Health Canada Santé Canada

Programmatic Guidelines for Screening for Cancer of the Cervix In Canada

Society of Canadian Colposcopists
Société Canadienne des Colposcopistes

The College of Family Physicians of Canada
Le Collège des médecins de famille du Canada

CANADIAN SOCIETY OF CYTOLOGY
SOCIÉTÉ CANADIENNE DE CYTOLOGIE

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The Society of Gynecologic Oncologists of Canada
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CERVICAL CANCER PREVENTION NETWORK

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Preamble

In 1976, a report was published on behalf of the Task Force on Cervical Cancer Screening under the principal authorship of Dr. Walton. The "Walton Report" has it has become known, has received citation internationally as well as in Canada. It was recognized that cervical cancer was a potentially preventable disease through screening and early detection. The essence of this report stated that all women who had ever had sexual intercourse were at risk for the development of cervical cancer and that only through organized screening programs with appropriate information systems support and programs of quality assurance would the burden of this disease be reduced further in Canada. Nonetheless, as so eloquently described by Dr. Marsha Cohen in a recent edition of the Canadian Medical Association Journal (1997), "There is no simple route to the prevention of cervical cancer."

Since the Walton Report, another Task Force Report was published in 1982 and a further Workshop convened in 1989 in order to document progress and facilitate new strategies for implementation. Interchange '95 was a further attempt to facilitate implementation plans at a provincial/territorial level. From this workshop in 1995, arose the concept of a Cervical Cancer Prevention Network that would serve as a catalyst for each of the jurisdictions in Canada. The purpose of the Network was articulated as "to foster the development of provincially based organized quality screening programs in Canada" and thereby reduce the incidence and mortality of cervical cancer. Three major outstanding issues were identified by the participants as priorities for further development if this goal was to be attained. These included quality management, information systems and public awareness and recruitment strategies. To address each of these issues, a working group was created with the mandate to provide a strategy to be made available to all Provinces/Territories for the purpose of implementing a programmatic approach to this problem. This document represents the product of the Quality Management Working Group.

This Working Group was comprised of representatives from each of the professional societies most committed to assuring that quality management guidelines were in place before any organized screening programs were implemented. The guidelines presented reflect the opinion and expertise of the contributing societies with the formal endorsement of same. These guidelines are intended to be used by health care personnel responsible for programs of population health. They are distinct from the definition of clinical practice guidelines as developed by the Canadian Medical Association to assist individual practitioners in patient care.

This document is not intended to stand apart from organized screening programmes, nor is it intended to replace the practitioner's judgement. It is intended to act as a tool, to provide guidance regarding the process and practices associated with the prevention of cervical cancer from an early detection perspective.

Since this document was written, it became clear that there was more than simply the process at issue. Ongoing and appropriate communication with the patient about what tests and procedures are being discussed and carried out is essential at all stages. Further, there are emerging issues which will continue to challenge the wisdom within these pages, e.g., recruitment of "hard-to-reach" women and Human Papillomavirus. It is our hope that this document will be updated on a regular basis and will be accompanied by other documents relevant to reducing the incidence and mortality of cervical cancer.

Acknowledgements

There are many people who we would like to thank for contributing to this project. Most important are the individual members of the Quality Management Working Group who were willing to take time from their busy schedules to share their expertise and without whom the Guidelines could not have be written.

We would also like to gratefully acknowledge the tireless drafting and re-drafting of the document by Dr. Jean Parboosingh and the leadership and wit of Dr. Gavin Stuart in chairing the Working Group. Finally, we would like to thank Ms. Suzanne Inhaber for facilitating and coordinating the development process for the Guidelines, and Dr. Michel Fortier for proof-reading and editing the French translation.

Contents

Tables

Figures

1.0 INTRODUCTION

The intent of this document is to provide systematically-developed statements to help physicians and patients make decisions about appropriate health care for specific clinical circumstances.

The Philosophy and Ethics embedded in the Canadian Medical Association's Guidelines for Canadian Clinical Practice Guidelines (Canadian Medical Association, 1994) include the following statements:

- The goal of clinical practice guidelines should be to improve quality of health care.
- Clinical practice guidelines should be sufficiently flexible to allow patients and physicians to exercise judgment when choosing among available options.
- Clinical practice guidelines should enable informed decision making by patients and physicians by enhancing professional learning, patient education and patient-physician communication.

These goals are echoed in this document which will also provide background information on why such guidelines are necessary in the area of cervical cancer screening at this time in Canada and will be relevant for health professionals at all points of the cervical screening pathway from recruitment to follow-up for treatment. These guidelines once adopted by practicing physicians can then be used to assess and manage the quality of care provided within an organized screening program.

It is recognized that these practice guidelines will form only one component of a quality management program of an organized screening program. Other components, such as recruitment strategies and information systems, require their own quality management program.

The following guidelines incorporate the existing approaches and documentation on practice and education of the relevant Canadian specialties where available and which are referenced.

1.1 Background and History of Cervical Screening in Canada

Cervical cancer is one of the most preventable cancers; the Papanicolaou (Pap) smear test has been used to screen for pre-cancerous lesions in asymptomatic women for the past 50 years. In Canada, as early as 1973, the Conference of Deputy Ministers of Health explored the need for comprehensive screening programs for cancer of the cervix. In 1976, the Walton Task Force recommended that health authorities support the development of cervical cancer screening programs and that all women be encouraged to participate (Walton, 1976). In 1980 a survey assessing the impact of the Task Force concluded that, the recommendations had not been, by and large, implemented at the provincial level (Kassirer, 1980). In response to this and concerns about the significance of new data, changing sociosexual patterns and wide variation in the implementation of the 1976 recommendations, the Task Force was reconvened in 1980 (Walton, 1982). Recommendations made in 1982 related to the frequency of screening, laboratory

quality control and follow-up mechanisms. Measures to improve the quality and sensitivity of screening programs, recruitment of women never screened and the development of government-sponsored registries were seen as essential components of an effective system and as potentially more effective than attempts to increase the frequency of screening.

In 1989, a National Workshop on Screening for Cancer of the Cervix reviewed the 1982 recommendations on screening for cancer of the cervix and recognized that programs in Canada were still not fully effective: not all women at risk were being screened; some physicians had not acquired the necessary skill to take satisfactory smears; some laboratories were too small to provide adequate experience for staff and adequate quality control; and some women with detected cytologic abnormalities were receiving inadequate follow-up and management (Miller, 1991). Conversely, some women were being screened too frequently, resulting in inappropriate use of resources. Recommendations reiterated the need for an organized approach and addressed the following issues: the frequency of screening; the management of abnormalities; information systems; training and quality control requirements for laboratories and programs. The recommendations were accepted by the Conference of Deputy Ministers of Health in November, 1990, who requested that a report of a regular review of developments be made to them on a periodic basis.

