The Papanicolaou Smear: Its Value and Limitations

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Although the Papanicolaou (Pap) smear is one of the most effective screening tests ever invented for a common cancer, it remains an imperfect test. The technical shortcomings of the Pap smear have been compounded by the general public's unrealistically high expectations of the test's accuracy, underestimations of the importance of regular smears, and the actions within the medico-legal system. To remedy some of the technical shortcomings, the Bethesda System, which better reflects our current knowledge about cervical neoplasia, has been proposed to replace the old Papanicolaou classification system. Although standardized cytologic criteria may reduce interobserver variability, the false-negative rate of Pap smears is at least 5%, even in the best laboratories. No amount of training or experience with human observers can reduce the error rate to zero. Automated Pap screening holds the promise of higher sensitivity, but no instruments to date have been approved as a sole means of primary screening. The family physician can play a unique role in overcoming the limitations of the Pap smear by educating patients about the value and limitations of the test, instituting patient-specific treatment or follow-up of abnormal smears based on clinical and cytologic findings, and encouraging patients to get regular smears at intervals based on risk.

Key words. Pap smear; gynecology, cytology, limitations.
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An unknown Greek immigrant named George Papanicolaou arrived on Ellis Island on October 19, 1913. He had a medical degree and a doctorate in zoology, but was unable to find work in the United States. He finally accepted a job selling carpets at Gimbels department store in New York City. On his second day of work, he saw someone he knew and was so embarrassed that he quit and took a job in a laboratory at New York Hospital. In 1916, while conducting research on the menstrual cycle of guinea pigs, he discovered that he could predict the stage of the menstrual cycle by examining vaginal smears of the animals. Unlike humans, guinea pigs do not have cyclic bleeding. This was a breakthrough, he thought, because many guinea pigs were needlessly sacrificed at the wrong time in the cycle while trying to obtain eggs. Thus, the first Papanicolaou (Pap) smears were used to stage the guinea pig's menstrual cycle. In 1920, he began examining smears from surgical specimens of human cervical cancers, and found that he could predict the presence of human cervical cancer from cytologic smears. By 1928, he had enough data to present his findings at the third so-called Race Betterment Conference in Battle Creek, Michigan. His findings were not well received; skeptics thought they were absurd. Undaunted, he continued his studies, and in 1942, published his famous monograph *Diagnosis of Uterine Cancer by the Vaginal Smear*,[1] which ushered in the era of modern cytopathology.

In the years since the publication of his monograph, knowledge of cervical neoplasia has greatly advanced. The original Papanicolaou classification is no longer consistent with this new knowledge. The expectations of society for what was once considered a screening test have greatly increased. The false-negative Pap smear has been trampled by the press in a series of exposés.[2] This paper is a review of the role of the Pap smear, the evolution of the new classification system based on current understanding of the neoplastic process, the value of the Pap smear, and its limitations.

Cervical Neoplasia and the Pap Smear

Human papillomavirus (HPV) has long been suspected to be the causative agent of cervical dysplasia and carcinoma.

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Recent epidemiological studies have proved that HPV is the cause of the great majority of cervical dysplasias,[3] and there is strong evidence that most cervical cancers are preceded by HPV-induced dysplasia.[4] For many reasons, it is difficult to determine the transit time between the earliest dysplasia and invasive carcinoma. Sampling errors occur in both cytologic and surgical studies. Biopsy removes some of the abnormal tissue and changes the natural history of the disease. Advanced lesions are seldom left untreated. In a recent review of the literature that critically examined transit times and progression rates,[5] however, reported transit times ranged from less than 1 year to more than 10 years. Moreover, many cases did not progress. Mild dysplasia regressed in 57% (range, 7% to 76%) of cases, moderate dysplasia in 43% (range, 16% to 60%), and severe dysplasia in 32% (range, 0% to 50%). Mild dysplasia progressed to invasive carcinoma in 1% of cases (range, 0% to 10%), moderate dysplasia in 5% (range, <1% to 10%), and severe dysplasia or carcinoma in situ in 12% (range, 0% to 75%).

The goal of the Pap smear is to screen for cervical dysplasia before it progresses to invasive carcinoma. At one time, a Pap smear was recommended annually for all adult women. With the knowledge that the transit time of most cases of dysplasia is long and that many actually regress, the recommendations for the frequency of smears have changed. In 1987, the American Cancer Society issued the following statement: *All women who are or have been sexually active or have reached age 18 should have an annual Pap smear and pelvic examination. After a woman has had three or more consecutive satisfactory normal examinations, the Pap test may be performed less frequently at the discretion of her physician.*

The United States Preventive Services Task Force recommends less than annual examinations following two consecutive annual negative Pap smears. Screening in Great Britain, Denmark, and Australia is performed every 3 years. The screening interval for an individual patient is left to the discretion of the physician, who must take into account such factors as history of previous abnormal Pap smears, reliability of the patient, and risk factors for HPV infection. There have been some cases of invasive cervical cancer following recent true-negative Pap smears.[6] These may represent cases of rapidly progressive disease or sampling error. Thus, it would seem prudent to advise patients with risk factors for HPV infection to have a Pap smear more frequently than every 3 years. That is, high-risk groups may benefit from more frequent screening.[7] Realistically, it may be difficult to determine who is really at high risk. There are no standard recommendations on the frequency of screening in high-risk groups or even on which epidemiologic factors would place a patient in such a high-risk group.

