Colposcopy was also serious because it could not detect the severe stage. Then colposcopy could not substitute the final tissue diagnosis from conization or hysterectomy.

Of the total case of 75, there were 56 cases who had satisfactory colposcope and 19 cases had unsatisfactory colposcope. The percentage of unsatisfactory group was 25.3 percent that is higher than other studies (Townsend,1970; Stafl and Mattingly, 1973; Benedet and Boyes, 1976).

The unsatisfactory colposcopic group were suggested to have further diagnostic conization without any exception.

Table 7 shows the result of conization of patients with unsatisfactory colposcopy. There were 4 patients that refused to be coned and did not agree to participate in this study.

In the satisfactory group, 2 patients refused to be coned. Twenty patients were admitted in follow up program. The final diagnoses of this group were composed of the combination between colposcopy results and follow up results. The histopathology of these patients were obtained from colposcopic directed biopsy.

Table 9 shows the result of histopathology of tissue gained from colposcopic directed biopsy in the

TABLE 6. The comparision between colposcopy results and the final histopathology results from conization, hysterectomy or colposcopy of invasive stage in 49 patients.

	HISTOPATHOLOGY OF FINAL TISSUE DIAGNOSIS					
COLPOSCOPY	CIN 0	CIN 1	CIN 2	CIN 3	CIV	TOTAL
NORMAL CIN 0	**5**	0	0	1	1	7
MILD CIN 1	1	**0**	0	0	0	1
MOD. CIN 2	0	1	**2**	7	0	10
SEVERE CIN 3	1	1	0	**19**	1	22
INVASIVE CIV	0	0	0	0	**9**	9
TOTAL	7	2	2	27	11	49
%	14.2	4.1	4.1	55.1	22.4	100.0

The correct agreement between colposcopy and final histopathology is the number in the diagonal line (bold letter) The correct agreement rate is 71.4% (35 from 49)

If we use the agreement in the acceptable range of plus and minus 1 stage, the agreement rate is 91.8 % (within the dark line space).

TABLE 7 The Result of conization of patients with unsatisfactory colposcope

		FREQ	PERCENT
Normal	CIN 0	2	13.3
Mild dysplasia	CIN I	1	6.7
Mod. dysplasia	CIN II	1	6.7
Sev. dysplasia	CIN III	9	60.0
Invasive	CIV	2	13.3
	TOTAL	15	100.0

VALID CASES 15 MISSING CASES 4

- -

TABLE 8 The distribution of Age of patients with unsatisfactory colposcope compared with satisfactory group

Unsatisfactory		Satisfactory	
MEAN	43.267	MEAN	34.339 ***
RANGE	42.000	RANGE	37.000
MINIMUM	21.000	MINIMUM	20.000
MAXIMUM	63.000	MAXIMUN	57.000
STD ERR	3.304	STD ERR	1.270
STD DEV	12.798	STD DEV	9.507

*** Significantly Difference $P < 0.05$

Table 9 The result of histopathology of tissue gained from colposcopic directed biopsy in the satisfactory colposcopic group.

		ABSOLUTE	RELATIVE FREQ
		FREQ	PERCENT
Normal Epithelium	CIN 0	17	30.4
Mild Dysplasia	CIN I	3	5.4
Moderate Dysplasia	CIN II	11	19.6
Severe Dysplasia	CIN III	19	33.9
Invasive Carcinoma	CIV	6	10.7
	TOTAL	56	100.0

satisfactory colposcopic group.

To answer the research question "what is the false positive rate of Pap smear evaluated by Cytology unit at Bhumipol Hospital?", the calculation is false positive Pap smear cases divided by total abnormal Pap smear cases. The false positive cases are abnormal Pap smear women whose final diagnoses indicate the absence of diseases (17 cases). The total cases were all abnormal Pap smear cases who had final histopathology diagnosis (90 cases, 80 from colposcopy group and 10 from frank carcinoma). The false positive diagnosis of Pap smear is 18.9 percent.

The incidence of cervical neoplasia in women who have abnormal Pap smear in Gynecology Unit of Bhumipol Hospital is 81.1 percent(True Positive cases).

In the sense of sequential diagnostic test. (colposcopic directed biopsy then followed by conization or hysterectomy or follow up program). The final histopathology was the most serious disease stage diagnosed from all methods. For example, If a patient, Mrs. A, had colposcopic directed biopsy followed by conization and followed by hysterectomy and the histopathology results were CIN III, CIN 0 , CIN 0, then the final histopathology was CIN III (from the colposcopic directed biopsy) because CIN III was the most serious disease stage diagnosed from the three methods.

