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INCIDENCE OF CERVICAL DYSPLASIA IN WOMEN WITH AND WITHOUT CYTOLOGY SUGGESTIVE OF HUMAN PAPILLOMAVIRUS

by

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Abstract

Significant controversy has existed in the areas of management of women with cervical cytological diagnoses of atypical squamous cells of undetermined significance (ASCUS) and ASCUS suggestive of human papillomavirus (HPV). The purpose of this study was to determine the incidence of cervical dysplasia in women with and without cytology suggestive of HPV in order to improve patient management. The Bethesda System was utilized as the basis for a conceptual physiological framework. Orem's self-care theory was shown to support the framework. The researcher hypothesized that there would be no difference in the incidence of cervical dysplasia in women with cytology suggestive of HPV and women without cytology suggestive of HPV. This retrospective study utilized a convenience sample (N = 58) drawn from a population consisting of records of women (N = 442) with cytology reported as ASCUS from an area in the southeastern United States. Descriptive and inferential statistics were employed for data analysis. Descriptive statistics confirmed an incidence of cervical dysplasia in women with ASCUS (n = 42) of 30.95% and an incidence of cervical dysplasia in women with ASCUS suggestive of HPV (n = 16) of 18.75%. This finding

represents a 65% higher incidence of cervical dysplasia in the women with Pap reports of ASCUS without evidence of HPV. Utilizing contingency tables and chi-square analysis, no significant difference between the two subsets and the incidence of dysplasia emerged, $X^2(1, N = 58) = 0.8629$, $p < .05$, $p = 0.353$. Therefore, the researcher concluded no difference in the incidence of cervical dysplasia in women with cytology reports of ASCUS and women with cytology reports of ASCUS suggestive of HPV existed and accepted the null hypothesis. Findings indicated the need for further research and closer monitoring of patients with cytologic diagnosis of ASCUS and ASCUS suggestive of HPV. Nurse practitioners must assume responsibility to conduct research in the area of ASCUS and ASCUS suggestive of HPV to extend theory and knowledge while functioning as primary care providers for women. Management of cytology reports will be an important component of clinical practice and involve intervention, educative and supportive nursing functions.

Dedication

To my wonderful family.

To my husband, Mack, who along with his unending encouragement, support, and love, has done an incredible job functioning as both Mom and Dad this past year, and to my children, Lindsey Kathrynn and Mary Leigh, who have made my life worthwhile and have been extremely sweet and understanding throughout this endeavor--I give you all my love.

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Table of Contents

List of Tables

List of Figures

Chapter I

The Research Problem

Significant controversy has existed in the areas of management of women with a cytological diagnosis of atypical squamous cells of undetermined significance (ASCUS) (ACOG Technical Bulletin, 1993; Schaffer & Philput, 1992; Slawson, Bennett, & Herman, 1993) and women with the diagnosis of ASCUS suggestive of human papillomavirus (HPV) (American College of Obstetricians and Gynecologists, 1994; Kurman, Henson, Herbst, Noller, & Schiffman, 1994; Schaffer & Philput, 1992). Gaining additional knowledge regarding the incidence of progression of ASCUS to cervical dysplasia will have provided more direction in the management of women with ASCUS and ASCUS suggestive of HPV. The purpose of this study was to determine the incidence of cervical dysplasia in women with and without cytology suggestive of HPV in order to provide improved and appropriate management to women with ASCUS.

Further controversy has existed in the area of cervical cytology. While the Papanicolaou (Pap) smear has remained the most successful screening tool for cervical cell abnormalities, refinements in diagnosing cervical cytology have continued. Terminology used to define gradations of

cervical disease, classifications to describe test results, and appropriate techniques for collecting adequate cervical cell specimens have been targeted for change (Fowler, 1993). The Bethesda System has remained the accepted standard for cervical cytology diagnosis since the early 1990's.

Establishment of the Problem

One of the major classifications of The Bethesda System scrutinized has been that of atypical squamous cells of undetermined significance (ASCUS). Kurman and Solomon (1994) indicated ASCUS results reflected either an exuberant benign change or a potentially serious lesion, and, therefore, were interpreted to be of undetermined significance. Abdul-Karim and Willis (1994) reported numerous studies attempted to determine the biological significance of atypical squamous cells without much consistency.

> The available data indicate that for many specimens demonstrating ASCUS, patients do not have a significant lesion, and follow-up smears or colposcopic biopsies are normal. In a proportion of patients, however, the abnormality will persist and in a significant number of these, further evaluation will detect a squamous intraepithelial lesion. (Kurman & Solomon, 1994, p. 42)

Significant controversy has existed in the management of women with ASCUS. Guidelines for management established by the American College of Obstetricians and Gynecologists (ACOG) were presented in the ACOG Technical Bulletin of August 1993. If the patient with cytological diagnosis of ASCUS was determined to be reliable, she could be scheduled to return for repeat Pap smears every six months.

Recommendation was for colposcopic examination after two or more cervical cytology reports of ASCUS. With a potentially non-compliant patient, initial colposcopy was recommended for consideration. Conversely, Schaffer and Philput (1992) suggested a decision for management be based on the patient's resources and history while Slawson, Bennett, and Herman (1993) recommended immediate colposcopy for atypical smears.

Another dilemma was the diagnosis of ASCUS suggestive of human papillomavirus (HPV) on cervical cytology smears. HPV has been recognized as being highly prevalent in the general population and spread through sexual contact (Morrison, 1994). The possibility of HPV opened a whole new arena for exploration. Of initial importance was, according to Dr. V. Cecil Wright, the latency period of HPV after exposure which may range from six weeks to twenty years (personal communication, December 4, 1994). In 1992, Schaffer and Philput reported there was no documentation of the risk of latent HPV progression over time. Even so, ACOG (1993) reported that women with HPV were at increased risk for preinvasive cervical lesions. ACOG also reported that a progression to high grade squamous intraepithelial lesion (SIL) occurred in approximately 15% of women with HPV and that spontaneous regression occurred in approximately 60%. ACOG did not propose the outcomes of the other approximate 25%. High rates of false negative results have indicated the

need for histologic confirmation. Low grade SIL, which included HPV, and ASCUS classifications represented, according to Kurman, Henson, Herbst, Noller, and Schiffman (1994), the greatest problem for the clinician from the standpoint of management and the largest volume of patients that required evaluation. Not surprisingly, controversy over management of these findings also has existed.

ASCUS suggestive of HPV had cytologic changes that when observed could possibly have been related to the type of HPV infection. Thus colposcopic examination proved helpful in the increased rate of detection of HPV. Management of ASCUS suggestive of HPV, however, and controversies surrounding the diagnosis, remained similar to those of ASCUS (Abdul-Karim & Willis, 1994).

There has been substantial controversy in the management of women with atypical squamous cells because of the identification of undetermined significance. Some literature suggested practitioners watch and wait while others supported an aggressive approach which utilized immediate colposcopy for diagnostic determination. Kline and Kannan (1994) indicated the need to further study the biologic behavior of ASCUS. Due to frequent changes in cytology reporting, inconsistencies between reportings, and lack of current literature, further investigation was necessary.

Significance to Nursing

As the incidence of cervical dysplasia in women with and without cytology suggestive of HPV has been quantified, additional information has been added to the body of existing knowledge in nursing as well as other medical fields. Research, along with improved and consistent management of women with ASCUS, has strengthened not only the role of the nurse practitioner, but has also contributed to the current body of scientific research in the areas of ASCUS and ASCUS suggestive of HPV. This study quantified the incidence of cervical dysplasia and therefore has strengthened the support for specific guidelines for management of patients with cervical cytologic ASCUS classification. Nurse practitioners have the responsibility to provide supportive and educative services to their clients. This research will benefit practitioners' services by strengthening the scientific body of knowledge in management of women with Pap smear reports of ASCUS and ASCUS suggestive of HPV by determining the incidence of subsequent cervical dysplasia. Not only compliance but timely follow-up has been indicated to optimize the outcomes of these patients. As nurse practitioners' roles expand in the primary care arena, nurse practitioners must assume greater responsibility for management of women with abnormal cytology.

Physiological Conceptual Framework

The Bethesda System served as the basic physiological framework of this research to facilitate the conceptualization of the study and support the contributing information. Dorothea Orem's self-care theory supported women's measures in obtaining cervical screening and follow-up as well as the nurse practitioner role in their management.

The Bethesda System was adopted in December 1988 to promote communication between the laboratory and the clinician by providing uniform diagnostic terminology. The design of The Bethesda System was to facilitate categorization and reporting of cytologic diagnoses. The cytologic diagnosis was based on the most abnormal cells present on a smear (Kurman & Solomon, 1994) (see Appendix A for the complete Bethesda System).

The Bethesda System was amended and modified in April 1991. It was emphasized that The Bethesda System was only a recommended terminology not specifically mandated by legislation. Use of traditional terminology was still acceptable for use in conjunction with The Bethesda System (see Appendix B for terminology comparisons between classification systems). The predominant strength of The Bethesda System identified by Fowler was the use of terminology that closely followed the histopathologic

vocabulary utilized in reporting cervical cytologic diagnoses (Valente & Shantz, 1993).

Specimen adequacy held high priority at the second Bethesda conference held in 1991. Specimen adequacy was correlated to collection of both squamous epithelium cells and squamous metaplastic cells. Columnar and squamous epithelium comprise the cervix. The cervical transformation zone, an area of change, was identified as an area of squamous metaplasia. Squamous metaplasia was defined as the process by which columnar cells evolve into squamous cells, and mature squamous epithelium occurs when the tips of columnar papillae grow together (Rubin & Lauver, 1990). A fully satisfactory Pap smear included cell samples of squamous epithelium cells and squamous metaplastic cells and was correlated with specimen adequacy. The cells were most easily sampled using a Cytobrush and Ayre wooden spatula. The Pap smear was not promoted as a diagnostic tool, but specificity was reported to be high if the results were positive (Buck, 1994).

Other sections of The Bethesda System included general categorization, which was optional, and descriptive diagnoses. Epithelial cell abnormalities included ASCUS. The Bethesda System reports had to qualify ASCUS as to whether a reactive or premalignant (suggestive of HPV) or even a malignant process was favored. The specimen adequacy was considered along with the Pap smear results. Appropriate

management was supported based on the adequacy of the specimen and the cervical cytology results. Management also was aided by the consistency of reporting--the descriptive diagnoses, and the criteria for interpretation as was outlined in The Bethesda System (Valente & Schantz, 1993).

While the physiologic framework of this study was developed around The Bethesda System, the theoretical framework was developed utilizing Dorthea E. Orem's Self-Care Deficit Theory of Nursing. Orem (1991) acknowledged her theory as a general theory composed of three related theories. The first was the theory of self-care in which self-care was described and explained:

> Self-care is learned, goal-oriented activity of individuals. It is behavior that exists in concrete life situations directed by persons to self or to the environment to regulate factors that affect their own development and functioning in the interests of life, health, or well-being. (Orem, 1991, p. 64)

Orem's second theory, the theory of self-care deficit, described and explained why people can be helped through nursing. The theory of nursing systems was Orem's third theory. In her theory of nursing systems, Orem described and explained relationships that must be brought about and maintained for nursing to occur (Orem, 1991).