Classification Systems

The original Papanicolaou classification system consists of five classes numbered from I to V: class I, normal; class II, benign atypia; class III, suggestive of malignancy; class IV, strongly suggestive of malignancy; and class V, consistent with malignancy.[8] While this system is adequate for differentiating benign from malignant, it is inconsistent with our current understanding of the dysplasia-carcinoma process. Laboratories tried to incorporate the concept of dysplasia into the Papanicolaou system, but the result was inconsistent assignment of meaning to each class. Interlaboratory comparison was impossible. In addition, there was no tissue equivalent for classes II through IV.

To alleviate some of the shortcomings of the Papanicolaou numerical system, some laboratories adopted the dysplasia-carcinoma system, while others used the cervical intraepithelial neoplasia (CIN) system. The dysplasia-carcinoma system reports abnormal Pap smears in a manner similar to the classifications on cervical biopsy: mild dysplasia, moderate dysplasia, severe dysplasia, carcinoma in situ (CIS), and squamous cell carcinoma. This classification system has the advantages of being directly comparable to tissue biopsy and being well understood by clinicians and pathologists. The CIN system is somewhat similar to the dysplasia-carcinoma system: CIN I is mild dysplasia; CIN II is moderate dysplasia; and CIN III combines severe dysplasia and carcinoma in situ. Pathologists cannot reliably differentiate severe dysplasia from CIS, even with a biopsy specimen[9]; CIS implies inevitable invasion without treatment, whereas severe dysplasia may regress. Since these were not easily differentiated, they were combined as CIN III.

Despite the advantages of the new classification systems, there were still many problems because many laboratories continued using the old Papanicolaou classes. The diagnosis of moderate dysplasia or CIN II had much interobserver variability, and there was a persistent problem with class II Pap smears[10] because this classification served as a heterogeneous catchall that contained both reactive and preneoplastic lesions. The diagnosis of class II offered little guidance to the clinician. These shortcomings led to a meeting of clinicians and laboratorians sponsored by the National Cancer Institute in 1988 and again in 1991 in Bethesda, Maryland.[11,12] The result of the meetings was a series of guidelines and recommendations that became known as the Bethesda System. In the words of the National Cancer Institute: *The groups of the Papanicolaou system do not reflect the current understanding of cervical neoplasia and the Papanicolaou classes do not have an equivalent in tissue diagnostic terminology.* The Bethesda System was designed to bring uniformity into the

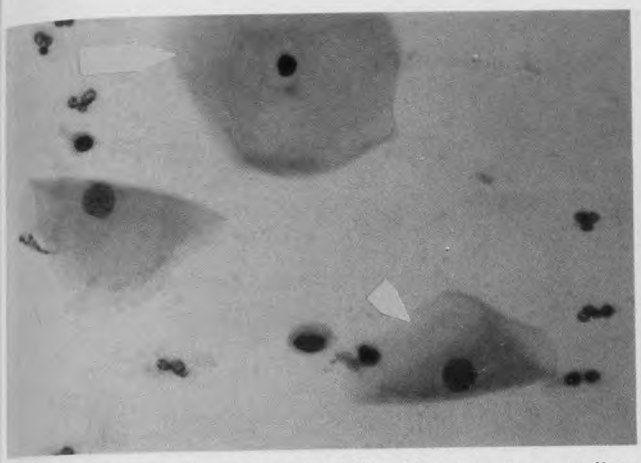

Figure 1. Normal Pap smear (×400). The two intermediate squamous cells have larger, open nuclei (short arrows) and a superficial cell has a smaller, darker nucleus (long arrow). Normal squamous cells are large and polygonal. The nuclear/cytoplasmic ratio is low. Intermediate cells are found in the presence of progesterone or low level estrogen stimulation. They are the most common cells found in normal women of childbearing age. Increased superficial cells are found with high levels of estrogen stimulation, such as occurs at ovulation.