The table 10 shows the result of histopathology of the cervical tissue from colposcopic directed biopsy compared with final histopathology in the satisfactory colposcopy group.

The accuracy of colposcopy is the percentage of CIN lesions (detected by colposcopic directed biopsy) that were

TABLE 10. The result of histopathology of the cervical tissue gained from colposcopic directed biopsy compared with histopathology result of FINAL diagnosis in 54 satisfactory patients.

COLPOSCOPY	FINAL HISTOPATHOLOGY					
	CIN 0	CIN 1	CIN 2	CIN 3	CIV	TOTAL
NORMAL CIN 0	**15** 26.8	1 1.8	0 0.0	0 0.0	1 1.8	17
MILD CIN 1	0 0.0	**3** 5.4	0 0.0	0 0.0	0 0.0	3
MOD. CIN 2	0 0.0	0 0.0	**6** 10.7	5 8.9	0 0.0	11
SEVERE CIN 3	0 0.0	0 0.0	0 0.0	**16** 28.6	1 1.8	17
INVASIVE CIV	0 0.0	0 0.0	0 0.0	0 0.0	**6** 10.7	6
COLUMN TOTAL	15 26.8	4 7.1	6 10.7	21 37.5	8 14.3	54 100.0

within one degree of the final histopathological staging (same staging plus one higher and one lower staging)(Benedet, 1976).

From the table 10, accuracy is the number between diagonal lines of the table. The accuracy of histopathology diagnosis of colposcopic directed biopsy was 98.14 percent.

If the accuracy was defined as the exact agreement between colposcopy and final histopathology, the accuracy was 85.18 percent (bold letter in the table, 46 from 54).

From this table, 17 patients diagnosed as CIN 0 by colposcopy, 2 patients were wrong diagnosis. One patient was invasive adenocarcinoma of uterus invading cervix. One patient was mild dysplasia. In mild dysplasia, the error was acceptable. The percentage of wrong diagnoses in this group was 11.8 % (2 from 17). Diagnostic performance of colposcopy in this group can be accepted.

In the moderate dysplasia (CIN II) group, 5 patients were wrong diagnosis. Percentage of wrong diagnosis is 45.5%. Fortunately, the wrong diagnosis were in the acceptable range.

In the severe dysplasia and CIS (carcinoma in situ) group (CIN III), one invasive case was miss diagnosed by colposcopy. Although it was in the range of plus or minus 1 stage, this error can not be accepted, because missing invasive disease is very dangerous to the patients. The diagnostic performance of colposcopy in this situation cannot be accepted.

The sensitivity of satisfactory colposcopy in diagnosis of cervical neoplasia is 94.87% (37 from 39). The application of colposcopy must carefully avoid the wrong diagnosis of disease from upper genital tract such as uterine cancer.

In the satisfactory colposcopy group, 34 patients had further tissue diagnosis from conization or hysterectomy. Table 11. show the comparison between colposcopy results and final histopathology results from conization and hysterectomy.

From this table, 4 patients diagnosed as CIN 0 by colposcopy, 1 patient was wrong diagnosis. She was invasive adenocarcinoma of uterus invading cervix. The percentage of wrong diagnoses in this group was 25.0 % (1 from 4). Diagnostic performance of colposcopy in this group could not be accepted.

In the moderate dysplasia (CIN II) group, 6 patients were wrong diagnosis. Percentage of wrong diagnosis is 75.5%.

In the severe dysplasia and CIS (carcinoma in situe) group (CIN III), one invasive case was miss diagnosed by colposcopy. Although it was in the range of plus or minus 1 stage, this error can not be accepted. Because missing invasive disease is very dangerous to the patients. The diagnostic performance of colposcopy in this situation can not be accepted.

There were 3 patients (8.8 %) whose colposcopy were more severe than final histopathology from conization or hysterectomy.

The correct agreement rate was 67.64 %(23 from 34). The agreement in the acceptable range was 88.23 %. Not only the satisfactory colposcopy had low accuracy but the wrong diagnosis is also serious, then colposcopy could not replace final tissue diagnosis from conization or subsequent hysterectomy.

TABLE 11 show the comparision between colposcopy results and final histopathology results from conization and hysterectomy in the 34 satisfactory colposcopy patients.