Orem's (1991) theory of self-care related directly to women seeking Pap smear screening. Self-care requisites fostered health and well-being. The role of the nurse practitioner in providing information and explanations to

facilitate knowledge of an illness or potential illness fostered competency in the women to manage an illness. The client was, more than likely, her own self-care agent--"the provider of self-care" (Orem, p. 117). Nurse practitioners enabled women desiring health promotion and disease prevention the ability to act as their own self-care agents. The nurse practitioner functioned in the nursing system by not only providing the screening and education that allowed the woman to make informed decisions, but the practitioner also provided some of the follow-up procedures for a possible abnormal Pap smear result.

In summary, The Bethesda System provided a framework in which to conceptualize the problem of ASCUS and HPV while Orem's theory of self-care provided a theoretical framework for the problem. The Bethesda System functioned to provide more consistency in the interpreting and reporting of cervical cytology results by use of terminology closely associated with surgical diagnoses. Additionally, Orem's theory of self-care supported women with health seeking behaviors and integrated the role of the nurse practitioner into the patient's mechanism for action.

Assumptions

For this study, the assumptions were the following:

1. For the specimens utilized in this study there was consistent cytology reporting over time and between specimens.

2. For the specimens utilized in this study there was consistent tissue diagnosis over time and between specimens.

3. Women practiced activities they initiated and performed on their own behalf in maintaining life, health, and well-being.

Purpose of the Study

The purpose of this study was to determine the incidence of cervical dysplasia in women with and without atypical squamous cells of undetermined significance suggestive of human papillomavirus.

Statement of the Problem

Significant controversy has existed among women health experts concerning the management of women with abnormal Pap smears. While some experts recommend follow-up with repeat pap smears (ACOG, 1993), others recommend immediate colposcopy (Slawson, Bennett, & Herman, 1993). ASCUS and ASCUS suggestive of HPV as defined by The Bethesda System have been the focus of much controversy. Little research has been published in the area of ASCUS and ASCUS suggestive of HPV with significant contributions to patient management. This study addressed the question: What is the incidence of cervical dysplasia in women with and without cytology suggestive of human papillomavirus? in order to contribute to the body of knowledge in clinical management of women with cytological findings of ASCUS and ASCUS suggestive of HPV.

Hypothesis

The hypothesis of this research was that there is no difference in the incidence of cervical dysplasia in women with and without cytology suggestive of human papillomavirus.

Definition of Terms

For the purpose of this study, the following terms were defined:

Cervical Dysplasia

Theoretical. Cervical dysplasia as defined by The Bethesda System is an abnormal differentiation in proliferating cells which results in an abnormal degree of variation in size, shape, and appearance of cells and a disturbance in the usual arrangement of such cells (Abrams, 1992).

Operational. Cervical dysplasia was considered to be any level of cervical dysplasia identified by surgical tissue (biopsy) diagnosis.

Women

Theoretical. Women are defined theoretically as female persons.

Operational. Women were those female persons with abnormal cervical cytology.

Cytology

Theoretical. Cytology is defined as microscopic examination of cells desquamated by means of aspiration,

washing, smear, etc. from a body surface in order to detect malignancy and microbiologic changes in accordance with The Bethesda System (Friel, 1981).

Operational. Papanicolaou smear reports of atypical squamous cells of undetermined significance were the functional definition of cytology.

Atypical Squamous Cells of Undetermined Significance (ASCUS)

Theoretical. According to The Bethesda System, cells with abnormalities that are greater than those attributable to reactive changes but are quantitatively or qualitatively less than those abnormalities of a squamous intraepithelial lesion (Kurman & Solomon, 1994).

Operational. Cytology reported on a Pap smear result according to The Bethesda System guidelines served as the operational definition of ASCUS.

Atypical Squamous Cells of Undetermined Significance (ASCUS) Suggestive of Human Papillomavirus (HPV)

Theoretical. ASCUS with other abnormal cells that give the impression that HPV may be present but are not identified as a definitive squamous intraepithelial lesion according to The Bethesda System.

Operational. For this study, ASCUS suggestive of HPV was the cytology result reported on Pap smears according to The Bethesda System.

Summary

Controversies have existed in the area of cervical cytology. The Bethesda System was established to provide continuity and clarification of cervical cytology. The Bethesda System's classification of atypical squamous cells of undetermined significance fell under much scrutiny. No consistency was found in determining the biological significance of atypical squamous cells nor was there any consensus in the management of women with ASCUS or of women with ASCUS suggestive of human papillomavirus.

Orem's theory of self-care directed the role of nurse practitioners as supportive and educative systems in enabling women who desired health promotion and disease prevention to act as their own self-care agents. While Orem was utilized as the theoretical framework for this study, The Bethesda System was established as the physiologic framework. The Bethesda System aided the conceptualization of the problem of ASCUS and ASCUS suggestive of HPV. The Bethesda System provided consistency in reporting Pap smear results and in the criteria for diagnostic interpretation.

Chapter II

Review of the Literature

An exhaustive search of the literature revealed a lack of current research reports on cervical cytology diagnosis of ASCUS and ASCUS suggestive of HPV. Only two recent studies, one from 1993 and one from 1994, specifically addressed the ASCUS designation from The Bethesda System. Both studies were Harrisburg, Pennsylvania area network (HARNET) studies.

The 1993 study was titled "Follow-up Papanicolaou Smear for Cervical Atypia: Are We Missing Significant Disease?" (Slawson, Bennett, & Herman). The purpose of the research outlined in this study was to examine two objectives:

> (1) the prevalence of undetected CIN [cervical intraepithelial neoplasia] among women in primary care settings with a Pap smear showing atypia of undetermined significance, and (2) the accuracy of a single follow-up Pap smear performed with an endocervical Cytobrush and a wooden spatula in identifying those women subsequently found to have biopsy-proven CIN (Slawson et al., p. 290).

The researchers surmised that the data on which many investigators based their recommendations for colposcopy may have been misleading due to the referral population of women with identified risk factors, the method by which the Pap smears were obtained, and the adaptation of the results to The Bethesda System for cytological analysis. Consequently,

the authors stated that the risk in women with cervical atypia and no evidence of HPV or dysplasia, which was classified as squamous atypia of undetermined significance, was uncertain (Slawson et al., 1993).

The design included a population of 7,458 women (N = 7,458) that presented for an initial Pap smear in one of six family practice offices in the Harrisburg, Pennsylvania area. Major population differences between the sites were not identified. Each Pap smear was obtained using a Cytobrush and wooden spatula. All abnormal Pap smears identified by a cytotechnologist were reviewed by a board certified pathologist that had no knowledge of the study. Atypia of undetermined significance was identified in 442 patients and 159 remained eligible for continuation in the study (n = 159). Out of this sample, 37 chose immediate colposcopy while 121 women consented to wait four to six months before returning for a repeat Pap smear and colposcopy. Colposcopic directed biopsies were performed by trained and certified practitioners and were reviewed by board certified pathologists (Slawson et al., 1993).

The prevalence rate of CIN determined by colposcopic directed biopsies among women whose screening Pap smears showed atypical cells of undetermined significance was 35%. Single follow-up Pap smears had a false negative rate of 57%. One third of the high grade lesions were not identified by Pap smears (Slawson et al., 1993).

Of the women (n = 37) choosing immediate colposcopy, 15 (40%) were identified as having CIN I and none with a more severe lesion. Those that waited (n = 121) had a 34% incidence of CIN and more significantly a 12% incidence of CIN II/III. These results may have indicated that progression of cervical disease occurred during the four to six month waiting period or that normal reparative healing was not allowed to occur in the sample that underwent immediate colposcopy (Slawson et al., 1993).

Based on data analysis, Slawson et al. (1993) recommended that all women with cervical atypia of undetermined significance undergo colposcopic examination. Repeat Pap smears were encouraged every four to six months for one to two years if initial colposcopic studies were refused. If any abnormal cytology occurred during follow-up, colposcopy was recommended.

One-third of the women in this study with cervical atypia on an initial Pap smear had CIN after cervical biopsy. The Pap smear obtained failed to detect one-half of the cases of biopsy-proven CIN. Slawson et al. (1993) recommended further studies regarding the use of supplementary screening methods. In comparison with The Bethesda System, CIN corresponded to low grade and high grade squamous intraepithelial lesions. These results indicated a need for further study and the current study pursued the meaning of ASCUS in another setting.

Slawson, Bennett, Simon, and Herman (1994) published another study titled "Should All Women With Cervical Atypia Be Referred for Colposcopy: A HARNET Study. The purpose of the research was to determine the optimal management of women whose Papanicolaou (Pap) smears showed atypical squamous cells of undetermined significance (ASCUS). In the previous HARNET study, it was concluded that a Pap smear follow-up four to six months later failed to accurately predict abnormal colposcopic biopsies. Therefore, additional tests to augment the follow-up Pap smear were evaluated which included a human papillomavirus (HPV) screen and a naked eye examination after a five percent cervical acetic acid wash (Slawson et al., 1994).

Initial Pap smears were performed on 7458 women who attended six Harrisburg, Pennsylvania area family clinics. The population was from urban, suburban, and semirural areas. ASCUS was found on 442 Pap smears ($N = 442$). Consenting subjects ($n = 122$) waited four to six months then returned for follow-up. A repeat Pap smear was performed and was augmented by HPV screen (ViraPap), and naked eye examination of the cervix after a five percent acetic acid wash before colposcopic directed biopsies and endocervical curettage (Slawson et al., 1994).

Augmenting the follow-up Pap smear with the acetic acid wash predicted 73% of the abnormal colposcopic biopsies. Use of the ViraPap had no additional effect. When identifying

all grades of cervical lesions, the negative predictive value was low, but with respect to high grade lesions, 93% were detected. The Pap smear alone failed to detect one third of the high grade lesions (Slawson et al., 1994).

Findings from the second HARNET study were that (1) among women with cervical atypia, one-third of the cases of high-grade disease went undetected with a single follow-up Pap smear and (2) detection increased with a follow-up Pap smear plus an acetic acid wash. The implication presented by the researchers for practice was that the combined use of a Pap smear and an acetic acid wash would reliably guide clinical management of cervical atypia. Slawson et al. (1994) recommended further research of additional screening methods that might improve reliability for identifying CIN in women with cervical atypia. Randomized controlled trials comparing cost-effectiveness and prevention of cervical cancer were recommended. Determining the incidence of cervical dysplasia in women with ASCUS in an area in which collection and interpretation of Pap smears and tissue specimens are consistent, as attempted in this current study, may prove cost-effective with clearer indications for follow-up recommended for cervical atypia.