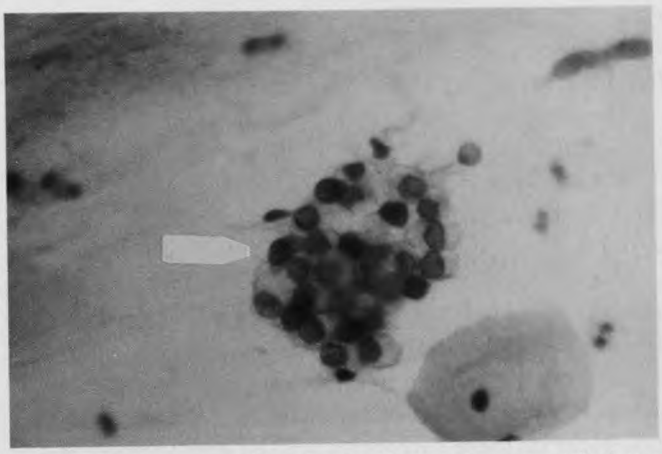

Figure 2. Normal endocervical cells in a honeycomb-shaped group (arrow) next to a larger superficial squamous cell (×400). The endocervical cells are much smaller than squamous cells and have a cuboidal to columnar shape. There is clear mucus in the cytoplasm. The presence of two or more well-preserved groups of endocervical cells implies adequate sampling of the squamocolumnar junction.

reporting of cervical Pap smears and to implement a system that was congruent with the current understanding of the neoplastic process. It also represented an attempt to decrease interobserver variability by decreasing the number of diagnostic categories. The Bethesda System has now been adopted by most laboratories in the country.

The Bethesda System

There are three parts in a Pap smear reported under the Bethesda System: statement of adequacy, general categorization, and descriptive diagnoses. A recommendation may be appended to an abnormal smear report. In each of the three parts, further statements are made to further classify the lesion.[13] Most Pap smears are satisfactory for evaluation (Figures 1 and 2).

One of the greatest advances of the Bethesda System is the statement of adequacy. A smear may be satisfactory for interpretation or satisfactory but limited by one or more factors. Interpretation is less precise if, for example, there is excessive obscuring blood, inflammation, poor fixation, or scant cellularity. If the adverse factors are severe, the smear may be deemed unsatisfactory for interpretation (Figure 3). The lack of endocervical cells, which may imply suboptimal sampling of the transformation zone in a premenopausal woman who still has a cervix, will cause a smear to be judged satisfactory but limited, rather than unsatisfactory.[14] The clinical management of a satisfactory but less-than-optimal smear depends on the clinical context and the current and previous cytologic findings. Follow-up differs depending on the clinician's philosophy. For example, if a woman who has had normal satisfactory Pap smears in the recent past now presents with a satisfactory but limited smear because of inflammation, many physicians may choose to continue screening at routine intervals rather than repeat the Pap smear following treatment. On the other hand, if a similar normal but limited smear is reported in a woman in whom a dysplastic process has been recently diagnosed, the report may be interpreted as a possible false negative, and appropriate follow-up instituted. Before the Bethesda System,

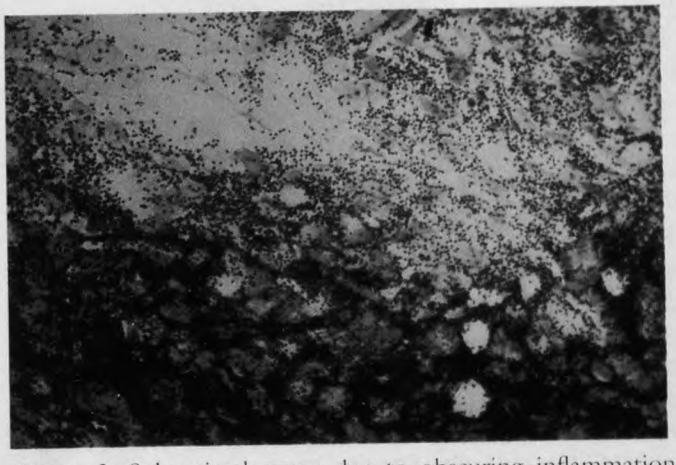

Figure 3. Suboptimal smear due to obscuring inflammation (×100). The small, dark nuclei of the polymorphonuclear neutrophils nearly totally obscure the underlying larger squamous cells. If 50% to 75% of the slide is obscured, the smear is classified as adequate for evaluation but limited by obscuring inflammation. If more than 75% of the slide is obscured, the smear is unsatisfactory.

no statement about adequacy was made. Thus, some apparently normal smears probably should have been considered unsatisfactory in certain clinical situations.

The general categorization is a statement of whether the smear is normal or abnormal. As many as 90% of Pap smears are within normal limits or show benign cellular changes.[15] If a smear is abnormal, the general categorization refers the clinician to the descriptive diagnoses.

The descriptive diagnoses are the "heart" of an abnormal Pap smear report. There are several general categories of descriptors: infection, reactive and reparative changes, epithelial abnormalities, nonepithelial malignant neoplasm, and hormonal evaluation (vaginal smears only). Most of these categories are self-explanatory. Reactive and reparative changes refer to minor epithelial changes that are not normal but are not considered preneoplastic. These do not require further workup. Most significant abnormalities fall into the category of epithelial abnormalities.