The Society of Obstetricians and Gynaecologists of Canada, the Gynaecologic Oncologists of Canada and the Society of Canadian Colposcopists supported the development of formal screening programs. The recommendation with respect to a screening interval of 3 years concerned these groups in the absence of adequate information systems and high-quality laboratory services; also of concern was the recommendation for repeat smears without colposcopy for low-grade squamous intraepithelial neoplasia. These groups suggested that until patient information systems and high-quality laboratory services are in place, annual screening of sexually active women should continue to be the standard of practice (Stuart, 1991).

As a follow-up to these activities supported by Health Canada and to review the situation within the provinces with respect to the development of organized screening programs, another workshop, Interchange '95, was held in 1995 (Interchange '95, 1995). The purpose of this Workshop was not to make recommendations but to identify whether the previous recommendations were still relevant, and, if so, to identify the barriers to implementing these recommendations and the best approaches to overcoming these barriers. The Workshop focused on three specific but interrelated components of a comprehensive cervical cancer screening program namely, information systems, quality improvement and recruitment. Provincial and territorial representatives involved in cervical cancer screening on a clinical or programmatic level attended the workshop along with policy makers from the federal and provincial governments and other national organizations.

The majority of the recommendations of the 1989 Workshop were seen to be still relevant; however, concerns were raised that the recommendations on quality assurance programs only related to cytology. It was felt that the recommendations needed to be updated particularly in relation to enhanced community involvement in policy and program development; broader quality improvement processes to incorporate guidelines for smear taking and clinical care, as well as for cytology. Specifically, it was suggested that there should be a mechanism to ensure the quality of smear-taking, smear-preparation, interpretation of the smear and follow-up of both normal and abnormal smears, as well as indicators that the program as a whole was functioning to ensure that all at-risk women were recruited and retained within the system. It was noted that, in the past, little attention has been paid to the integration of quality assurance or

quality improvement activities within each of the relevant disciplines; where practice guidelines or quality assurance processes have been developed, this has occurred in isolation.

Participants at Interchange '95 requested a continued presence of the federal government in encouraging and facilitating information exchange between the provinces and providing some direction and leadership in the area of standards and quality of care. To this end, all provinces and territories were invited to participate in the Cervical Cancer Prevention Network (CCPN), an informal association of federal and provincial representatives with the relevant clinical professional bodies. Represented are the Society of Obstetricians and Gynaecologists of Canada, the College of Family Physicians of Canada, the Canadian Society of Cytology, the Gynaecologic Oncologists of Canada, the Society of Canadian Colposcopists and the Canadian Nurses Association.

The purpose of the CCPN is to continue to reduce the morbidity and mortality from cervical cancer and its precursors in Canada by facilitating the implementation or enhancement of organized screening programs. Three Working Groups of the CCPN have focused their attention on the development of the following three components of an organized screening program: effective recruitment strategies, information systems and an integrated set of practice guidelines as the basis of a quality management program within the provincially-based screening programs. The latter is the subject of this document, which is based on existing Canadian recommendations and quality assurance documentation where this exists.

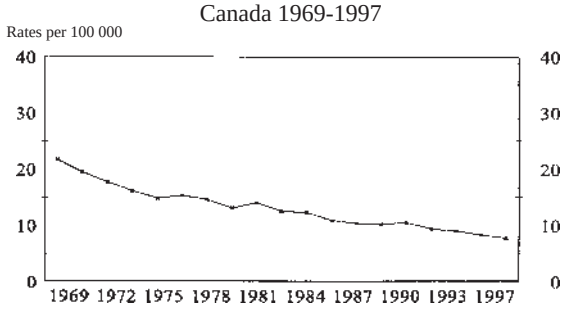
1.2 Statistics on Morbidity and Mortality from Cancer of the Cervix

The mortality and morbidity rates have fallen significantly since screening began in Canada (Figures 1 & 2). More specifically, over the past three decades in Canada, there has been an overall reduction in the age-standardized mortality rates from invasive cervical cancer from 7.4 per 100,000 females in 1969 to 2.4 per 100,000 females in 1992 and a reduction in incidence rates from 21.6 per 100,000 in 1969 to 10.4 per 100,000 in 1990; however, since the mid-70s the rate of decline in incidence rates has slowed, particularly among women under 50 (Laboratory Centre for Disease Control; unpublished data).

However, data from British Columbia indicate that, while mortality and incidence rates of invasive cancer have decreased since the introduction of an organized program in 1949, there has been an increase in the number of cases of in-situ carcinomas from 12.3 per 100,000 in 1955 to 133.6 per 100,000 in 1985 (Anderson, 1988). This increase is probably due to changing lifestyles (e.g. early onset of sexual activity, multiple partners etc) and is simply being picked up by screening.

Figure 1

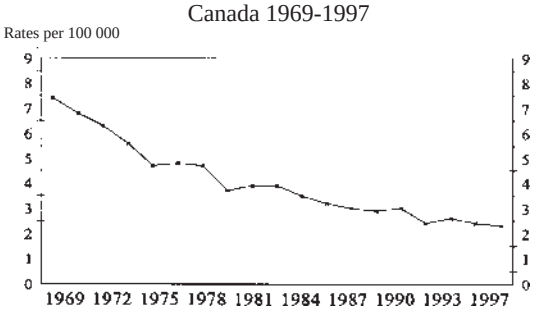
Age-Standardized Incidence Rates,
Canada 1969-1997



Estimated Rates - 1993 to 1997
Source: Health Statistics Division, Statistics Canada

Figure 2

Age-Standardized Mortality Rates,
Canada 1969-1997



Estimated Rates - 1993 to 1997
Source: Health Statistics Division, Statistics Canada

1.3 Participation In Screening for Cancer of the Cervix

Currently, objective information on screening rates is not readily available in most provinces on a routine basis. British Columbia, Nova Scotia, Newfoundland and, most recently, Prince Edward Island are the only provinces that currently have cervical cancer screening registries. At the present time, none are able to generate comprehensive screening rates. Reasons include an inability to obtain denominator data by linking with population databases which may not themselves be accurate; an inability to exclude women who have had a hysterectomy from the denominator; problems with data quality and comprehensiveness including absence of a unique identifier; and changes in terminology over the years. Furthermore, administrative databases at the provincial level, such as physician billing data, cannot be used for the most part as they may not include separate billing codes for Pap smears and, even if they do, do not allow for distinction between smears done in asymptomatic women and those done for reasons other than screening e.g. follow-up.