Soutter, Wisdom, Brough, and Monaghan (1986) addressed atypical Pap smears much earlier than the previous two studies. The purpose of the research, titled "Should Patients With Mild Atypia in a Cervical Smear Be Referred

for Colposcopy?" (Soutter et al., 1986, p. 70) was constructed to answer this specific question. The researchers believed that patients who were referred for colposcopy because of a mildly abnormal cervical smear often were found to have a more severe lesion than had been detected on the cervical smear (Soutter et al., 1986).

The design was a retrospective survey. The population was identified as women who attended a colposcopy clinic at the Regional Gynaecological Oncology Unit (RGOU), Gateshed in Great Britain. Their initial abnormal cervical cytology had revealed atypical but not dyskaryotic (dysplastic) cervical cells. The cervical smear that prompted the referral was termed the "index smear" (Soutter et al., p. 70).

Two populations were identified and samples of convenience were utilized. Group 1, referred to RGOU from July 1, 1983, to October 30, 1983, was initially comprised of 199 women but 10 were excluded due to pregnancy ($\underline{N}$ = 189). Of these, 24% were referred for cervical atypia ($\underline{n}$ = 45). Group 2 was identified from 22,245 computerized cytology records from RGOU for the year 1983. The sample ($\underline{n}$ = 102) was reduced from 1,515 women with cervical atypia ($\underline{N}$ = 1,515) due to a varied rate of follow-up, default by some, and the burden of performing colposcopy on all. Additionally, the sample of women ($\underline{n}$ = 102) recently had their first abnormal Pap smears which indicated

cervical atypia.

> These women were matched for age with the year's population of women with atypical smears, and were chosen so that at least 6 months had elapsed since the initial atypical smear had been reported to allow time for follow-up data to have been obtained. (Soutter et al., 1986, p. 71)

Instrumentation included cervical smears performed on all women in each sample followed by colposcopically directed biopsies of any areas of atypical epithelium. If more than one biopsy was taken from an individual, the most severe diagnosis was used. If a cervical conization was indicated, the patient was referred back to her physician for surgery (Soutter et al., 1986).

Descriptive analyses of data reported 37% to 39% of women in the first group with cervical atypia had final diagnoses of CIN II (moderate dysplasia) or worse. Within the second group, 27 patients were lost to follow-up, 56 had a normal cervical smear and did not undergo colposcopy, and 9 had another abnormal cervical smear but a histological diagnosis was not obtained. The remaining 10 women did undergo colposcopically directed biopsies. One was diagnosed with CIN I, three with CIN II, and six with CIN III (Soutter et al., 1986).

Soutter et al. (1986) concluded that women with even mildly atypical or dyskaryotic smears were at considerable risk of having CIN. The authors recognized that most colposcopy clinics in Britain were unable to cope with the increased load of colposcopies for women with only one

atypical cervical smear. Therefore, recommendation was for colposcopy referrals for any degree of dysplasia on a cervical smear. Due to increased risk for CIN in patients with cervical atypia and inability of existing clinics to cope with the additional load, further recommendation was for a compromise which suggested a colposcopy if two smears taken at an interval of at least 3 months were atypical. Finally, a confirmatory Pap smear six months after a second negative Pap smear was deemed prudent (Soutter et al., 1986).

Following a review of current literature, findings warranted a need for more aggressive follow-up. If the findings were significant as reported, then the burden of premalignant cervical disease would seem to outweigh any facility burden. The most significant statistic seemed to be the false negative rates of Pap smears which ranged anywhere from 2.4% to 69%. This research attempted to determine the incidence of cervical dysplasia in women with cytologic findings of ASCUS and ASCUS suggestive of HPV. With the determination of such statistics, practitioners would gain better understanding for follow-up measures.

Information derived from Soutter et al.'s (1986) study is relevant. Despite the age of the study, it holds the implication that atypia may be more important or significant than anyone was aware of then and now. Atypia must be followed closely through current literature, experience, and

continued research. Researchers must remain aware as classification systems for cervical cytology reporting are changed or updated. Studies are strengthened when research is conducted integrating current terminology.

Schaffer and Philput (1992) addressed HPV in their study, "Predictors of Abnormal Cervical Cytology: Statistical Analysis of Human Papillomavirus and Cofactors". The purpose of the research was to "develop and compare cohort profiles for cervical-cytology smears done from 1977 to 1989 at the student health center of a large southeastern university" (Schaffer & Philput, 1992, p. 47). Cervical cancer was the most common cancer in women less than 35 years old. The Centers for Disease Control (CDC) recognized a 460% rise in the incidence of HPV between 1966 and 1981. The oncogenic contribution of HPV was substantiated and the rise of HPV was felt to correlate with the dramatic rise of cervical cancer. However, the numbers of women with HPV without cervical cancer indicated that other cofactors along with HPV might lead to cervical-cytology abnormalities. The research questions were these: "Has the incidence of abnormal cervical cytology changed over the study period? Can factors associated with abnormal cervical-cytology be predicted by knowledge of the risk factors implicated in the current professional literature?" (Schaffer & Philput, p. 47). The researchers hypothesized that by identifying statistically significant cofactors in association with HPV,

they could then identify those individuals at greater risk for abnormal cervical cytology (Schaffer & Philput, 1992).

Schaffer and Philput's research was a retrospective study and utilized a sample of convenience. All patient records at the student health center were reviewed. The authors identified 2,919 records (n = 2,919) out of 9,057 women's records (N = 9,057) with at least one cervical cytology report done between September 1977 and May 1989. Those 33% met the study criterion and comprised the sample (Schaffer & Philput, 1992).

Schaffer developed the instrument, Cyto 4400, from a literature review on cervical cancer. The instrument included age at first sexual intercourse, cigarette smoking, exposure to exogenous hormones, exposure to herpes, HPV, Gardnerella, Chlamydia, history of a previous abnormal cervical cytology smear, as well as the dates and results of cervical cytology, specific infections present at the time of each smear, treatments ordered for infections, and whether clients were referred to a specialist, and treatment provided by the specialist (Schaffer & Philput, 1992).

A cervical cytology severity rating scale was used. Scale validity was determined by asking experts in women's health to rate a list of commonly used cytology terms in order of severity. Validity was determined to be 0.99. Some women had more than one cervical smear and so their severity scores were added and then divided by the number of cytology

reports. This allowed comparison between women with different numbers of cytology reports. However, the study was weakened when (1) inflammation and (7) carcinoma could be averaged and (4) mild dysplasia was not indicative of the whole picture (Schaffer & Philput, 1992).

The most prevalent infections were Gardnerella, HPV, and Chlamydia. There was a 10.8% rate of HPV. HPV occurrence was significantly higher in 1987 (ANOVA, $F[10, 2105] = 6.36$, $p = .0001$) (Schaffer & Philput, 1992).

The 2,919 participants had 6,224 cervical smears done during the study time of which 34.9% were abnormal. Cervical cytology by year (ANOVA, $F[10, 2,077] = 17.50$, $p = .0001$) indicated abnormal cervical cytology and HPV infection peaked the same year. Chi-square analysis revealed cervical smears of women exposed to HPV had significantly more atypias and dysplasias. Additionally, women over 30 years old did not have disproportionately high cytology severity (Schaffer & Philput, 1992).

A stepwise regression analysis used the dependent variable and entered three independent variables. The researchers indicated that incomplete data sets were excluded. HPV, the year of the cervical smear, and genital herpes infection were the independent variables. The overall R squared was 10%. The stepwise regression analysis did not identify a significant model to predict cervical cytology severity (Schaffer & Philput, 1992).

An additive effect between HPV, herpes, and smoking was determined by ANOVA and Duncan's multiple range test. Women with all three variables had mean Pap smear scores of 3.33. This was consistent with squamous atypia (Schaffer & Philput, 1992).

Over the course of the study the increases in sexually transmitted diseases, especially HPV, coincided with the increase of abnormal cervical cytology . The researchers concluded that further study was needed because "concurrent increases in HPV infection and cervical-cytology severity" (Schaffer & Philput, 1992, p. 50) indicate an association between the two.

The researchers felt the stepwise regression model was disappointing although it was significant. Schaffer and Philput (1992) indicated that if the majority of cervical abnormalities were resultant of HPV then HPV must not have been detected reliably through routine Pap smear screens. Underdiagnosis was thought to be due to inadequate cervical sampling.

In conclusion, HPV and herpes at the time of the Pap smear were the best predictors of abnormal Pap smears. The addition of smoking further increased the risk for abnormal cytology. Practitioners were cautioned to be aware of significant risk for cervical cytology severity. False-negative screening rates in high risk women were thought to be reduced with more frequent cytological screening.

Persistent inflammation of squamous koilocytotic atypias was indicated for additional screening; colposcopy and biopsy were felt to be justified to be certain that neoplasia did not exist (Schaffer & Philput, 1992).

Schaffer and Philput (1992) highlighted the importance and impact of cervical HPV infection. Their study provided a foundation for this researcher to investigate the suggestion of HPV infection on cytologic smears diagnosed as ASCUS and the incidence of cervical dysplasia. In an attempt to determine the impact of HPV, the researcher strived to present a greater understanding of the effects of HPV and management of cytological findings of the same.

In summary, there was a scarcity of literature regarding the incidence of cervical dysplasia in women with cytologic diagnosis of ASCUS with and without suggestion of HPV. Two HARNET studies focused on cytologic findings of cervical atypia. Slawson, Bennett, and Herman (1993) questioned whether or not significant cervical disease was being missed in primary care settings with single follow-up Pap smears for abnormal cervical cytology classified as atypia. In 1994, Slawson, Bennett, Simon, and Herman questioned whether all women with cervical atypia should be referred for colposcopy. In both studies, cervical cytology alone failed to be reliably predictive of cervical pathology. The HARNET studies supported a much earlier study by Soutter, Wisdom, Brough, and Monaghan (1986). The earlier

study concluded that women with even mildly atypical cytology results were at considerable increased risk of having cervical dysplasia. Human papillomavirus effects were addressed by Schaffer and Philput (1992). They concluded that women with cytological evidence of HPV required additional screening including colposcopy and biopsy to ascertain the presence of dysplasia.

None of the studies reviewed addressed the specific incidence of cervical dysplasia in women with cytologic results of ASCUS as defined by The Bethesda System and results of ASCUS suggestive of HPV, another The Bethesda System classification. Similarly, all except Schaffer and Philput addressed the significance of cytologic findings of cervical atypia although not in the context of The Bethesda System. Only Schaffer and Philput (1992) studied the effect of human papillomavirus on cervical pathology. This research has synthesized the results of these studies to provide a basis for determining the incidence of cervical dysplasia in women with and without ASCUS suggestive of HPV.