Squamous Epithelial Abnormalities

The most common significant lesions detected by the Pap smear are squamous abnormalities of the cervix. The Bethesda System replaces all previous classification systems with a completely new one. For squamous lesions, the descriptors are atypical squamous cells of undetermined significance (ASCUS), low-grade squamous intraepithelial lesion (LGSIL), high-grade squamous intraepithelial lesion (HGSIL), and squamous cell carcinoma (SCC).

The descriptor ASCUS refers to cells that are more abnormal than cells seen in reactive or inflammatory lesions, but do not fulfill all the criteria for LGSIL or HGSIL (Figure 4). Between 10% and 45% of these cases will turn out to be SIL on follow-up after 6 to 12 months.[15] The SIL may be high grade, especially if atypical metaplastic cells were seen.[16] Although a statement may be made on which process is favored, there is much overlap. According to the interim guidelines developed in 1992 by the National Cancer Institute (NCI),[17] a patient with ASCUS and severe infection should have the smear repeated in 2 to 3 months following treatment of the infection in order for the reparative process to subside. When ASCUS is found in a postmenopausal woman not taking hormones, she should have a smear following topical estrogen because parabasal cells seen in atrophic smears may be difficult to distinguish from cells arising from SIL. Patients with ASCUS, favor reactive, or ASCUS not otherwise classified, should be followed with Pap smears every 4 to 6 months for 2 years. Routine screening may be resumed after three consecutive negative smears. ASCUS, favor SIL, should be followed like LGSIL. Persistent ASCUS, ASCUS in a high-risk patient, or ASCUS

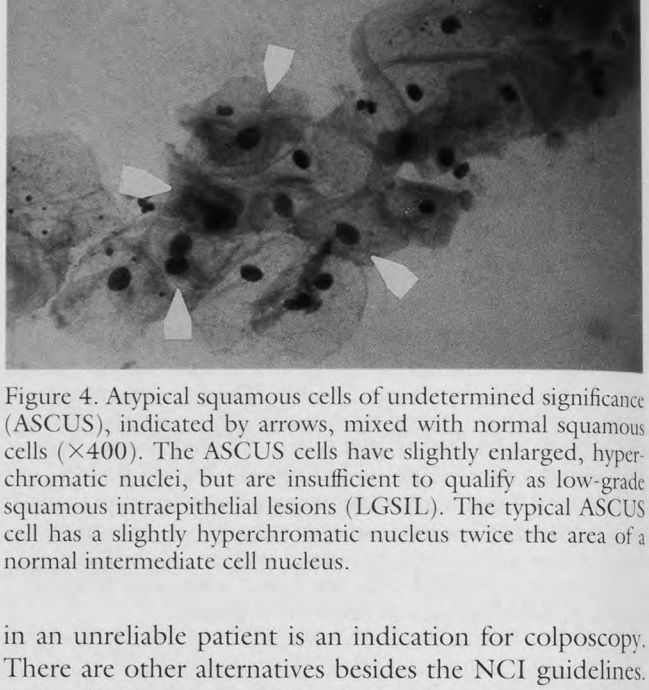

Figure 4. Atypical squamous cells of undetermined significance (ASCUS), indicated by arrows, mixed with normal squamous cells (×400). The ASCUS cells have slightly enlarged, hyperchromatic nuclei, but are insufficient to qualify as low-grade squamous intraepithelial lesions (LGSIL). The typical ASCUS cell has a slightly hyperchromatic nucleus twice the area of a normal intermediate cell nucleus.

in an unreliable patient is an indication for colposcopy. There are other alternatives besides the NCI guidelines. Some clinicians may go directly to colposcopy and biopsy following a cytologic diagnosis of ASCUS, since the histologic examination may be more advanced than cytologic examination. At best, management remains controversial.

The descriptor LGSIL encompasses both mild dysplasia and condyloma acuminatum (Figures 5 and 6). The combination of these two lesions into one diagnostic category is a controversial aspect of the Bethesda System.

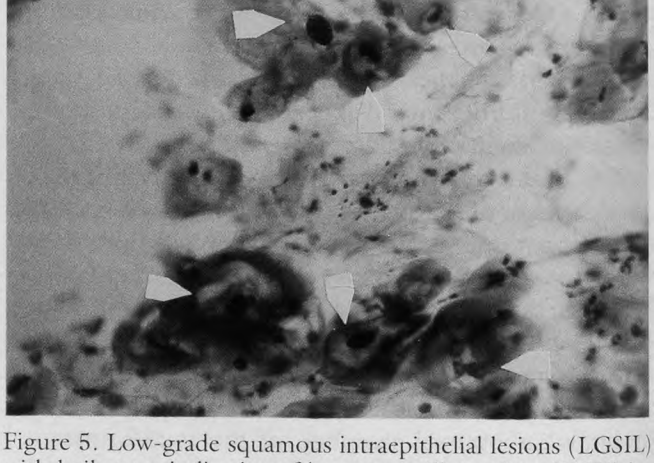

Figure 5. Low-grade squamous intraepithelial lesions (LGSIL) with koilocytes indicative of human papillomavirus (HPV) infection (arrows) (×400). The infected cells have enlarged, hyperchromatic, wrinkled nuclei and prominent clear perinuclear halos. Many years ago, findings such as these were termed koilocytotic atypia. Today, we know these cells are highly specific for HPV infection.