Self-reports from women in national and provincial health surveys and small area studies are thus the only sources of information on the current status of cervical cancer screening in Canada. The Health Promotion Surveys of 1985 and 1990 revealed that in 1990 twice as many women in the 25 to 44 age group reported never having had a Papanicolaou smear as in 1985; and, in 1990, 27% of women over 65 had never been screened (Stephens, 1993). The 1994 National Population Survey revealed that 16% of women over the age of 18 had never had a smear; 35% of women aged 18 to 24, 11% of women aged 25-34, 9% of women aged 35 to 64 and 29% of women over 65 had never been smeared. Of those women who had had a smear, 99% of the women aged 18 to 24 had had one within the previous 3 years compared to 94% of women aged 25 to 34, 81% of women between 35 and 64 and 55% of women over 65 (Maxwell, 1996).

In a study of invasive cancer of the cervix in British Columbia (Anderson, 1992), almost half of the newly diagnosed cases fell into the category of "no cytology or cytology longer than 5 years ago". Aboriginal women, recent immigrants and women over 60 were disproportionately represented in these statistics and it was felt by the authors that special efforts were needed to attract these groups. In an analysis of data from the Ontario Health Survey, factors related to low utilization of cervical cancer screening were increased age, recent immigration, low level of education and not having English or French as their first language (Goel, 1994). Studies in Prince Edward Island, and Manitoba have also identified women at risk of not being screened (Sweet, 1991; Cohen, 1989).

However, evaluation of the literature on self-reporting of cervical cancer screening rates suggests that women may under-report having smears as they may not know whether a smear has been taken, but they also tend to underestimate the time interval between smears.

The lack of good information on screening practices in Canada reinforces the need for provincial information systems to allow for surveillance and monitoring of screening for cancer of the cervix.

1.4 The Effectiveness of Organized Screening Programs

Screening for cancer of the cervix, using the Pap smear, became generally accepted and introduced into practice without any formal evaluation of its effectiveness by means of a randomized trial. As a result, evaluation has been based upon historical studies, case-control studies, observational studies of established programs and mathematical models of the natural history of the disease. These studies indicate the effectiveness of the multiple steps on the screening pathway in combination without being able to determine the relative contributions of each step.

The most well-known studies are those comparing incidence and mortality trends in Iceland (Johannesson, 1978) and in the five Nordic countries (Hakama, 1982; Laara, 1987). Before screening was introduced in Iceland, mortality had been rising but fell by 50% within ten years of introduction of screening. In the Nordic countries, the decline in cumulative incidence rates over a 15-year period, between 1966-70 and 1981-85, was related to the coverage and extent of the organized programs. In Norway where only 5% of the population had been screened opportunistically, the incidence rates fell by 20% in comparison to Finland, with a national population-based program, where incidence fell by 65%.

In the absence of control groups in these time series, it is possible to interpret declining rates as no more than a continuation of a pre-existing reduction in rates; conversely, a lack of change in rates may result from a failure of screening. Failure of opportunistic screening has been postulated as the cause of the absence of a fall in incidence rates in the UK, despite screening being available from the mid-60's; the NHS Cervical Screening Programme has focused on recruitment and quality assurance and results now show a decrease in mortality, particularly in older women (Sasieni, 1995).

Studies in Canada (Miller et al, 1976), the US (Cramer, 1974) and Denmark (Lynge, 1983) have related changes in incidence and mortality from cervical cancer to the intensity of screening. Parkin et al (1985) estimated that the increase in incidence in younger women in the UK between 1963 and 1978 would have been 50% greater in the absence of screening and that an increased incidence at older ages had been largely prevented.

Case control studies of screening efficacy were initially pioneered in Canada by Clarke and Anderson in 1979; these studies all show a lower risk of cervical cancer in screened than in unscreened women. A review of 15 such studies (albeit with varied definitions of the exposure being studied from ever/never having been screened to screening within a variety of time frames) showed that the estimated relative risks varied from 0.1 to 0.51 (Parkin, 1997).

1.5 Frequency of screening

Recommendations for age to start and stop screening and for screening interval vary from country to country and between professional organizations; they also have changed over time. The recommendations of the 1989 National Workshop on Screening for Cancer of the Cervix (Miller, 1991) are that all women age 18 and over who have had sexual intercourse should be screened, initially with two smears one year apart; if these smears are satisfactory then rescreening every three years is advised until the age of 69, if they have had no significant abnormality in the past. For women over 67 or older, if they have never been screened, two smears at 6-monthly intervals are recommended, following which, if normal, they

may cease having smears. These recommendations are supported by the IARC study (Day, 1986) which showed that the effect of screening every year between 20 and 64, requiring 35 smears, reduced the cumulative incidence of invasive cancer of the cervix by 93.3%, whereas three yearly smears after an initial 3 smears for a total of 14 smears reduced the rate by 90.1%. Eddy (1990) provided estimates of the consequences of different options for screening intervals under different assumptions; in general, as screening becomes more intensive, the gains become smaller while the costs and inconvenience increase. In general, he recommended that women should be screened at least every three years starting in their early 20's and continuing into their 60s.

The recommendation for a three-yearly interval is predicated on the presence of a system for recall and quality assurance within an organized screening program. Currently, opportunistic screening, based on annual screening, depends entirely on the individual woman's and/or her physician's initiative.

After an initial smear result that is within normal limits, a woman who is infected with the human immunodeficiency virus should have at least one additional smear obtained within 6 months to rule out the possibility of false-negative results on the initial smear. If the repeat smear is normal, annual smears are advised (Hankins, 1994; Wright, 1996; Maiman, 1997). For other immunosuppressed women, annual smears are also recommended.

If a woman has not had a smear in the past five years, it is suggested that she should have two normal ones one year apart before getting into the routine 3 yearly interval.

1. 6 Need for Organized Programs in Canada

Opportunistic screening has occurred in Canada since the 1970's; the overall incidence and mortality have declined considerably since then. However, it is now necessary to address cervical cancer screening in a systematic manner for the following reasons:

- cancer of the cervix is a potentially preventable disease, yet a significant number of cases occur in Canada each year;
- it is economically sound to prevent the disease;
- since the 1970's, there have been recommendations for the establishment of provincially-based organized programs;
- there has more recently been a decrease in the rate of decline of invasive cancer of the cervix in women under 50 in Canada, in contrast to an increase in in-situ disease, a pre-invasive condition;
- opportunistic screening does not achieve optimal screening coverage and appears to have reached the limit of its effectiveness;
- women who are diagnosed with the disease are those who have not been screened;
- organized programs have been shown to be effective;
- the costs of organized programs are probably less than that of opportunistic screening; and
- organized programs allow for the evaluation and monitoring of screening and follow up activities.

Clinical practice guidelines are only one component of the quality of an organized screening program. Other components include recruitment strategies at both public, patient and professional levels; information systems; continuous management of the quality of care provided; and professional education. The ability to assess new research findings that provide new information or evidence for change in practice is a key concept for programs to adopt.