Chapter III

The Method

This retrospective study, "Incidence of Cervical Dysplasia in Women With and Without Cytology Suggestive of Human Papillomavirus", was conceptualized to address the problem of an undetermined significance of cervical atypical squamous cells and an undetermined significance of cervical atypical squamous cells suggestive of HPV. A chart audit was conducted of medical records obtained from an OB/GYN practice. Medical records were selected for audit by an examination of pathology reports obtained from a local pathology laboratory utilized by the OB/GYN practice. Sampling design was one of convenience. Data were recorded and quantitative analysis performed.

Variables

The independent variable was cervical cytology reports suggestive of HPV. The dependent variable was cervical dysplasia as determined by histologic diagnosis. Control variables included the consistency of the clinicians in obtaining specimens of both a cytologic and histologic nature and the consistency of the same cytotechnologists and pathologists interpreting specimens. Intervening variables that may have affected the research included the length of

time between collection of a specimen and when the specimen was fixed, knowledge obtained and utilized in collection or diagnosis of specimens, change in equipment utilized for collection or diagnosis of specimens, misdiagnosis, incorrect recording of results, and client variables such as age at first intercourse, number of sexual partners, current sexual activity or preferences, last menstrual period, birth control method, smoking, elapsed time before follow-up or biopsy, presence of other diagnosed and/or undiagnosed cervical or vaginal infections, and age at time of ASCUS diagnosis.

Setting, Population, and Sample

The setting for this research was a college town in the southeastern United States. The town was located in a rural area approximately 70 miles from a large metropolitan center. The population of the town combined with the population of the campus included approximately 10,000 females. The area medically served was approximately 49% Caucasian and 49% African-American. The college was approximately 10% African-American and approximately 85% Caucasian. Foreign students comprise about 5% of the college population. Approximately 40% of the college students were classified as out of state; 60% were classified as residents (Board of Trustees of State Institutions of Higher Learning, 1994).

For the purpose of this study, the population (N = 442) included cervical cytology reports of women whose Pap smears were reported as ASCUS or ASCUS suggestive of HPV from March 1994 through May 1995. The sample (N = 58) included all medical records of women presenting to one obstetric and gynecologic (OB/GYN) practice for follow-up of cytology indicating ASCUS or ASCUS suggestive of HPV that culminated in colposcopically directed cervical biopsies. Two board certified obstetrician/gynecologists (OB/GYNs) performed biopsies. The Pap smears and biopsies were diagnosed by one pathology group which was comprised of two board certified pathologists and two certified cytotechnologists.

The first cytology report of ASCUS or ASCUS suggestive of HPV was termed the index smear. Two sample subsets were established based the reported presence of HPV on the index smear report. The first sample subset consisted of cytology reports of ASCUS (n = 42) while the second subset consisted of cytology reports of ASCUS suggestive of HPV (n = 16).

Methods of Data Collection

Instrumentation and Procedure

Permission to conduct this study was granted by the Internal Review Board of Mississippi University for Women (see Appendix C) and also the pathologists and OB/GYNs of the charts reviewed. The permission form illustrated in Appendix D was utilized to obtain permission from the physicians. Names of the practices were inserted before

presenting the forms. The forms were explained to the physicians and each signed appropriately. The forms remained in the possession of the researcher to assure anonymity.

Names of clients with cytologic diagnosis of ASCUS were obtained from the pathology group. The corresponding charts in the office of the OB/GYNs were utilized to obtain results of follow-up cervical biopsies. Demographic observations were made of the sample utilizing the Registration Slip and Patient Questionnaire forms which had been provided to all patients at the OB/GYN practice and the GYN Cytology and Pathology forms from the pathology laboratory (see Appendixes E, F, G, and H for respective forms). Not all information requested was given by the patient but some consistency in information reported was noted.

Information normally reported by patient and/or physicians that could be considered intervening variables (Schaffer & Philput, 1992), as well as demographic characteristics, was recorded for the purpose of sample description. Due to the retrospective nature of this study, accessible data consisted of race, year of birth, age at the time of the first ASCUS or ASCUS suggestive of HPV report and biopsy date, date of the last menstrual period preceding the index cytology report and preceding the biopsy, smoking, birth control methods, evidence of candida, herpes simplex virus, bacteria, and chlamydia, pregnancy, and the number of previous abnormal Pap smears in the pathology laboratory

before the biopsy. After data collection was completed, a set of 200 random numbers was generated using the Lotus 123 @RAND function. These numbers were then assigned to individual cases and names were deleted to assure anonymity (see Appendix I for raw data).

Method of Data Analysis

Descriptive and inferential statistics were utilized for data analysis. The incidence of cervical dysplasia in women with ASCUS and the incidence of cervical dysplasia in women with ASCUS suggestive of HPV were reported as percentages of occurrences in the sample subsets. A chi-square analysis was utilized to determine statistical significance of the incidence of cervical dysplasia in the sample subsets at $\alpha = 0.05$.

Limitations

Many limitations were encountered throughout the research. The first limitation was the lack of current published research evaluating ASCUS and ASCUS suggestive of HPV. The studies that did exist did not utilize The Bethesda System.

Along with changes in classification systems over recent years, changes in cervical cell collection techniques also occurred. This affected the generalization to and comparison with previous studies. Another limitation encountered was the potential inconsistency in adapting one classification system to another.

Follow-up Pap smears were not augmented with additional screening techniques by the gynecologists in this study. The gynecologists' normal follow-up for one Pap smear result of ASCUS with or without suggestion of HPV was to repeat the Pap smear in three to six months. If the patient was pregnant and colposcopy indicated, follow-up was sometimes delayed. If the patient was not trusted to follow-up, a colposcopy was sometimes performed instead of a repeat Pap smear. False negative rates of cytologic interpretation were unknown.

The fact that the sample was one of convenience has inherent weaknesses. Neither variables nor randomization could be controlled. Exposure of the clinicians and clients to increased knowledge of HPV had to be identified as a potential limitation. With increased knowledge about and awareness of HPV by the clinicians, bias may have also increased. With public education, more women have identified themselves at increased risk for HPV and present sooner and more often for Pap smears than in previous years. The incidence of cervical dysplasia may have appeared increased only due to the increased presentation of those clients at increased risk.

In summary, the quantitative research design was introduced along with its relevance to this study. Independent and dependent variables were stated. Many intervening variables were outlined. Descriptions were given

of the setting, population, and sample. Instrumentation of data collection was presented along with the procedures for data collection and recording. The methods of data analysis requiring calculations of percentages and a chi-square value were presented. Limitations were acknowledged as affecting the outcome of the research.

Chapter IV

The Findings

The purpose of this study was to determine the incidence of cervical dysplasia in women with and without atypical squamous cells of undetermined significance (ASCUS) suggestive of human papillomavirus (HPV). This retrospective study addressed the problem of an undetermined significance of cervical atypical squamous cells and ASCUS suggestive of HPV. Sampling was one of convenience. Chart audits were performed on medical records from an OB/GYN group for the purpose of data collection and quantitative analysis.

Description of the Sample

The sample was derived from a population of Pap smear reports of ASCUS by the pathology laboratory. From the list of 442 Pap smear reports of ASCUS and ASCUS suggestive of HPV (N = 442), 58 smears culminated in biopsies. Those Pap smears that culminated in cervical biopsies comprised the sample set (N = 58) and were the focus of this study.

The 58 cases in the sample set were selected on the basis of several criteria. First, the subjects must have had a Pap smear and/or biopsy within the time frame of the study, March of 1994 through May of 1995. Second, an index smear reporting ASCUS or ASCUS suggestive of HPV must have

been satisfactory for evaluation according to The Bethesda System. Two subsets, ASCUS (n = 42) and ASCUS suggestive of HPV (n = 16), were determined by the index smear report. Third, the index smear must have culminated in a colposcopically directed cervical biopsy. Biopsies were performed subsequent to one abnormal Pap smear in 62.1% of the cases, subsequent to two abnormal smears in 36.2% of the cases, and subsequent to three abnormal smears in 1.7% of the cases. Subjects were eliminated if there was a cytology report of any dysplasia preceding the index smear or if treatment with cervical cryotherapy, conization, or laser vaporization was noted.

One Asian, 16 African Americans, and 41 Caucasians were identified during chart audits of the sample (N = 58). Ages reported on index Pap smears ranged from 17 to 53 years. Figure 1 illustrates the distribution of ages. A summary of sample demographics is presented in Table I.

Results of Data Analysis

The null hypothesis was that there is no difference in the incidence of cervical dysplasia in women with and without cytology suggestive of human papillomavirus. Both descriptive and inferential statistics were utilized for analysis of sample data. Descriptive results indicated an incidence of cervical dysplasia in women with ASCUS (n = 42) of 30.95%, and an incidence of cervical dysplasia in women with ASCUS suggestive of HPV (n = 16) of 18.75%. This