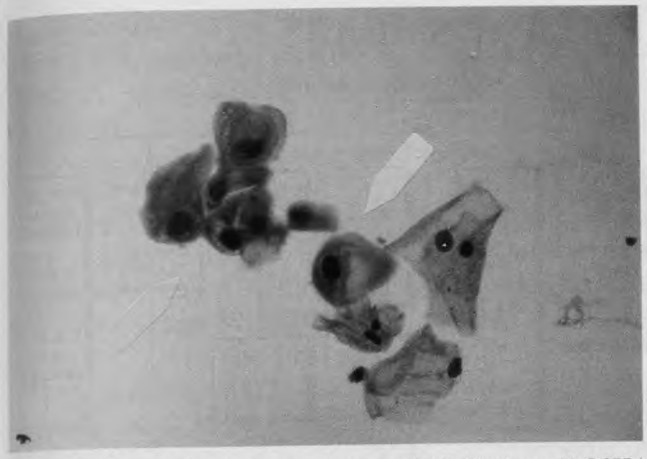

Figure 6. Low-grade squamous intraepithelial lesions (LGSIL) (arrows) (×400). The nuclei of the abnormal cells are enlarged and hyperchromatic. The nuclear/cytoplasmic ratio is increased, but the cells still have a polygonal shape. The nucleus of a cell in LGSIL is typically at least three times the area of the nucleus of a normal intermediate cell.

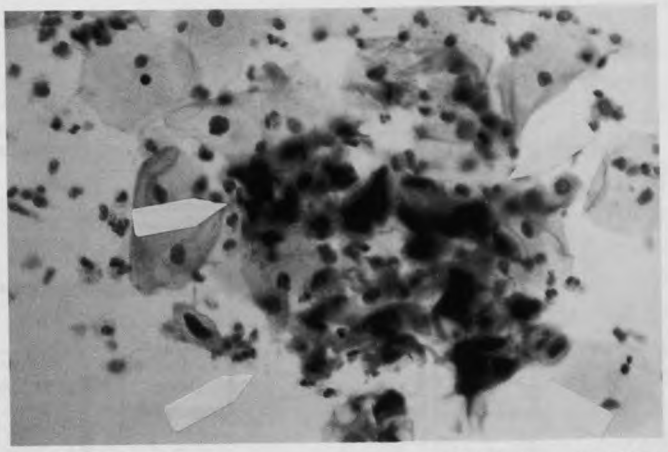

Figure 7. High-grade squamous intraepithelial lesions (HGSIL) (arrows) (×400). The nuclei of the abnormal cells are even larger and more hyperchromatic than those seen in low-grade squamous intraepithelial lesions (LGSIL). The nuclei occupy a large part of the cytoplasm. The cells have an oval or metaplastic shape rather than the normal polygonal shape.

The rationale for combining them is the similarity in natural history and treatment. The treatment and follow-up of these patients is controversial. The interim guidelines allow follow-up Pap smears every 4 to 6 months as one option. Colposcopy and biopsy are indicated for persistent LGSIL. Routine screening can be reinstituted following three consecutive negative smears. As previously indicated, most lesions either remain stationary or regress. Another alternative is to proceed directly to colposcopy and biopsy because the lesion may be more advanced than is indicated by the Pap smear.

Moderate dysplasia, severe dysplasia, and carcinoma in situ are included in HGSIL (Figure 7). These are serious lesions that require biopsy and treatment. Thus, they are combined into one diagnostic category. Patients with these lesions may have had LGSIL that has progressed, or may not have had regular Pap smears, resulting in late detection of the lesion. This broad approach to categorization leads to fewer discrepancies in reporting.

The diagnosis of SCC represents failure of a Pap screening program (Figure 8). In the majority of cases, it represents the failure to get regular Pap smears.[18] Although microinvasive or invasive squamous cell carcinoma can often be successfully treated, the 5-year survival ranges from 80% to 90% in stage I to 10% to 15% in stage IV.[19]

Glandular Epithelial Abnormalities

Glandular lesions of the cervix are less common than squamous lesions. The cytologic abnormalities are much more difficult to recognize, even for cytopathologists. The Bethesda System recognizes atypical glandular cells of undetermined significance (AGCUS) and endocervical adenocarcinoma as diagnostic categories. There is no category called "endocervical gland intraepithelial lesion" analogous to squamous lesions. The microscopic criteria for diagnosis of glandular lesions are not as clear-cut as for squamous lesions. The workup and management of glandular lesions lack consensus. The NCI guidelines recommend cone biopsy if adenocarcinoma in situ is suspected. A finding of AGCUS should be followed by a Cytobrush sampling of the endocervical canal or by endocervical curettage, depending on the history and physical findings;