The reasons for developing these guidelines at this time are thus:

- Multiple health care providers are involved in the screening pathway and cooperation and collaboration is essential for an effective and efficient program.
- These health care providers need to share common terminology.
- A standardized approach to screening, follow-up and treatment is needed so that there is equitable care for the women of Canada.
- Program evaluation and inter-provincial comparisons can only be carried out if such a standardized approach is in place.

2.0 PRIMARY CARE PROVIDER PRACTICE

2.1 Information for women prior to having a smear

Primary care providers should have patient education material available or should inform women that the purpose of the smear is to identify pre-cancerous lesions in order to prevent cervical cancer. Many women find the procedure embarrassing and uncomfortable. To encourage women to return, practitioners should explain the procedure, answer questions and communicate throughout the procedure; a sensitive environment will contribute to the alleviation of anxiety.

The woman should be informed, at the time the appointment is made, that certain conditions are better than others for screening and that she should not douche the vagina for 48 hours prior to the examination.

Smears should not be taken during menstruation. The optimal time is mid-cycle or just before ovulation and the woman should be informed that the date of her last menstrual period will be required. However, if these conditions cannot be met, and it is possible that she will not return, a Pap smear should be done.

The primary care provider and his or her office staff should have an agreed upon policy for advising the patient of her results and should inform the patient of the method of communicating the information to her.

2.2 Primary Care Practitioner

The majority of historical series cite sampling problems as the cause of over half of the false-negative smears (Department of Health and Human Services, 1989; Gay, 1985). The reasons for sampling errors may be the location of the lesion (e.g. within the endocervix), specific patient variables (e.g. presence of blood or inflammatory material), or incomplete sampling (i.e. poor technique).

2.2.1 Training and maintenance of competence in taking a smear, interpretation of results and appropriate follow-up or referral.

Within the medical school the following should be taught:

- that cervical cancer is a potentially preventable disease;
- that the Papanicolaou smear is an effective screening test ;
- that all women who have ever been sexually active are at risk;

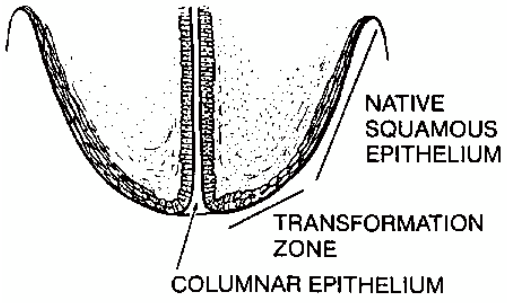
- that regular smears are recommended for women with normal smears; and
- that there are nationally-accepted recommendations for follow-up and treatment of women with abnormal smears.

Practitioners should recognize that opportunities for screening or for reminding women about regular screening include routine visits for chronic care, pregnancy, contraception and visits related to hormone replacement therapy.

2.2.2 How to take a smear

- The medical student, resident or other health care provider should be able
  - to expose the cervix with a bivalve speculum in such a manner that it is visible,
  - to describe the transformation zone,
  - to identify a normal cervix from a cervix with obvious abnormalities,
  - to identify the appropriate tool(s) with which to take a smear,
  - to take the smear, transfer material to the slide and fix the smear, and
  - to take the relevant history for completing the cytology requisition form.

- There are three sampling areas of the cervix (see diagram): the exocervix (covered by squamous epithelium), the transformation zone (covered by metaplastic epithelium) and the endocervix (covered by columnar epithelium). During high oestrogen states, such as puberty and pregnancy, the visible squamocolumnar junction may become more exposed to the outside portion of the cervix and visible to the naked eye. It is this area of the visible squamocolumnar junction from which cervical cytology samples should be obtained.



Three types of epithelium on the cervix

Figure 3: (Reprinted with permission from Wright VC, Lickrish GM, Shier RM (eds): Basic and Advanced Colposcopy Part Two: A Practical Handbook for Treatment; 1996, Biomedical Communications, Houston)

- Post-menopausally, the squamocolumnar junction tends to recede into the endocervical canal and cannot be readily visualized. For this reason, it may be necessary to use an endocervical sampling device in addition to a spatula to obtain an adequate sample from older women.

- The equipment required includes: an examining table, good illumination, various sizes of bivalve specula, a wooden spatula (wood allows good adherence of the sample before transfer to the slide; e.g. Ayre type), an endocervical sampling device, a glass microscope slide with frosted end, a pencil for labelling the slide, a cytology spray fixative (unless otherwise informed by laboratory to which slide is being sent), a container for transporting slides to the laboratory and requisition forms.

  NOTE: Do NOT use lubricating jelly on the speculum.

- Several sampling techniques are acceptable. Both the spatula and the endocervical sampling device should be used, if the transformation zone is not visible and easily sampled. An endocervical sampling device alone should not be used. The spatula is used by applying it to the exocervix, incorporating the squamocolumnar junction, and performing a 3600 scrape keeping contact with the cervix continuously. An endocervical brush should be rotated 900 only. If an endocervical sampling device is to be used, the woman should be informed that it may be uncomfortable and that spotting may occur.

- The smear should be spread on one slide only and fixed immediately unless air-drying is the choice of the receiving laboratory. Spraying evenly across the slide with a cytologic spray fixative at a distance of 6 to 10 inches is recommended. Details of the patient as required by the laboratory is written in pencil on the frosted end of the slide.

- The requisition form is completed by the smear taker and should include the following relevant clinical information: age; date of LMP; whether pregnant, on oral contraceptives or hormone replacement therapy; presence of an IUD; history of previous abnormal smear; history of hysterectomy identified as total or sub-total as appropriate; suspicious appearance of cervix; history of previous treatment for an abnormality of the cervix. Demographic information such as name, health number, physician name may be determined by each provincial jurisdiction.

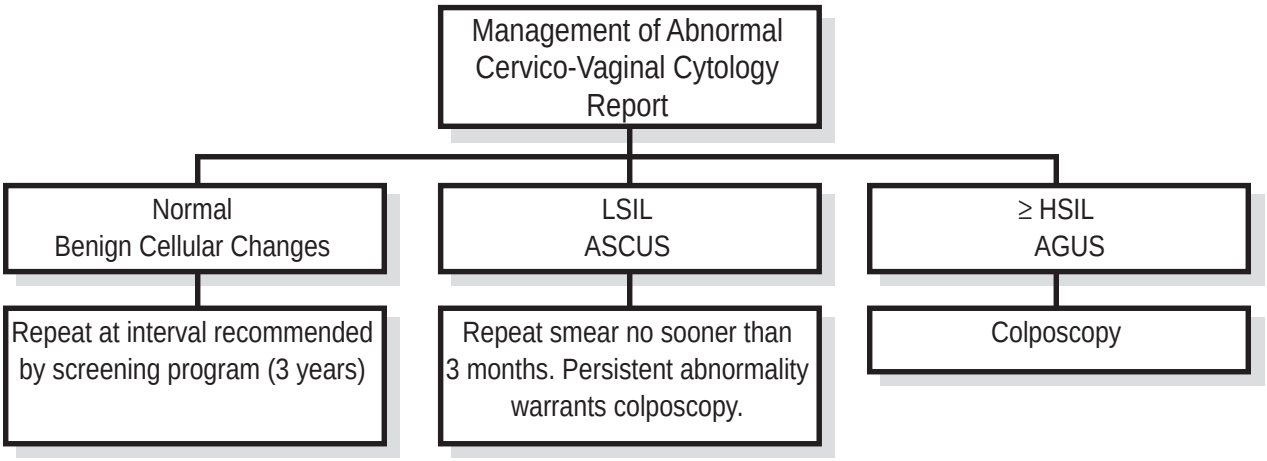
- The medical student/resident/primary care practitioner should understand the terminology used in reporting of the cytology results and the reasons behind the recommendations for follow-up.