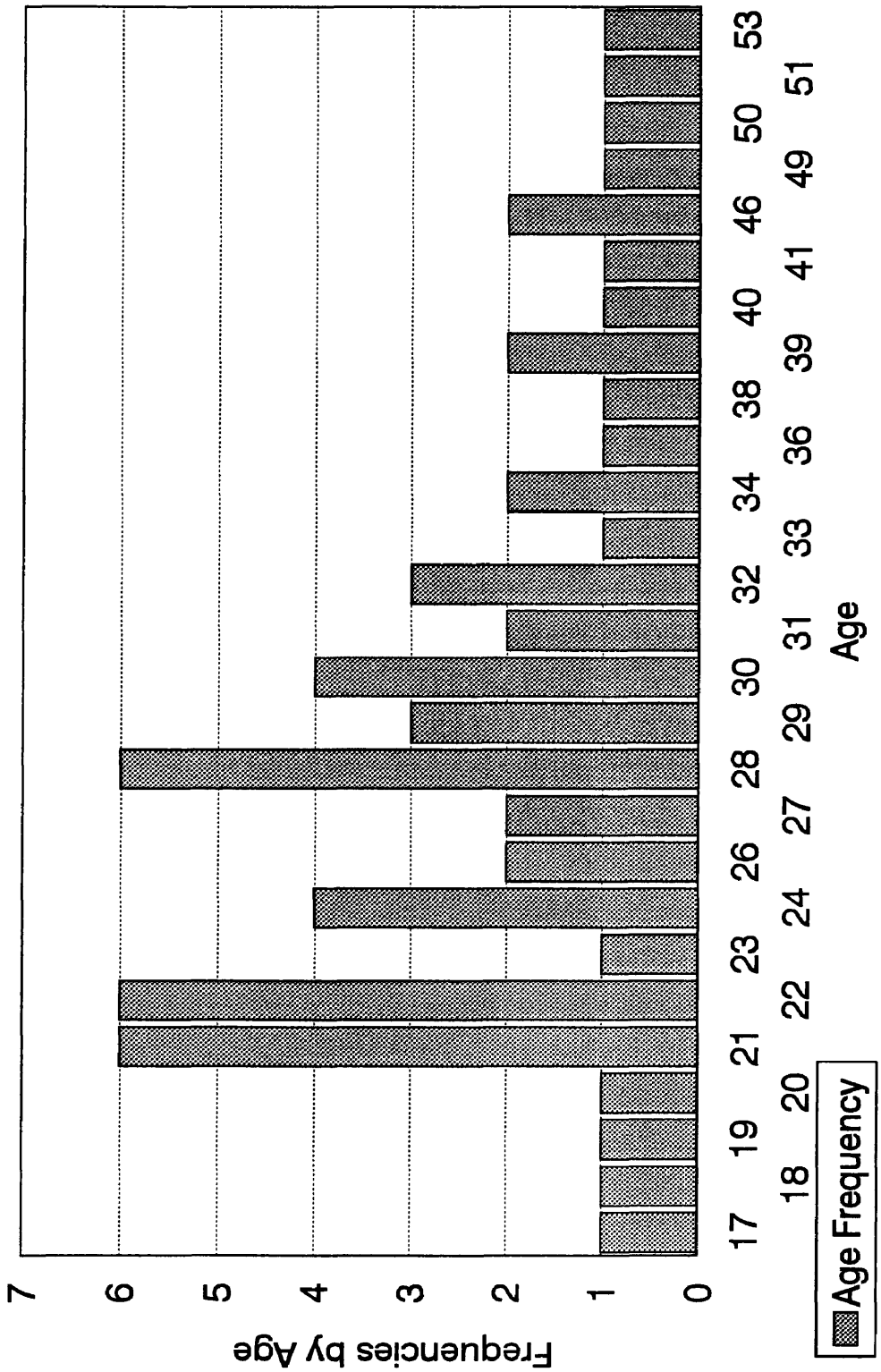

Figure 1. Distribution of sample (N = 58) according to age frequencies.

Table I

Summary of Demographic Characteristics by Subsets, ASCUS and ASCUS suggestive of HPV, using Frequencies (f) and Percentiles (%)

Demographic Characteristics	ASCUS (n = 42) f	%	ASCUS Suggestive of HPV (n = 16) f	%	Total (N = 58) f	%
Race						
African-American	11	26.19	5	31.25	16	27.59
Asian	0		1	6.25	1	1.72
Caucasian	31	73.81	10	62.50	41	70.69
Smoker	9	21.43	7	43.75	16	27.59
Birth Control Method						
Oral contraceptives	20	47.62	10	62.50	30	51.72
Tubal sterilization	6	14.29	1	6.25	7	12.07
Natural/rhythm	0		1	6.25	1	1.72
Diaphragm	0		1	6.25	1	1.72
Condoms	3	7.14	1	6.25	4	6.90
Norplant	1	2.38	0		1	1.72
None/unknown	9	21.43	2	12.50	11	18.97
Post-menopausal	3	7.14	0		3	5.17
Pregnant	3	7.14	0		3	5.17
Infection on cytology						
Candida	6	14.29	2	12.50	8	13.79
Herpes Simplex Virus	2	4.76	0		2	3.45
Bacteria	5	11.90	1	6.25	6	10.34
Chlamydia	1	2.38	0		1	1.72

represents a 12.2% point difference between the two subsets and a 65% higher incidence rate of cervical dysplasia in the women with Pap smear reports of ASCUS without evidence of HPV. Table II further illustrates these findings. Subjecting data to analysis utilizing contingency table and chi-square

statistics revealed $X^2(1, N = 58) = 0.8629$, $p < .05$, $p = 0.353$.

Table II

Incidence of Cervical Dysplasia in Women with ASCUS and in Women with ASCUS Suggestive of HPV

Cytologic diagnosis	Cervical dysplasia	No cervical dysplasia	(n) Total
ASCUS	13	29	42
	30.95%	69.05%	100%
ASCUS suggestive of HPV	3	13	16
	18.75%	81.25%	100%

Using subsets of cytology reports of ASCUS ($n = 42$) and ASCUS suggestive of HPV ($n = 16$) and the frequency of dysplasia and no dysplasia on biopsy, a chi-square value with one degree of freedom was derived. The chi-square value obtained was 0.8629. This represents a probability value of 0.353 or approximately a 35% chance that a distribution of observations exists that would be more likely to show a dependency, or relationship, between cytological diagnosis of HPV and biopsy proven cervical dysplasia. Therefore, using the chi-square results, the null hypothesis cannot be rejected at a level of $\alpha = .05$. Table III further illustrates these results.

Additional Findings

Many additional findings surfaced during collection and analysis of the data from chart audits. Of the biopsies

Table III

Contingency Table and Chi-Square Results for Cervical Dysplasia by HPV on Cytology

		No HPV	HPV	Total
No Dysplasia	Frequency	29	13	42
	Total Percent	50.00	22.41	72.41
	Row Percent	69.05	30.95	
	Column Percent	69.05	81.25	
Dysplasia	Frequency	13	3	16
	Total Percent	22.41	5.17	27.59
	Row Percent	81.25	18.75	
	Column Percent	30.95	18.75	
Total	Frequency	42	16	58
	Percentage	72.41	27.59	100.00

Note. Chi-Square Value with 1 df = 0.864, $p = 0.353$. Chi-Square rejection value with 1 df at $\alpha = 0.05$ is 3.71.

($N = 58$), 74.14% or 43 biopsies confirmed dysplasia and/or HPV. Dysplasia was recorded on 16, or 27.59%, of the pathology reports, and of these 16 reports, 14 also recorded HPV. HPV without dysplasia was recorded in 28 cases or 48.27% of the pathology reports. A total of 42 pathology reports indicated HPV (72.4%).

While 16 index smears had cytology consistent with ASCUS suggestive of HPV, only 11 of them confirmed HPV by biopsy. No pathological diagnosis of HPV was given on five reports. Mild dysplasia was diagnosed in three of these 16 biopsies; of these three, two were also diagnosed with HPV. Only one of these observations indicated no HPV on cytology yet diagnosed dysplasia on biopsy.

HPV was not noted in 42 of the index cytology reports. In this subset (n = 42), HPV was diagnosed by biopsy in 31 of those observations while 13 reports of dysplasia were noted. There was only one observation in which dysplasia was diagnosed without HPV. Biopsies revealed 19 observations of HPV without dysplasia. Twelve of the 42 reports of ASCUS without evidence of HPV culminated in biopsies with diagnoses of both dysplasia and HPV.

Out of the 58 biopsy reports, three revealed high grade dysplasia--approximately 5% of the total sample. Chart audits of these three revealed all to be Caucasian and oral contraceptive users 21, 28, and 30 years of age. Two were smokers, and none had index cytology suggestive of HPV. All histopathology indicated HPV along with high grade dysplasia. Elapsed times between the index smear and biopsy were 175 days, 187 days, and 229 days. The mean elapsed time was 197 days for these three observations.

Elapsed time (Schaffer & Philput, 1992; ACOG, 1993) from date of index smear to date of biopsy ranged from 0--that is, the biopsy was done immediately following the index Pap smear, to 517 days. The mean elapsed time from the date of the index Pap smear to the biopsy date was 143.67 days for the sample (N = 58). Pap smears reporting ASCUS (n = 42) had a mean elapsed time of 148.2 days prior to biopsy. Reports of ASCUS suggestive of HPV (n = 16) had a mean elapsed time of 131.7 days prior to biopsy. The mean elapsed

time was 140.7 days for smears that culminated in biopsy proven dysplasia and 144.5 days for cytology that culminated in HPV. Four of the observations that culminated in biopsies identifying cervical dysplasia had elapsed times of 35 days or less.

Chart audits also revealed four clients used condoms for birth control. Of those four, all had pathology reports of HPV. Three of the pathology reports also diagnosed mild dysplasia.

Eight index Pap smears revealed Candida. Two of these also suggested HPV while only one of the two had a HPV diagnosis from biopsy. HPV was diagnosed from biopsies of three of the index smears that revealed Candida without HPV. Only one index Pap smear that reported Candida culminated in a biopsy with dysplasia without HPV while the cytology report also gave no evidence of HPV.

Summary

In summary, the null hypothesis, there is no difference in the incidence of cervical dysplasia in women with and without cytology suggestive of HPV, failed to be rejected based on inferential analysis with a chi-square value, $X^2(1, N = 58) = 0.8629$, $p < .05$, $p = 0.353$. However, descriptive statistics revealed an increase of 65% in the incidence of cervical dysplasia in cases of women without evidence of HPV as reported on the index Pap smear over cases with evidence of HPV as noted on the index cytology

report. The descriptive statistics along with the chi-square analysis does seem to indicate a relationship although weak and statistically non-significant. Additional findings from chart audits have been presented. The findings reveal information regarding the pathological diagnosis of HPV and dysplasia.

Chapter V

The Outcomes

Notable controversy has existed in the areas of management of women with a cytological diagnosis of atypical squamous cells of undetermined significance (ASCUS) and women with the diagnosis of ASCUS suggestive of human papillomavirus (HPV). Due to frequent changes in cytology reporting, inconsistencies between reportings, and lack of current literature, further investigation into the areas of cervical cytology reportings of ASCUS and ASCUS suggestive of HPV was deemed necessary. A null hypothesis, there is no difference in the incidence of cervical dysplasia in women with and without cytology suggestive of HPV, was proposed. The purpose of this retrospective study was to determine the incidence of cervical dysplasia in women with ASCUS and in women with ASCUS suggestive of HPV in order to provide improved and appropriate management to both groups of women. This chapter presents a summary of the significant findings, additional findings, discussion, review of the physiological conceptual framework, conclusions, implications for nursing, and recommendations for further study.

A chart audit was conducted of medical records from an OB/GYN medical practice. Observations were made of medical records containing Pap smears with the diagnosis of ASCUS

and ASCUS suggestive of HPV that had culminated in cervical biopsies. The setting was an area of the southeastern United States. The population (N = 442) included medical records of women with cytologic diagnosis of ASCUS and ASCUS suggestive of HPV made by a pathology group utilized by the OB/GYN group for cervical screening and diagnosis. Descriptive and inferential statistics were utilized for data analysis.

The null hypothesis, there is no difference in the incidence of cervical dysplasia in women with and without cytology suggestive of HPV, failed to be rejected based on chi-square analysis at $\alpha = 0.05$. Descriptive statistics did, however, indicate a 65% greater incidence of HPV in women with cytology reports of ASCUS than in women with cytology reports of ASCUS suggestive of HPV. The descriptive statistics do highlight a possible relationship but the chi-square analysis indicates a weak, statistically non-significant relationship at best. Additional findings revealed information pertaining to the histological diagnosis of HPV and dysplasia.

Summary of Findings

The sample, N = 58, was comprised of Pap smear reports of ASCUS (n = 42) and ASCUS suggestive of HPV (n = 16) that culminated in cervical biopsies. An array of demographic factors was identified through chart audits.