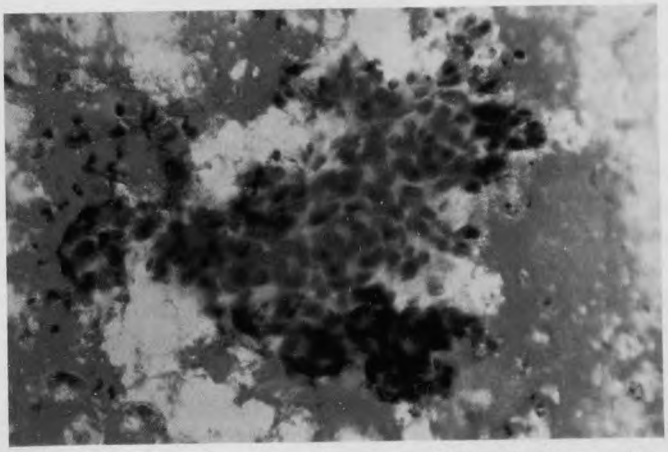

Figure 8. Squamous cell carcinoma (×400). The large, pleomorphic group of malignant cells have hyperchromatic, irregular nuclei. The nuclei are more irregular than those seen in high-grade squamous intraepithelial lesions (HGSIL), but the nuclear/cytoplasmic ratio is actually lower. The necrotic blood in the background, called tumor diathesis, is suggestive of an invasive lesion.