- The primary care practitioner should be aware of new information regarding cervical cancer screening and screening programs and maintain his/her competence in taking and interpreting the reports of cytology results and the recommendations for follow-up.

- The primary care practitioner should also be aware that a patient with a visibly abnormal cervix or abnormal vaginal bleeding should be subjected to further investigation including a biopsy, regardless of the cytological findings.

2.2.3 Management recommendations of an abnormal smear

- Management of an abnormal smear should conform with the following algorithm:



Note: In the absence of a clinical abnormality, an unsatisfactory smear should be repeated in no fewer than 2 months.

2.2.4 Office Management Issues

- A woman is at risk if she has ever had sexual intercourse and should be screened.

- Ideally, within the context of an organized screening program, there should be a mechanism within each office to ensure that results are obtained from the laboratory in a timely manner. If the results are not received, the office staff should communicate with the laboratory to ensure that the smear was received by the laboratory and that a report will be forthcoming.

- Results need to be communicated to the patient. If the result is normal requiring no immediate follow-up or if the smear needs to be repeated for technical reasons, a member of the office staff could call the patient with this information, remind them to return at the appropriate time if a normal result has been obtained or give her an appointment for a repeat smear when this is indicated. If the results are abnormal and follow-up or referral is required, the physician should inform the patient him/herself in a sensitive manner, giving an appointment for further discussion and appropriate information re possible diagnostic procedures as required.

- It is imperative that an efficient process be in place for the recall of women with abnormal smears for a repeat smear or referral in order to ensure that these women have the appropriate care.

- Policies with respect to recruitment and recall will differ by province; each physician should be cognizant of the policies for their province. Areas of variation include: ability of program to recruit women by linking with a population dataset; and whether recruitment/recall letters are sent by laboratories or by a central register; and whether these letters are sent to physicians or directly to women.

- If recruitment/recall letters are sent to the physician to contact the woman, the physician's office should determine their own mechanism for ensuring contact with the woman and for ensuring that the woman has a smear.

- Provincial information systems will remind physicians that follow-up has not been carried out, but the responsibility for contacting patients with abnormal smears remains with the physician who has taken the smear. Once women have been treated for an abnormality or for cervical cancer and discharged by the specialist back to the primary care physician, follow up should be ensured.

- Physicians should be aware of the screening coverage of their patient population and their individual adequacy and abnormality rates either by quantifying feedback from the laboratory or screening program or by carrying out audits of his/her own practice.

3.0 CYTOTECHNOLOGISTS, CYTOPATHOLOGISTS AND LABORATORY PRACTICE

3.1 Training and Maintenance of Competence of Cytotechnologists, Cytopathologists and Laboratory Practice

All cytopathology laboratories should consider the 1996 Canadian Society of Cytology Guidelines for Practice and Quality Assurance in Cytopathology in the following areas:

- qualifications, training, continuing education and maintenance of competence of cytotechnologists and cytopathologists
- physical facilities and equipment
- processes for accessioning, preparing and staining of cytologic specimens
- internal and external quality control practices
- screening and diagnostic practices
- performance indicators

3.2 Performance Indicators

Laboratory performance indicators should include:

- cyto-histological correlation rates for each grade of squamous intraepithelial lesion and for carcinomas measured against follow-up surgical material or clinical outcome
- the false-negative rate of the laboratory. The false-negative rate of the laboratory and individual cytotechnologists should be separately measured. A false-negative result is defined as a screening miss of an abnormality in a satisfactory smear >/= "ASCUS" or its equivalent if an alternate terminology is in use (Canadian Society of Cytology, 1995-96).
- the rate of satisfactory, satisfactory but limited and unsatisfactory smears at the laboratory and smear-taker levels

- the total number and rates of abnormal gynecological diagnoses and specific diagnostic categories for the laboratory

- the turnaround time. Clinicians and laboratories should establish a mutually agreed upon turnaround time from the date the smear is received in the laboratory to the date of the finalized report; an optimal time could be approximately one month.

3.3 Screening practices

- Cytotechnologists' total workload should be determined by the relative proportions of different types of slides (nature, type of preparation, routine, follow-up of previous abnormality, non-gynecological specimens), but should not be higher than 60-80 cervical-vaginal smears per 6-8 hour workday for a technologist screening full-time.

- Normal gynecological smears from women with atypical histories, smears with an abnormality equal to or greater than ASCUS (atypical squamous cells of undetermined significance) or AGUS (atypical glandular cells of undetermined significance) should be referred for a second screening and/or directly to a pathologist for reporting. If a current smear is determined to be equal to or greater than CIN 1 (cervical intraepithelial neoplasia)/HPV effect /LSIL (low grade squamous intraepithelial lesion), all smears from the previous 5 years for that woman should be rescreened by a cytotechnologist and referred to a pathologist.

3.4 Reporting Terminology

- It is recommended by the Canadian Society of Cytology (Canadian Society of Cytology, 1995-96) that The Bethesda System (TBS) (National Cancer Institute Workshop, 1989) be used in conjunction with dysplasia and/or CIN systems (Table 1). The obsolete numerical Papanicolaou class system of reporting should not be used. Within a provincial jurisdiction, it is preferred that one terminology be used; however, the choice of which terminology to use is to be determined by each jurisdiction.

3.5 Specimen inadequacy

- If a specimen is limited or unsatisfactory or considered not to be representative of the stated tissue site and precludes interpretation, this should be stated and recommendations made for submission of an adequate smear.

3.6 Histology

- Terminology used in histologic reporting of cervical biopsies should facilitate cytologic correlation. Ideally, the same terminology, e.g. the Bethesda System, should be used for both cytology and histopathology reporting.

- The Canadian Assocaition of Pathologists has a subcommittee that is currently developing quality assurance guidelines in histopathology. When available, the principles of these guidelines should be applied to cervical histopathology.