Significant Findings

The incidence of cervical dysplasia was found to be greater in women with cytology reporting ASCUS than in women with cytology reporting ASCUS suggestive of HPV. The incidence of cervical dysplasia in women with ASCUS (n = 42) was 30.95% while the incidence of cervical dysplasia in women with ASCUS suggestive of HPV (n = 16) was 18.75%. These findings represent a 65% increase in the incidence of biopsy proven cervical dysplasia after index Pap smears of ASCUS over the incidence of cervical dysplasia after index Pap smears of ASCUS suggestive of HPV. Inferential analysis utilizing contingency tables and a chi-square value indicated a statistically non-significant relationship between the incidences of cervical dysplasia in the two subsets, $X^2(1, n = 58) = 0.8629$, $p < .05$, $p = 0.353$. Therefore, the researcher failed to reject the null hypothesis at $\alpha = 0.05$.

Additional Findings

While 74.14% of the cervical biopsies (N = 58) confirmed HPV and/or dysplasia, HPV was found to have a higher incidence of occurrence than dysplasia. A total of 42 pathology reports, 72.4%, diagnosed HPV while a diagnosis of dysplasia was reported in only 27.59% of the sample. Of the subset reporting ASCUS (n = 42), 30.95% had biopsy proven dysplasia; of the subset reporting ASCUS suggestive of HPV (n = 16), 18.75% had biopsy proven dysplasia.

Approximately 5% of the cases in the sample (N = 58) diagnosed high grade dysplasia. All three cases revealed Caucasian race and oral contraceptive users. None had evidence of HPV on cytology but HPV was confirmed along with the high grade dysplasia in each of the biopsies.

All clients reporting condom use for birth control were found to have HPV on biopsy. Mild dysplasia was also reported in 75% of those cases of HPV in condom users.

Further findings resulted from additional examination of demographic variables. Of the 58 cases in the sample set, 70.69% of the women were reported to be Caucasian while 27.59% were African Americans and 1.7% were Asian. The sample revealed a positively skewed bimodal distribution of ages. Ages ranged from 17 years to 53 years at the time of the index Pap smear. The mean sample age was 29.6 years. The mean age for the subset of reports demonstrating ASCUS was 29.29 years and for the subset demonstrating ASCUS suggestive of HPV was 30.56 years. Smoking was reported in 27.6% of the sample. Chart audits revealed 51.7% of the sample reported use of oral contraceptives for birth control.

Discussion

The researcher failed to reject the null hypothesis, there is no difference in the incidence of cervical dysplasia in women with and without cytology suggestive of HPV. Although inferential statistical analysis using chi-

square found no significant relationship in differences of incidences of cervical dysplasia, descriptive statistics did seem to indicate a relationship between cytology suggestive of HPV and biopsy proven dysplasia. However, the inferential analysis reveals this relationship to be weak and not statistically significant.

Utilizing descriptive statistics, a greater incidence of biopsy proven dysplasia with ASCUS than with ASCUS suggestive of HPV is noticeable. In part, this may appear so because there exists a morphologic overlap in cytology. Subjective variations between cytotechnologists and pathologists exist thus creating diagnostic dilemmas. The assumption was made, however, that within the pathology laboratory utilized, there would be consistency in reporting over time and between specimens. Some confusion does continue to exist in pathology in classifying ASCUS and HPV on cytologic smears. The need is thus demonstrated that ASCUS with or without evidence of HPV must be followed closely.

Paps reflecting ASCUS diagnoses culminated in many biopsy proven cases of HPV when no evidence of HPV was seen on the Pap smear, 31 out of 42. Again, this may be due to the morphologic overlap in pathology reporting. Perhaps some criteria was met for HPV classification on cytology but not all criteria was met. Results may be skewed, however, due to the large number of assumed sexually active college women

having more than one partner. The local college has demonstrated a higher than national average in the diagnosis of HPV on cytology. Conversely, HPV suggested by Pap smear but not identified by biopsy, causes some concern. This inconsistency may be due in part to biopsy sampling error or overdiagnosis by the pathology laboratory. However, it is most likely due to reactive or inflammatory changes of cells collected for cytologic evaluation.

Some concern has existed as to whether or not the presence of Candida interferes with the ability to make an accurate cytologic diagnosis as Candida may mimic changes seen with ASCUS and thus lend to some overcall of ASCUS. Interference by Candida is not obvious from this data. The pathology laboratory utilized has not been steered to wrongful diagnoses in the presence of Candida.

Condom users in this study demonstrated a 100% biopsy proven HPV rate. One must take into consideration whether or not condoms were used consistently, and if HPV was present before condoms were utilized. Assuming 100% compliance, inference can be made that condoms are hardly protective of HPV transmission.

Interest and concern surface as a result of the diagnoses of high grade dysplasia in 5% of the sample. Enough atypia was identified on the Pap smear that the cases were not lost. This, however, represents a broad spectrum of pathology that can be high grade but sampling on a Pap smear

can lead to errors in diagnoses. Sampling errors may be the result of the size of the abnormal lesion--if the lesion is minuscule, there would be a decreased chance of obtaining those cells. The location of the lesion may not be easily accessible and thus may not be reached with the Cytobrush or Ayre wooden spatula, especially if the lesion lies within the glands of the cervix.

After biopsies, 74.14% of the sample (N = 58), ASCUS and ASCUS suggestive of HPV, demonstrated confirmed cervical dysplasia and/or HPV. This appears to represent a strong relationship between cytologic atypia and histologic atypia.

Problems with the design of the study may have affected the results. It was hoped that the use of one OB/GYN group and one pathology laboratory would strengthen the study. Inherent, however, is the acknowledgement that this may also be a theoretical shortcoming of the design. Two different doctors performed colposcopies, and biopsy specimens were interpreted by two different pathologists. Pap smears were interpreted by two cytotechnologists and two pathologists. This does not appear to be a fatal flaw, but it may account for some of the subjective variations in classifications. Another inherent limitation was the sample size and time frame of the study. While specific guidelines for management are not established, the time frame limits the inferences that can be drawn with respect to management. The time frame of this study did, however, allow for consistency in

cytological classifications utilizing The Bethesda System. There will be questions as to whether or not a larger sample or a longer time frame would have significantly altered results in either the descriptive or inferential analyses. Also, extension of the results of this study to the general population may be difficult as the sample population may not adequately reflect the populations in other geographic areas.

Findings of this study lend support to most but not all of the current published literature. Kurman and Solomon (1994) indicated ASCUS results reflected either an exuberant benign change or a potentially serious lesion, and, therefore, were interpreted to be of undetermined significance. The sample utilized in this study, $\underline{N}$ = 58, revealed biopsy proven HPV and/or dysplasia in 74.14% of the cases. Only 25.86% of the biopsies were benign. These results strengthen the case for ASCUS findings representing potentially serious lesions.

Slawson et al. (1993) reported a 35% prevalence rate of biopsy proven CIN among women whose screening Pap smears showed ASCUS while this study revealed a prevalence rate of dysplasia in a subset of women whose index Pap smears showed ASCUS ($\underline{n}$ = 42) of 30.95% and in the total sample ($\underline{N}$ = 58) of 27.59%. However, 74.14% of this total sample had an occurrence of biopsy proven dysplasia and/or HPV.

Slawson et al. (1993) also reported results that may indicate progression of cervical disease occurred during the four to six month waiting period after an initial ASCUS. Results of this study revealed a mean elapsed time from the index Pap smear to biopsy of 143.67 days or approximately 5 months in which, again, a rate of 74.14% of biopsy proven dysplasia and/or HPV was identified. While Slawson et al. reported that the Pap smear alone failed to detect one third of the high grade lesions, this study demonstrated that none of the high grade lesions with HPV on biopsy were predicted by Pap smears and were classified as ASCUS (with no evidence of HPV). Thus, this study supports Slawson et al. in both the prevalence rate and the elapsed time measures. This research was even more definitive in recognizing that Pap smears alone may fail to detect the presence of high grade lesions.

Soutter et al. (1986) concluded that women with even mildly atypical or dyskaryotic smears were at considerable risk of having CIN. Despite the date of the study, the implication that atypia may be more important or significant than realized is supported by this current study. Their conclusions will continue to be strengthened with replications studies in which current terminology is integrated.

Schaffer and Philput (1992) found a significant chi-square relationship between exposure to HPV and cervical

atypias and dysplasias on cytology. However, this research, while not testing for atypias, found a high percentage of biopsy proven HPV in women with ASCUS. While Schaffer and Philput concluded that women with cytological evidence of HPV required additional screening to ascertain the presence of dysplasia, the prevalence of dysplasia in this study was greater in the subset of reports of ASCUS than in the subset of reports of ASCUS suggestive of HPV.

The Bethesda System was utilized exclusively by the pathology laboratory in reporting cervical cytology during the time frame of this study. This consistency in classification and use of terminology closely related to histopathologic vocabulary strengthened this study. Knowledge of specimen adequacy as satisfactory was utilized as part of the criteria for inclusion in this study as was the cytological classifications of The Bethesda System.

Orem's theory of self-care provided the basis for the assumption that women practice activities they initiate and perform on their own behalf in maintaining life, health, and well-being. With additional knowledge gained from this study, nurse practitioners will be able to function in the educative-supportive role in the nursing system to foster health and well-being through disease prevention and health promotion related to cervical cancer screening. With detection of abnormal cervical cytology, nurse practitioners will have additional knowledge to support the educative

efforts in promoting women's understanding of the risks associated with any abnormal Pap smear.

Conclusions

Scarcity of current published research on the dilemma of diagnosis and management of women with ASCUS and ASCUS suggestive of HPV prompted this study. A null hypothesis was proposed: There is no difference in the incidence of cervical dysplasia in women with and without cytology suggestive of HPV. Descriptive statistics and inferential analysis suggested a weak statistically non-significant relationship between cytologic diagnosis of HPV and biopsy proven dysplasia. Thus, the researcher, using chi-square analysis at a rejection level of $\alpha = 0.05$, failed to reject the null hypothesis. Findings indicate the need for further research and closer monitoring of patients with cytologic diagnosis of cervical ASCUS with or without suggestion of HPV.

While no previous studies have addressed this specific problem, some studies do parallel this research in examining cervical cytology reports and/or histopathology reports (Slawson et al., 1993; Slawson et al., 1994; Soutter et al., 1986; Schaffer & Philput, 1992). The identified prevalence rate of dysplasia on cervical biopsy reports of 30.95% supports findings reported by Slawson et al. (1993). Elapsed time between the Pap smear and progression of cervical disease from ASCUS or ASCUS suggestive of HPV of

approximately five months also lends support to Slawson et al.'s study. Five percent of seemingly mild Pap smear abnormalities resulted in diagnoses of high grade dysplasia on biopsy. This is consistent with the findings of Slawson et al. reported in 1994 and also with findings reported by Soutter et al. in 1986. The greater prevalence of HPV identified on cervical biopsy than on cervical cytology found in this research supports findings reported by Schaffer and Philput (1992).