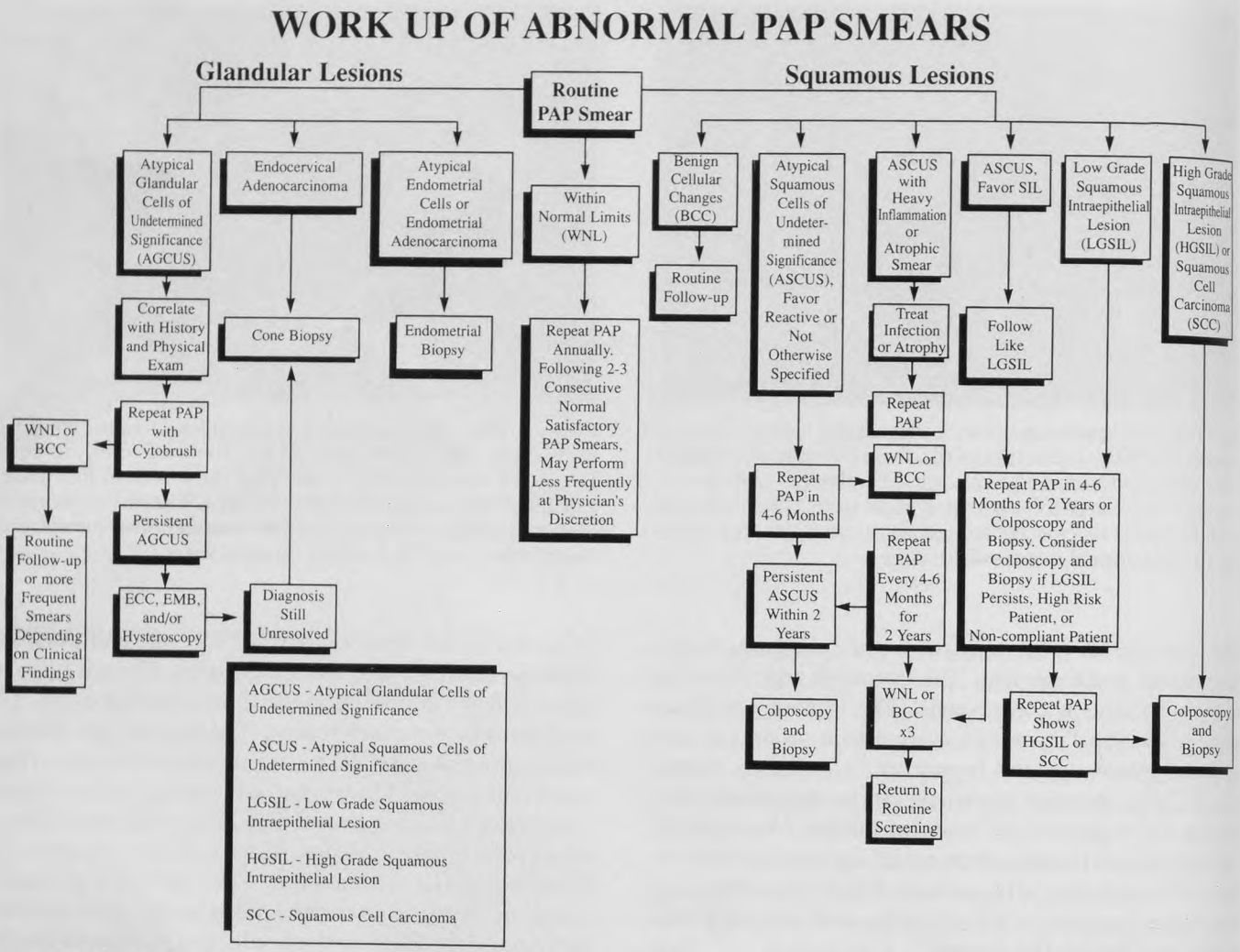

Figure 9. Algorithm for the management of abnormal cervical cytologic findings. ECC denotes endocervical curettage; EMB, endometrial biopsy.

however, they are by no means the only accepted means of follow-up.

The Pap smear plays little or no role in the primary screening of endometrial or ovarian cancer. It is very insensitive. Not uncommonly, cytologically benign endometrial cells are seen incidentally on Pap smears of asymptomatic postmenopausal women. The NCI guidelines do not address this issue. It is unclear what workup, if any, these women need. Some clinicians may perform an endometrial biopsy, whereas others may choose to just follow the patients.

An algorithm for the workup of abnormal cervical cytology, based mostly on NCI recommendations, is presented in Figure 9. There are many acceptable alternatives to these guidelines, especially in the controversial areas of ASCUS and LGSIL management. In addition, some clinicians may use other triage tests such as cervicography, cervical acetic acid wash, or HPV testing. Certainly, factors such as previous Pap history, epidemiologic risk factors, comfort level of the patient and clinician, and reliability of the patient may affect the workup and management of the patient with an abnormal Pap smear. The family physician is in a unique position to weigh all these factors since he or she usually has a long and ongoing relationship with the patient.

The Value of the Pap Smear

The Pap smear is one of the most effective screening tests for a common cancer ever invented. In developed countries with screening programs, cervical SCC is the 10th most common cancer among women. In third world countries without such programs, it is the most common malignancy among women.[20] Following the adoption of a Pap screening program in the 1960s, the incidence of

SCC in Iceland and the Nordic countries fell by 15% to 60% in 1975, compared with the incidence in 1955.[21] In Canada, an intense screening program in 1966 correlated significantly with a decreased incidence of SCC in 1970 to 1972, compared with that of 1960 to 1962.[22] On the other hand, the incidence of SCC in Norway, which did not adopt a nationwide Pap screening program in the 1960s, rose 28% between 1955 and 1975.[21] In 1961, 30% of US women had at least one Pap smear test. The incidence of SCC was 32.6/100,000. In 1987, 87% of US women had at least one Pap smear test. The incidence of SCC was 8.3/100,000.[23] These and many other epidemiologic studies point to the efficacy of the Pap smear in reducing the incidence of squamous cell carcinoma in screened populations, and it is perhaps the only known effective screening test for cancer today.[24]

The Limitations of the Pap Smear

An ideal screening test should have 100% sensitivity. It should detect all patients who have the disease. Specificity, or the ability to correctly classify patients without disease, is less important, although a false positive could lead to patient anxiety and additional diagnostic procedures. Few screening tests are 100% sensitive, and the Pap smear is no exception. A recent study conducted by the College of American Pathologists defined the limits of the Pap smear[25]: if a positive smear is defined as LGSIL or worse, the false-negative rate is 5%. If a positive smear is defined as ASCUS or worse, the false-negative rate is 12.5%. These recent findings are in accord with those of other studies. Koss[26] recently found a false-negative rate of 2.6% to 5.1% in a retrospective review of his laboratory findings. Krieger and Naryshkin[27] suggest that it may not be possible to reduce the false-negative percentage below 5%. These errors refer to false negatives of laboratory origin only; they do not include false negatives due to sampling error. The most common cause of a laboratory-generated false negative is a smear with a few poorly preserved atypical cells that were either overlooked or misinterpreted.[28] It would be impossible to detect such a small number of difficult-to-interpret cells in the time usually allotted to screen a slide.[28] Such errors, although often unavoidable, may lead to litigation. Plaintiffs' experts are often able to "treasure hunt" slides previously diagnosed as normal in search of "litigation cells."[29,30] Most cases with so-called litigation cells will be diagnosed as within normal limits when submitted for blind screening to another laboratory along with the regular workload.[31] Thus, plaintiffs' attorneys have been successful in arguing for zero tolerance for error, even though this is an impossible standard to achieve.

Perhaps the best protection against the inevitable false-negative Pap smear with current technology is a Pap smear test at regular intervals. It is possible for a woman with a significant lesion to have had one or more recent Pap smears falsely interpreted as normal, given the limitations of the test. Given the long preinvasive phase of cervical SCC, however, it is statistically unlikely that a significant lesion will be missed on a Pap smear at every screening opportunity. The patient must have regular Pap smear tests at intervals based on risk. Again, the family physician plays a crucial role in educating the patient about the need for regular smears and the limitations of the test. This cannot be overemphasized.