- The following specific guidelines should be included:

    - There should be correlation between the screening Papanicolaou smear diagnosis and follow-up cervical biopsy, when the smear diagnosis is ASCUS, favour SIL or greater.
    - When Initial histology sections of a cervical biopsy following a Papanicolaou smear reported as HSIL or greater do not reveal a pre-neoplastic or neoplastic lesion:
        - At least three deeper sections should be examined.
        - The abnormal Papanicolaou smear should be re-secreened and reviewed by the same laboratory reporting the histology, prior to referral for an excisional procedure.

Table 1: Cervico-vaginal Reporting Terminologies

The Bethesda System	**CIN/Modified Walton System**
Unsatisfactory: state reason	Unsatisfactory: state reason
Within normal limits	No abnormal cells; metaplasia noted
Benign cellular changes Trichomonas vaginalis Fungal organisms morphologically consistent with Candida spp. Cellular changes associated with Herpes Simplex virus	Abnormal cells consistent with reactive atypia (non-dysplastic) Trichomonas effect Yeast effect Viral effect (Herpes type)
Benign cellular changes Reactive cellular changes associated with: inflammation radiation other	Abnormal cells consistent with reactive atypia (non-dysplastic) Inflammatory effect Irradiation effect other
ASCUS*	Abnormal cells consistent with atypia (possibly dysplastic) Atypical metaplasia Atypical parakeratosis Other (add comment)
LSIL**	Abnormal cells consistent with condyloma (HPV§ effect)
LSIL HSIL*** HSIL	Mild dysplasia/CIN§§ I Moderate dysplasia/CIN II Severe dysplasia/CIS/CIN III
Carcinoma Squamous cell carcinoma Adenocarcinoma Unspecified	Abnormal cells consistent with malignancy Consistent with invasive squamous carcinoma Consistent with adenocarcinoma Type unspecified
AGUS****	
Other	Abnormal cells not specifically classified Add Comment)

ASCUS = atypical squamous cells of undetermined significance
LSIL = low grade squamous intraepithelial lesion
HSIL = high grade intraepithelial lesion
AGUS = atypical glandular cells of undetermined significance
HPV = human papillomavirus
CIN = cervical intraepithelial neoplasia

4.0 COLPOSCOPY

4.1 Training and maintenance of competence of colposcopists

Points to Consider:

- Colposcopy is a procedure which combines a variety of clinical and mechanical skills to assess and evaluate individuals with abnormal cytology and potential neoplasia of cervix.
- Colposcopy has a role in vaginal, vulvar and perianal disorders, as well as in cervical disorders.
- Colposcopy should be performed if possible at hospital or designated clinics.
- The colposcopist should possess knowledge in cytology and histopathology and the natural history of pre-invasive and invasive diseases of the lower female genital tract.
- The colposcopist should understand the normal and abnormal colposcopic patterns and be able to define low and high grade lesions in order to avoid missing advanced disease and to obviate over-treatment for low grade lesions.
- The colposcopist should possess knowledge and therapeutic skills in therapeutic regimens (surgical and chemotherapeutic) in the management of patients with lower genital tract disease.
- The colposcopist should understand and actively participate in quality control and audit to maintain a high standard of care.
- The colposcopist should sustain a volume and spectrum of new referrals to maintain diagnostic and treatment skills.
- The colposcopist is expected to remain current by attending scientific meetings and postgraduate courses related to colposcopy and treatment.
- If an adequate volume and spectrum of referrals cannot be maintained, additional supervised experience in colposcopy is necessary on a regular basis by means of a preceptorship under the supervision of a competent colposcopist in a recognized academic centre.
- Clinical practice using colposcopy is done in such a manner to ensure

- a continuous adequate case load of abnormal cervices.
- ongoing reviews with a pathologist correlating cytology, colposcopy and histology.
- appropriate referral to a colposcopy consultation service when deemed necessary, for example for a colposcopy during pregnancy.

• The colposcopist should be familiar with the "Guidelines for Training Requirements in Colposcopy and Its Related Treatment Modalities" (The Society of Canadian Colposcopists).

4.2 Procedure

4.2.1 Interpretation of Referral Letter and Smear Report

• It is frequently helpful to have a referring letter where applicable and a copy of the Pap smear of concern. Colposcopy is rarely undertaken without prior knowledge of the smear report. The colposcopist may choose to repeat the Pap smear at the time of colposcopy and directed biopsies to establish a correlation system (cytology, colposcopy, histology) within the same institution. A discussion of the Pap smear and its significance should occur with the patient.

4.2.2 Indications for colposcopy

• There is agreement that all patients with a cytology smear reported as CIN II/HSIL or greater should be advised to undergo colposcopic examination. Debate exists on the relative value of colposcopy in those patients with smears reported as ASCUS/CIN I/LSIL. Generally, a repeat smear should be recommended in 6 months for women with this degree of abnormality; if there is evidence of cytological progression or persistence of the abnormality, colposcopy should be arranged (SOGC, 1998b).

• Women infected with the human immunodeficiency virus or otherwise immuno-suppressed should be referred for colposcopy if a smear shows any degree of abnormality.

• The presence of atypical glandular cells of undetermined significance (AGUS) on cervical cytology should be investigated by colposcopically-directed biopsies, endocervical curettage and endometrial biopsy when indicated (Zweizig, 1997).

4.2.3 Colposcopic Terminology

• The transformation zone is the origin of intraepithelial lesions of the cervix and thus forms the basis of the classification system. In 1990 the International Federation of Cervical Pathology and Colposcopy (IFCPC) has formulated such a classification (Table 2) (Stafl, 1991). This system includes lesions extending outside the transformation zone as not uncommonly seen with papillomavirus infection, although their neoplastic potential is small.

Table 2. International Colposcopic Terminology

Normal colposcopic findings Original squamous epithelium Columnar epithelium Normal transformation zone Abnormal colposcopic findings Within the transformation zone Acetowhite epithelium* Flat Micropapillary or microconvoluted Punctation* Mosaic* Leukoplakia* Iodine negative Atypical vessels Outside the transformation zone, e.g., ectocervix, vagina Acetowhite epithelium* Flat Micropapillary or microconvoluted Punctation* Mosaic* Leukoplakia* Iodine negative Atypical vessels	Colposcopically suspect invasive carcinoma Unsatisfactory colposcopy Squamocolumnar junction not visible Severe inflammation or severe atrophy Cervix not visible Miscellaneous findings Nonacetowhite micropapillary surface Exophytic condyloma Inflammation Atrophy Ulcer Other

* Indicates minor or major changes: Minor changes = acetowhite epithelium, fine mosaic, fine punctation, and thin leukoplakia. Major changes = dense acetowhite epithelium, coarse punctation, thick leukoplakia, atypical vessels, and erosion.

Ratified by the International Federation of Cervical Pathology and Colposcopy, May 1990, Rome, Italy.