While support is given to previous studies, some different findings also exist. The most significant difference, however, is the chi-square value obtained in this research. Analysis identified a non-significant relationship between the incidences of dysplasia in women with index Pap smear reports of ASCUS and ASCUS suggestive of HPV. Schaffer and Philput (1992) utilized chi-square statistics and determined that women exposed to HPV had significantly more atypias and dysplasias.

Implications for Nursing

The body of nursing knowledge has increased as a result of this study and the areas of research, theory, practice, and education have been strengthened. Validation of the importance of ASCUS and ASCUS suggestive of HPV through research helps to identify nursing actions that are within the realm of nursing practice and helps delineate the unique role of nursing in health care today. When findings from

studies are similar, nurses will have a greater impact on patient outcomes. As suggested in this study, ASCUS and ASCUS suggestive of HPV have a much higher incidence of pathological changes on cervical biopsy than is indicated by Pap smears. Through understanding of the pathology of ASCUS and ASCUS suggestive of HPV, risk factors, screening, diagnosis and treatment, nurse practitioners can interrupt the spread of HPV, decrease pathogenic consequences of both ASCUS and HPV, and thus, avoid greater consequential outcomes as in the reduction of the incidence of cervical cancer. Nurse practitioners will also have the opportunity to evaluate progression or regression of cervical ASCUS and ASCUS suggestive of HPV. The educative effort of the nurse practitioner follows Orem's nursing system as does the intervention. If HPV is detected, counseling the infected woman on transmission, treatment, and prevention of reinfection is a large educative effort.

Nurse practitioners today are involved not only in counseling, education, and cervical cytology screening for women, but many have assumed a greater role to include performing colposcopies along with colposcopic directed biopsies. Nurse practitioners must demonstrate proficiency in this area in order to assure acceptance and respect by members of the health care profession and the communities in which they serve.

Nurse practitioners have the responsibility to identify needs of the profession. They must remain abreast of current research, treatment, technology and educational issues. All four areas must be integrated into nurse practitioner curriculums to effectively prepare students for the role of primary care providers. Practitioners must remain aware of changes or updates in the classification systems for cervical diagnosis through networking and continued education.

Not only will the client and the nurse practitioner benefit from this study, but other health disciplines will also benefit as they acknowledge the integral role that nurse practitioners and nursing research play in today's health care.

Recommendations for Further Study

Recommendations for further study have been derived from lack of current published research on the importance of ASCUS and ASCUS suggestive of HPV. Questions have surfaced related to a lack of complete information and to time restraints. Continued research in this area will improve the scientific base for not only nursing practice but also the practice of other health professionals. Recommendations for further study are the following:

1. Follow-up longitudinal study on the incidence of cervical dysplasia in women with cytology reportings of ASCUS and ASCUS suggestive of HPV.

2. Follow-up study on the incidence of cervical dysplasia in women with cytology reportings of ASCUS and ASCUS suggestive of HPV in other settings with different populations.

3. Follow-up study on the incidence of cervical dysplasia in women with cytology reportings of ASCUS and ASCUS suggestive of HPV with cytology sampling and cervical biopsies done by others and evaluation of cytology and histopathology by others.

4. Identification of HPV strains in this area and their relationship to cervical smears and biopsies.

5. Identification of demographic variables of groups of ASCUS and groups of ASCUS suggestive of HPV and their relationships.

6. Identification of significance of numbers of reports of ASCUS or ASCUS suggestive of HPV prior to biopsy and cervical diagnostic severity.

7. Identification of significance of elapsed time between index smear of ASCUS and ASCUS suggestive of HPV and the incidence of biopsy proven cervical dysplasia and/or HPV.

8. Correlation of cervical cytology diagnoses and histopathologic diagnoses with Pap smears and colposcopic directed biopsies performed by nurse practitioners.

9. Establishment and implementation of a colposcopy training program for nurse practitioners.

10. Acceptance of nurse practitioners as primary care providers in women's health in Mississippi.

11. Development of a program for recording pertinent data that may be linked to Pap smear results and biopsies in order for relationships to be established.

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Appendix A
The 1991 Bethesda System

The 1991 Bethesda System

- Adequacy of the specimen
  - Satisfactory for evaluation
  - Satisfactory for evaluation but limited by (specify reason)
  - Unsatisfactory for evaluation (specify reason)

- General categorization (optional)
  - Within normal limits
  - Benign cellular changes: See descriptive diagnoses
  - Epithelial cell abnormalities: See descriptive diagnoses

- Descriptive Diagnoses
  - Benign cellular changes
    - Infection
      - Trichomonas vaginalis
      - Fungal organisms morphologically consistent with Candida species
      - Predominance of coccobacilla consistent with shift in vaginal flora
      - Bacteria morphologically consistent with Actinomyces species
      - Cellular changes associated with herpes simplex virus
      - Other

- Reactive Changes
  - Reactive cellular changes associated with
    - Inflammation (includes typical response)
    - Atrophy with inflammation ("atrophic vaginitis")
    - Radiation
    - Intrauterine contraceptive device; Other

- Epithelial Cell Abnormalities
  - Squamous cell
    - Atypical squamous cells of undetermined significance: Quality[1]
    - Low-grade squamous intraepithelial lesion encompassing HPV[2]; mild dysplasia/CIN 1
    - High-grade squamous intraepithelial lesion encompassing moderate and severe dysplasia, CIS/CIN 2, CIN 3
    - Squamous cell carcinoma

Glandular Cell
- Endometrial cells, cytologically benign, in a post-menopausal woman
- Atypical glandular cells of undetermined significance: Quality[1]
- Endocervical adenocarcinoma
- Endometrial adenocarcinoma
- Extrauterine adenocarcinoma
- Adenocarcinoma, NOS

Other Malignant Neoplasms: Specify

Hormonal Evaluation (applies to vaginal smears only)
- Hormonal pattern compatible with age and history
- Hormonal pattern incompatible with age and history: Specify
- Hormonal evaluation not possible due to: Specify

---

* HPV indicates human papillomavirus; CIN, cervical intraepithelial neoplasia; CIS, carcinoma in situ; and NOS, non-organ specific.

[1] Atypical squamous or glandular cell of undetermined significance should be further qualified, if possible, as to whether a reactive or a premalignant/malignant process is favored.

[2] Cellular changes of HPV previously termed koilicytosis, koilocytotic atypia, or condylomatous atypia are included in the category of low-grade squamous intraepithelial lesion.

Source. The Bethesda System Committee, The Bethesda System for Reporting Cervical/Vaginal Cytologic Diagnoses. American Journal of Surgical Pathology, 16,(9), 1992.

Appendix B
Comparisons of Cytology Classifications

Comparisons of Cytology Classifications

Class	Traditional	Cervical Intraepithelial Neoplasia (CIN)	Bethesda System
I	Negative	n/a	Within normal limits
I	Negative (Inflammation Trich, Candida, Bacteria)	n/a	Within normal limits
II	Atypical cells Reactive atypia Atypical Repair	n/a	Other - Reactive Atypia- atypical Repair- atypical Metaplasia
II	Atypical cells (Cannot exclude dysplasia)	n/a	ASCUS - AGCUS* Herpes- atypical Metaplasia of undetermined significance
III	HPV (Flat condyloma)		Low grade Squamous Intraepithelial Lesion
III	Mild dysplasia	CIN 1 with or without HPV	
III	Moderate dysplasia	CIN 2 with or without HPV	High grade Squamous Intraepithelial Lesion
IV	Severe	CIN 3 with or without HPV	
IV	Carcinoma - in-situ		Squamous carcinoma
V	Squamous carcinoma		

* Glandular atypia - Class II or III

Source. Adapted from Valente and Schantz, April 1993.

Appendix C
Mississippi University for Women
Committee on Human Subjects in Experimentation
Letter of Approval

MISSISSIPPI UNIVERSITY FOR WOMEN
Columbus, MS 39701

Vice President for Academic Affairs
P.O. Box W-1603
(601) 329-7142

February 22, 1995

Ms. Deanna Mackie
c/o Graduate Nursing Program
Campus

Dear Ms. Mackie:

I am pleased to inform you that the members of the Committee on Human Subjects in Experimentation have approved your proposed research with the requirement that permission to conduct the survey and to review the records be obtained from any clinics and/or M.D.'s in advance.

I wish you much success in your research.

Sincerely,

Thomas C. Richardson
Vice President
for Academic Affairs

TR:wr

cc: Mr. Jim Davidson
Dr. Mary Pat Curtis
Dr. Rent

Appendix D
Memorandum of Agreement Concerning Research Study

Memorandum of Agreement Concerning
Research Study

Title of Study:

Incidence of Cervical Dysplasia in Women With and Without Cytology Suggestive of HPV

Name of Practice:

Study discussed with and explained to:

The nature and purpose of this study have been defined. I understand that all information will be kept confidential and that this institution may withdraw at any time during the data collection.

By _____
Physician

_____
Physician

_____
Researcher

Appendix E
Registration Slip

REGISTRATION SLIP PLEASE PRINT!

Your Name_____ Your Date of Birth___/___/___

Your Address_____
(Mailing Address) (City) (State) (Zip Code

Home Phone Number_____ Work Phone Number_____

Your Social Security Number_____ Husband's Name_____

Your Employer_____ Husband's Employer_____

Your Occupation_____ Husband's Occupation_____

Your next of kin (other than husband) and relationship to you_____

This relative's address_____ Their phone number_____

Who referred you to our doctors? (Please specify)_____

INSURANCE INFORMATION **If you have an insurance card, please let the receptionist copy it

Primary Insurance	Secondary Insurance
Insurance Co. Name_____	Insurance Co. Name_____
Insured's Name_____	Insured's Name_____
Insured's Social Security #_____	Insured's Social Security #_____
Policy or ID #_____	Policy or ID #_____
Group Number/Name_____	Group Number/Name_____
Benefits Phone Number_____	Benefits Phone Number_____
Pre-cert Phone Number_____	Pre-cert Phone Number_____
Mail Claims To:_____	Mail Claims To:_____
_____	_____

ASSIGNMENT OF BENEFITS/AUTHORIZATION TO RELEASE INFORMATION: I hereby authorize payment of insurance benefits payable to me but not to exceed the regular charges for the current year directly to Oxford OB/GYN Associates, P.A. I understand that I am financially responsible to Oxford OB/GYN Associates, P.A. for charges not covered by this authorization. I hereby authorize Oxford OB/GYN Associates, P.A. to release medical information for the purposes of filing insurance claims with my insurance company (companies).

_____ _____
(Patient's signature/Parent's signature, if patient is a minor) (Today's Date)

Billing Address(If different from Mailing Address)_____

_____

Appendix F
Patient Questionnaire

PATIENT QUESTIONNAIRE

Name_____ Date_____

During the last year, your life may have changed and this may affect your health. Please help us to provide the best health care for you by completing this short questionnaire.