COLPOSCOPY	FINAL HISTOPATHOLOGY					TOTAL
	CIN 0	CIN 1	CIN 2	CIN 3	CIV	
NORMAL CIN 0	**3**	0	0	0	1	4
MILD. CIN 1	0	**0**	0	0	0	0
MODERATE. CIN 2	0	1	**1**	6	0	8
SEVERE CIN 3	1	1	0	**13**	1	16
INVASIVE CIV	0	0	0	0	**6**	6
COLUMN	4	2	1	19	8	34
TOTAL	11.8	5.9	2.9	55.9	23.5	100.0

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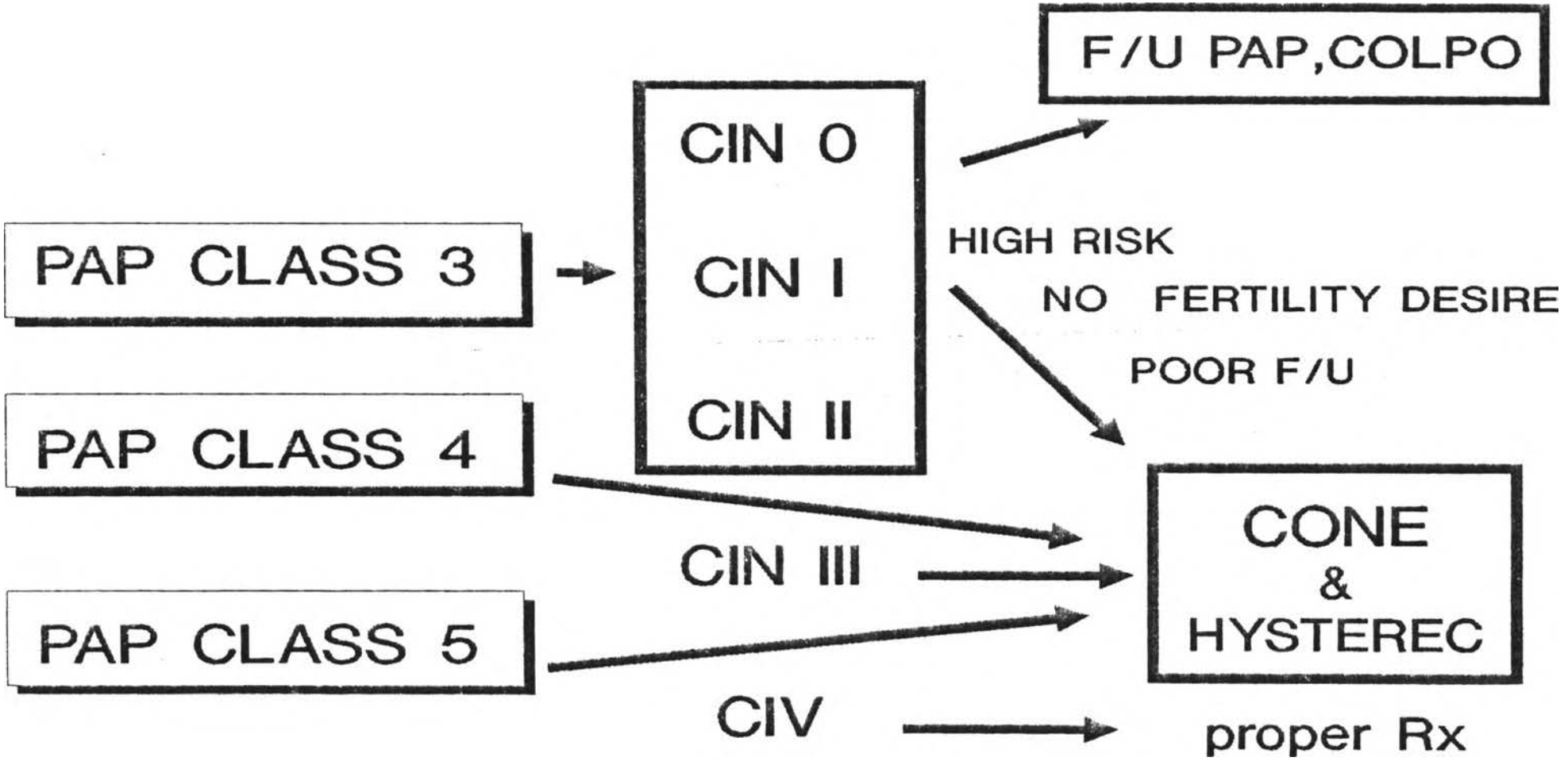

(CONFIRM BY GROUP OF CYTOLOGISTS AND PATHOLOGISTS)