4.2.4 Biopsy and Biopsy Findings

- The colposcopic provisional diagnosis is based upon evaluation of a number of epithelial characteristics. These include the surface contour, presence of a regular or irregular vascular pattern, calibre of vessels, whiteness of the epithelium, the intercapillary distance, the sharpness of the border against adjacent tissue, the findings of satellite lesions and the presence of atypical blood vessels suggestive of malignancy. Several colposcopic grading systems have been devised utilizing these parameters to help further quantify the colposcopic impression as to the severity of the lesion. It is from these recorded site(s) that colposcopic biopsy(s) are taken. The accurate recording of these findings should include:

  - whether the squamocolumnar junction was seen
  - presence or absence of a visible lesion
  - colposcopic opinion regarding the nature of the abnormality
  - the entire lesion is visualized.

- A correlative diagnosis is reached using the results of cytology, colposcopic impression, colposcopically directed biopsies and endocervical curettage (ECC) as indicated. Marked discrepancies or unsatisfactory colposcopy may require some method of cone biopsy. The biopsy results should be discussed with the patient as well as alternate methods of treatment.

- Correlation between Pap smear and subsequent biopsy diagnoses should be part of a quality assurance program.

- Glandular lesions should be considered as unique and managed separately in accord with existing guidelines (SOGC, 1998).

4.3 Methods of Treatment of Cervical Intraepithelial Neoplasia

4.3.1 Overview

Cervical intraepithelial neoplasia (CIN) refers to a spectrum of microscopic changes in the cervical epithelium that indicate a potential for the development of invasive carcinoma. Based on the degree of change observed, lesions are graded as one of three categories: CIN I, CIN II or CIN III, with the grade increasing with the severity of disease. Proposals have been put forward to group lesions into low grade squamous intraepithelial neoplasia (LSIL, corresponding to CIN I) and high grade squamous intraepithelial neoplasia (HSIL, corresponding to CIN II and III).

4.3.2 Role of Viral Typing

The human papillomaviruses (HPVs) have been implicated in the development of CIN. The different HPV types associated with genital disease are categorized as low or high risk, which reflects the percentages seen in invasive cancer (Table 3). At present, there is no evidence to support routine viral typing in the context of a cytology screening program; research is ongoing to determine the cost-effectiveness of HPV typing in the management of ASCUS/LSIL abnormalities.

Table 3: Viral Type by Risk*

Low-Oncogenic Risk	High-Oncogenic Risk
HPV 6,11,26, 40,42, 43,44, 53-55,57,59,66,68	HPV 16,18,31,33,35,39,45,51,52,56,58

* as of January 1998

4.3.3 Indications for Treatment

- CIN can occur in any woman who has ever had sexual intercourse. The disease can be found on the portio, in the canal or both, even extending onto the vagina. On the cervix the disease can involve crypts (glands) below the cervical surface. Radial linear length of lesions vary from 2-22 mm from distal to proximal borders (average 10 mm). Disease occurs higher up the canal with increasing age of the woman and the worst histology is found centrally/proximally.

- In general, most physicians treat all grades of CIN. The selection of the method depends upon location of disease, fertility, available equipment, and expertise of the physician.

- Controversy exists about the need for treatment of CIN I/LSIL/ASCUS since many such lesions will regress after biopsy. However it is possible that the CIN I/LSIL/ASCUS lesion may contain a carcinogenic HPV type. If the decision is not to treat, the patient must be informed of the need for surveillance with cytology and colposcopy every 6 months for 2 years. More advanced lesions must all be treated unless the patient is pregnant, in which case treatment is delayed until the post-partum period.

4.3.4 Treatment Options

The energy sources to manage CIN include lasers (CO2 laser), electrosurgical generators and cryosurgery equipment.[1]

The treatment options are:

- excision by scalpel, laser, electrosurgery
- laser ablation
- a combination of excision and ablation (laser or electrosurgery). The method(s) of treatment depend on the location and extent of disease and fertility considerations.
- cryosurgery

a. Excision

Excision is usually reserved for:

- dysplastic endocervical mucosa
- disease involving the endocervical canal
- inadequate correlation of cytology, histology and colposcopy
- differentiating micro-invasive from invasive squamous cancer
- differentiating between in situ and invasive adenocarcinoma
- unsatisfactory colposcopy

The methods of choice are CO2 laser, electrosurgery or scalpel.

b. Laser Ablation

- Laser ablation (usually with the CO2 laser) may be done for patients with ectocervical disease. It has an initial cure rate of 90% and an overall cure rate, with repeat procedures, of 98%. It is usually performed as an outpatient procedure using local anaesthesia. General anaesthesia may be required for the apprehensive patient.

c. Electrosurgery

- This can be done for both ectocervical lesions and lesions requiring excision for any reason. The overall cure rate is 90%. It is usually performed with the patient under local anesthesia but general anaesthesia may be necessary for the apprehensive patient or when required exposure would cause intolerable discomfort.

[1] To use these energy sources safely and effectively, the operator must thoroughly understand:
- how equipment for the energy sources is operated
- the different safety precautions for each energy source
- the effect of the energy source on tissue
- maintenance of equipment protocol

d. Cryosurgery

- Cryosurgery is reserved for patients with ectocervical CIN lesions. Overall cure rates are around 90% but larger lesions fail more often than smaller ones. It is usually performed as an outpatient procedure without local or general anaesthesia.

4.3.5 Follow-up Post-treatment

The initial follow-up should include cytology, colposcopy and/or biopsy as deemed necessary by the original biopsy. Persistent and/or recurrent disease is most likely found within six months after therapy. Retreatment is undertaken if lesions persist. Subsequent follow-up should include annual cytology, for the life of the woman. The patient should be informed of the follow-up schedule and referred back to the referring physician.

4.3.6 Outcome Indicators

Outcome indicators include, but are not limited to, the following:

- overall cure rates of 90% or more unless extensive disease is encountered or if cervical anatomical deformities exist
- patients with persistent disease are again submitted to colposcopic protocol and treatment is based upon histological and colposcopic findings
- based on the available evidence, the incidence of complications should be within acceptable limits. Complications include:
    - post-operative haemorrhage
    - delayed healing
    - cervical and pelvic infection
    - cervical incompetence or stenosis
    - persistent and recurrent intraepithelial neoplasia
    - anaesthesia problems

5.0 GYNECOLOGIST/ GYNECOLOGICAL ONCOLOGIST

5.1 Training and Maintenance of Competence

5.1.1 Training

During medical school, the medical student learns how to do a Pap smear and when he/she should refer the patient to a colposcopist or to a specialist.

During training, the gynecology resident acquires knowledge of the patho-physiology of cervical cancer, risk factors, and methods of management of an early lesion of the cervix. In the Canadian setting, the resident spends at least three months in a gynecological oncology unit.