	Circle one		If yes, please specify
Have you changed your occupation?	Yes	No	
Do you have any problems at home?	Yes	No	
Has there been any change in your relationship with your husband, partner, or boyfriend?	Yes	No	
Has there been a change in your periods?	Yes	No	
Date of your last period?			
Do you use a method of contraception?	Yes	No	Do you use it regularly?
If yes, what type? pills IUD diaphragm condoms natural/rhythm sponge spermicide other			Are you/your partner satisfied with this method?
Do you want any information about birth control?	Yes	No	
Date of your last Pap test?			
Do you have any questions about safer sex?	Yes	No	
Do you smoke cigarettes?	Yes	No	How many per day?
Do you use street drugs?	Yes	No	
Do you drink alcohol?	Yes	No	How often? How much?
Have you ever felt the need to cut down on your drinking?	Yes	No	
Are you exercising?	Yes	No	How often? What type?
Have you had any illnesses?	Yes	No	
Have you seen any of your other doctors recently?	Yes	No	
Are you taking any medicines now?	Yes	No	
Have you ever had a cholesterol test?	Yes	No	When?

Please answer if you are over 39:

Date of your last mammogram?_____

Date of your last stool test?_____

What brings you to our office today?

_____

_____

Do you have any questions, problems, or concerns that you would like to discuss with us today?

_____

_____

Appendix G
GYN Cytology Report Form

GYN CYTOLOGY REPORT

Patient:
Address:
Date of birth:
Age:
Sex:
Doctor:

Accession#:
Med Record#:
Social Security#:
Room#:

HISTORY / ADMITTING DIAGNOSIS

Anatomical Source:
LMP:
Number of Slides:
Clinical History:

Date of Specimen:
Date Received:
Date Reported:

SPECIMEN ADEQUACY:

DESCRIPTIVE DIAGNOSIS:

Appendix H
Pathology Report Form

PATHOLOGY REPORT

Patient:
Address:

Accession #:

Date of Birth:
Age:
Sex:
Physician:

Med. Rec. #:
Social Security #:
Room #:
Page: 1 of 1

History / Admitting Diagnosis

Date of Specimen:

Date Received:
Date Reported:

Clinical Data:

Postoperative
Diagnosis:

Anatomic Source:

GROSS DESCRIPTION:

A.

FINAL DIAGNOSIS:

A.

Appendix I
Data Collection Sheet and Raw Data with Code Descriptions

Code Descriptions

Rand#	Random number assigned to case to assure anonymity
RCE	Race
YOB	Year of Birth
AGE	Age at time of first ASCUS
ASCUS Date	Date of first ASCUS
ASCUS LMP	Date of last menstrual period at first ASCUS
HPV	Coded 1 if ASCUS suggestive of Human Papillomavirus Coded 0 if ASCUS not suggestive of Human Papillomavirus
WRT	Coded 1 if genital warts are present Coded 0 if genital warts are not present
SMK	Coded 1 if patient smokes Coded 0 if patient does not smoke
BCM	Records the birth control method used

OCP	Oral Contraceptive Pills
T	Tubal Sterilization
PM	Post-menopausal
X/UKN	None or unknown
NR	Natural/rhythm
D	Diaphragm
C	Condoms
N	Norplant

CND	Candida noted on cytology report Coded 1 if present
HSV	Herpes Simplex Virus noted on cytology report Coded 1 if present
GC	Gonorrhea Coded 1 if identified

BC	Bacteria noted on cytology report Coded 1 if present
CHL	Chlamydia Coded 1 if identified
BX Date	Date of colposcopically directed biopsy
LMP	Date of last menstrual period preceding biopsy
DX	Diagnosis coded 0 for negative biopsy Diagnosis coded 1 for dysplasia on biopsy
L/H	Coded 0 for low grade SIL Coded 1 for high grade SIL
BXH	Coded 1 for HPV on biopsy
BY	Coded 0 or 1 for physician identification performing biopsy
PG	Coded 0 for not pregnant at time of index smear Coded 1 for pregnancy
#AS	Number of abnormal cytology reports held by pathology laboratory including index smear before biopsy
ELT	Elapsed time in days between index smear and biopsy

Rand #	RCE	YOB	Age	ASCUS Date	ASCUS LMP	HPV	WRT	SMK	BCM	CND	HSV	GC	BC	CHL	BX Date	BX LMP	LD X	L/H	BXH	by	PG	#AS	ELT
49	b	64	30	05/03/94	40894	1	0	1	OCP						05/03/94	40894	0		1	1	0	1	0
194	c	62	31	04/05/94	120593	0	0	1	X			0			04/05/94	120593	0		1	1	1	1	0
191	c	61	32	04/14/94	33094	0	0	0	X						04/25/94	33094	0			1	0	2	11
114	c	57	36	01/12/94	120393	1	0	1	X	1	0				08/09/94	72894	0			1	0	1	209
179	b	54	39	08/15/94	80894	0	0	0	T						08/15/95	80894	1	0	1	1	0	1	365
102	b	60	34	08/22/94	72694	1	0	1	OCP				1		12/27/94		0		1	1	0	1	127
98	c	71	22	08/24/94	PP	1	0	1	OCP	0		0			01/11/95	122294	0		1	1	0	2	140
60	b	61	33	08/23/94	81594	1	0	0	T	0					02/08/95		0		1	1	0	2	169
63	b	68	26	08/29/94	80794	0	0	0	X						01/27/95	10695	0			1	0	1	151
185	c	48	46	09/22/94	90994	0	0	0	PM						02/13/95		0		1	1	0	2	144
92	c	75	18	09/22/94	90594	0	0	0	X						02/10/95	11495	0			1	0	2	141
99	c	43	51	09/26/94	91594	1	0	0	UKN						03/02/95		0		1	1	0	2	157
150	c	69	24	10/12/94	PP	0	0	1	T						12/02/94	112094	0		1	1	0	1	51
129	c	70	24	11/02/94	100194	1	0	1	NR	1	0				11/22/94	110894	0		1	1	0	2	20
139	b	65	29	11/14/94	90094	0	0	0	X	0	0				12/28/94		0		1	1	0	3	44
138	b	73	21	03/28/94	PP	0	0	0	T				1		12/08/94	112194	0			1	0	2	255
193	c	65	28	03/14/94		0	0	0	OCP						04/04/94		1	0	1	1	0	1	21
35	b	61	32	02/08/94	12994	0	0	1	OCP						03/08/94	30194	0		1	1	0	1	28
133	c	65	29	02/27/94	22095	0	0	0	OCP	0					03/30/95	22095	0		1	1	0	1	396
33	b	59	34	04/05/94	31694	1	0	0	OCP						03/27/95	22695	0			0	0	1	356
34	c	66	28	10/07/93	91093	0	0	0	OCP	1					02/15/95		0		1	0	0	2	496
188	c	64	30	06/02/94	52094	0	0	1	OCP				1		01/17/95		1	1	1	0	0	2	229
121	c	63	30	08/01/94	72694	0	0	0	OCP						08/31/94		0		1	0	0	2	30
165	c	56	38	08/18/94	80894	0	0	0	OCP						09/09/94		0			0	0	1	22
158	c	71	24	09/12/94	83094	1	0	0	OCP						10/06/94		0			0	0	1	24
113	c	73	22	05/05/93		0	0	0	OCP	1					10/04/94	91694	0		1	0	0	1	517
101	c	73	21	01/03/95	110094	0	0	0	OCP						03/09/95		0		1	0	0	1	65
50	a	54	40	02/20/95	20195	1	0	0	D						02/22/95	20195	1	0		0	0	1	2
59	b	64	30	02/22/95	20695	0	0	0	X				1		03/20/95		0		1	0	0	1	26
186	c	76	19	03/09/95		0	0	0	OCP						03/27/95		0			0	0	1	18

36	c	63	31	03/23/95		1	0	0	OCP				03/28/95		0		1	0	0	1		5
141	c	46	46	07/26/93	70293	0	0	0	X				09/21/94		0			0	0	1		422
97	c	74	21	06/16/94	52694	0	0	0	OCP			1	11/22/94	111594	0		1	1	0	1		159
126	c	74	21	09/22/94		0	0	1	OCP				03/28/95	31295	1	1	1	0	0	1		187
152	c	71	23	09/30/94	92094	0	1	1	C		1		1	10/12/94	92094	0		1	1	0	1		12
104	c	73	21	03/29/94	31094	1	0	0	OCP				11/04/94	100894	0		0	1	0	2		220
181	b	74	20	05/11/94		0	0	0	OCP				01/23/95	12095	1	0	1	0	0	1		257
83	c	70	24	01/25/94	11794	0	0	0	N	1			06/07/94	50794	0		1	1	0	1		133
110	b	68	26	06/08/94		1	0	0	OCP				02/01/95	10995	1	0	1	0	0	1		238
37	c	66	28	07/22/94	71394	0	0	0	OCP				01/13/95	10895	1	1	1	1	0	2		175
57	c	72	22	07/27/94	62894	0	0	0	OCP				12/13/94	112294	0		0	0	0	2		139
143	c	66	28	09/08/94	81594	1	0	0	C				01/25/95	123094	1	0	1	0	0	2		139
100	c	67	27	09/02/94	82494	1	0	1	OCP				12/22/94	121794	0		1	0	0	1		111
173	c	65	28	07/20/94		1	0	1	OCP				01/26/95		0		1	0	0	2		190
52	b	74	21	03/29/94	30194	0	1	0	X	1	1		10/11/94	62094	0		0	0	1	1		196
172	c	72	22	02/22/94		0	0	0	OCP				03/22/95		0		1	0	0	2		393
18	c	45	49	03/20/95	22395	0	0	0	PM				04/03/95	32195	0		1	0	0	1		14
131	c	65	29	12/27/94		0	0	0	OCP				04/04/95	31495	0		1	0	0	2		98
134	c	63	32	04/05/95	31695	0	0	1	T				04/24/95	41795	0		1	0	0	1		19
86	c	73	22	11/10/94	101194	0	1	0	C				04/26/95	32795	1	0	1	0	0	1		167
66	c	41	53	12/28/94	122594	0	0	1	PM				05/31/95		0		1	0	0	2		154
48	b	55	39	11/29/94	111094	0	0	0	T			1	05/03/95		1	0	1	0	0	1		155
46	c	77	17	09/28/94	90994	0	0	1	C				04/06/95		1	0	1	1	0	2		190
70	b	53	41	01/10/95	111694	0	0	0	X				02/14/95	111694	1	0	1	1	1	1		35
120	c	43	50	06/28/94	61394	0	0	0	T				11/22/94		1	0	1	0	0	1		147
184	c	71	22	07/25/94	71894	0	0	0	OCP	1			10/05/94		0		0	1	0	2		72
81	b	66	27	04/25/94		0	0	0	OCP				06/30/94		1	0	1	1	0	1		66
116	c	65	28	11/02/94	101294	0	0	0	OCP	1			11/28/94	101294	1	0	0	1	0	1		26