Even when a significant abnormality is recognized on a Pap smear, what the patient really has may not be the same as the cytologic diagnosis. Intraobserver variability, both overdiagnosis and underdiagnosis, is the main cause of misdiagnosis[32] and occurs among all observers, irrespective of the number of years of experience performing cytologic examinations. Interobserver variability also contributes to misdiagnoses, although this is influenced by the number of years of experience.[32] Sampling error both in cytologic examination and biopsy contributes to discrepancies between cytologic and histologic diagnosis. A recent study showed that only 50% of cases interpreted as LGSIL by cytologic examination could be confirmed on biopsy, and 11% were actually HGSIL.[33]

Leopold Koss, the best-known living cytopathologist today, summarizes the limitations of the Pap smear succinctly[34]: *In my experience, no laboratory can be expected to accurately and reproducibly recognize the atypical smear.*

Challenges for the Future

Despite the limitations of the Pap smear, it is still an excellent test. Challenges for the future include improving the test, educating clinicians and patients about its limitations, and developing strategies to overcome these limitations.

Automated Pap smear screening is one of the hopes for increasing the sensitivity of this test. Computer-assisted screening already exists in hematology. Peripheral blood smears are examined by computer-based image analysis, which is capable of recognizing abnormal cells. Normal smears are sent out without further workup, while apparently abnormal smears are flagged for examination by human observers. In cytologic examinations, a semiautomated screening technology called PAPNET is under development.[26] It uses neural networks, a type of artificial intelligence, to recognize and photograph abnormal cells. These photographs are then reviewed by human observers. In August 1995, a Food and Drug

Administration advisory panel recommended for approval the use of PAPNET in a quality-control mode (rescreening of apparently normal smears).[35] It has not yet been approved for primary screening.

Testing for HPV offers another potential means of increasing the sensitivity of detecting preneoplastic lesions. Since it is widely accepted that HPV causes most cases of dysplasia and cervical carcinoma, it would seem reasonable that a technology more sensitive than a Pap smear in detecting HPV infection would be efficacious. The polymerase chain reaction is a new technology that can detect small quantities of DNA by making many copies of the target sequences in an amplification process. Detection of HPV is not currently recommended as a primary screening modality, however, because of such observations as HPV-negative carcinomas, changing viral subtypes, ubiquity of the virus, unidentified subtypes, and lack of evidence that carriers of high-risk subtypes will necessarily develop a significant lesion.[36]

Clinicians and patients expect the Pap to be a perfect test: a false negative must mean someone made a mistake. In truth, false negatives are inevitable, no matter how experienced the observer. There has been a recent proposal to append the false-negative rate at the end of all Pap smear reports.[37] A Pap smear program is really a public health measure: it makes the promise of reducing the incidence of cervical squamous cell carcinoma in the population, but it makes no promise to detect all abnormalities in all women.[38] Clinicians and patients must understand that in order to be effective, Pap smears must be taken at regular intervals, with the actual interval dependent on the degree of patient risk. The media have done little to spread this truth; they have actually done the opposite by broadcasting exposés. Little is said of the inherent error rate of the test or of the responsibility of the patient to obtain regular smears. More frequent smears would reduce the rate of false negatives, but this too has limitations. Annual Pap smears would result in one-half the false-negative rate of those performed every 4 years but at four times the cost.[39] How much are we willing to pay?

The federal government has taken a keen interest in the operation of laboratories that screen Pap smears. The Clinical Laboratory Improvement Act of 1988 (CLIA '88) was the federal government's strategy to improve the quality of Pap diagnoses. This law limited the number of slides that could be screened per day, mandated continuing education, regulated the review of abnormal smears, and instituted a rigorous testing program. Although well intended, the result of CLIA '88 was a rapid rise in the cost of a Pap smear. This cost increase may cause some patients to have fewer Pap smears, as predicted by economic theory. Even if regulation increased the quality of interpretations, the decrease in number of smears performed may result in a greater number of undiagnosed cases of cervical neoplasia.[40] This is ironic considering that the patients least able to afford regular Pap smears and most sensitive to price increases are the population who are at increased risk for cervical neoplasia.

Conclusions

Despite its flaws, the Pap smear is still an excellent screening test if we keep in mind its value and limitations. The family physician has the dual role of being both advocate and educator to the patient. He or she must encourage the patient to get regular smears at intervals based on risk and to educate her on the limits of such testing. The patient also plays a significant role in this partnership. She must understand that no medical test is perfect and that there are things that she can do to minimize errors that could have clinical significance. If a strong alliance between physician, patient, and laboratory can be formed, based on realistic expectations of the Pap test, perhaps the negative sensationalism fostered by the media will take on much less significance.

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