For the fellow in gynecological oncology, training is at least two years. Since 1971 in the United States, there has been a recognized program by the American Board of Gynecologic Oncology and many of the practising gynecological oncologists in Canada were trained in the United States. In 1989, the Royal College of Physicians and Surgeons of Canada recognized gynecological oncology as a specialty and provides accreditation status to approved programs throughout Canada.

The Gynecological Oncologist is:
- an Obstetrician and Gynecologist;
- a pelvic surgeon with expertise in urological, gastro-intestinal and radical gynecological surgery;
- trained to give chemotherapy and participate in the decision to treat with radiation therapy;
- a promoter of programs to screen or to prevent gynecological oncology diseases;
- a teacher;
- a colposcopist; and
- a clinical researcher.

Such a specialist works in a gynecological oncology unit either at a University or a tertiary oncology centre.

5.1.2 Maintenance of competence

The general obstetrician and gynecologist maintains his/her competence:
- by maintaining a sufficient workload in his/her practice;
- by keeping up-to-date through journal reading, attending conferences and workshops etc;.
- by involvement in evidence-based practice;

- by membership in a sub-specialist society, such as the Society of Canadian Colposcopists; and
- by his/her participation in the Maintenance of Competence Program of the Royal College of Physicians and Surgeons of Canada.

In addition, the gynecologic oncologist maintains his/her competence:
- by working in a tertiary centre.
- by maintaining a caseload in gynecological oncology consisting at least 50% of his/her practice.
- by participation in multicentre clinical research; and
- by membership in a specialty, such as the Society of Gynecologic Oncology of Canada.

5.2 DIAGNOSIS AND INVESTIGATION

5.2.1 Diagnosis

The diagnosis of invasive cervical carcinoma requires a histo-pathologic diagnosis. Neither cytology nor colposcopy are diagnostic procedures, although each is important in the process. If a visible lesion is seen on the cervix, a biopsy of the lesion is indicated. When cytology suggests the presence of cells suspicious for invasive disease and no lesion is visible, colposcopy is invaluable in identifying the area to be biopsied. A surgical conization or ablation is indicated as discussed in the colposcopy chapter.

5.2.2 Investigation

The initial workup of invasive cervical cancer may include history and physical examination, chest radiography, intravenous pyelogram (IVP) or computed tomography (CT) scans of the pelvis, cystoscopy and proctosigmoidoscopy. Other radiological work-up is done as indicated.

5.2.3 Clinical Staging

The official FIGO staging system for cervical carcinoma is based on clinical assessment (Creasman, 1995), which may include an examination under general anesthesia at which cystoscopy and proctosigmoidoscopy are carried out. (These latter examinations may be omitted in patients with early stage disease.

5.2.4 Surgical Staging

Accumulating data continue to show the deficiency of clinical staging. The International Federation of Gynecology and Obstetrics (FIGO) staging system is based on the belief that cervical cancer is primarily a local disease in the pelvis, and that a surgical staging system cannot be widely done worldwide, especially in the developing countries.

Table 4: The FIGO Staging for Carcinoma of the Cervix Uteri (Montreal, 1995)

STAGE I The carcinoma is strictly confined to the cervix (extension to the corpus should be disregarded).

STAGE IA: Invasive cancer identified only microscopically. All gross lesions even with superficial invasion are Stage IB cancers. Invasion is limited to measured stromal invasion with maximum depth of 5.0 mm and no wider than 7.0 mm.

Stage IA-1
- Measured invasion of stroma no greater than 3.0 mm in depth and no wider than 7.0 mm.

Stage IA-2
- Measured invasion of stroma greater than 3.0 mm and no greater than 5.0 mm and no wider than 7.0 mm. The depth of invasion should not be more than 5.0 mm taken from the base of the epithelium, either surface or glandular, from which it originates. Preformed space involvement (vascular or lymphatic) should not alter the staging but should be specifically recorded so as to determine whether it should affect treatment decisions in the future.

Stage IB:Clinical lesions confined to the cervix or preclinical lesions greater that IA

Stage IB-1
- Clinical lesions no greater than 4.0 cm in size.

Stage IB-2
- Clinical lesions greater than 4.0 cm in size

STAGE II The carcinoma extends beyond the cervix but has not extended to the pelvic wall. The carcinoma involves the vaginal but not as far as the lower third.

Stage IIA
- No obvious parametrial involvement.

Stage IIB
- Obvious parametrial involvement.

STAGE III The carcinoma has extended to the pelvic wall. On rectal examination, there is no cancer-free space between the tumor and the pelvic wall. The tumor involves the lower third of the vagina. All cases with a hydronephrosis or nonfunctioning kidney are included unless they are known to be due to other causes.

STAGE IIIA
- No extension to the pelvic wall.

STAGE IIIB
- Extension to the pelvic wall and/or hydronephrosis or nonfunctioning kidney.

STAGE IV The carcinoma has extended beyond the true pelvis or has clinically involved the mucosa of the bladder or rectum. A bullous edema as such does not permit a case to be allotted to Stage IV.

Stage IVA
- Spread of the growth to adjacent organs.

Stage IVB
- Spread to distant organs.

5.3 Treatment

5.3.1 Treatment Overview

If abnormal lymph nodes are detected by CT scan or by lymphangiography, fine needle aspiration could be done for purpose of diagnosis and might affect the decision with respect to treatment intervention. Surgery and radiotherapy have comparable outcomes in selected patients with early stage small volume disease. Surgery, however, may be the preferred option in younger women in order to preserve ovarian function and to avoid vaginal atrophy and stenosis. The value of adjuvant treatments, such as chemotherapy, for patients with more advanced disease, is uncertain, and enrolment in clinical trials may be appropriate for patients with disease more advanced than stage II, or with lymph node involvement.

Survival is related to tumor volume; treatment may, therefore, vary within each stage as currently defined by FIGO dependent on tumor bulk and pattern of spread.

Incidental invasive cervical carcinoma diagnosed in a hysterectomy specimen: Fortunately, many of these patients have early disease and can have an excellent prognosis with appropriate treatment. Patients, who are radical surgical candidates and who have no gross residual disease, can be treated with radical parametrectomy, upper vaginectomy and regional lymphadenectomy. This procedure is especially valuable in young patients where preservation of normal ovarian and vaginal function is important. Radiation therapy is otherwise a suitable alternative to radical parametrectomy. In women whose hysterectomy specimen reveals that cancer has been cut-through, prognosis is poor and radical parametrectomy, upper vaginectomy and node dissection is inadvisable.

Surgical or radiation therapy for patients with cancer of the cervical stump is effective, yielding results comparable to those seen in patients with an intact uterus. In this group bowel complications due to treatment may be increased.

During pregnancy, no therapy is warranted for preinvasive lesions of the cervix, although colposcopic examination is recommended to exclude invasive cancer.

Treatment of invasive cervical cancer during pregnancy depends upon the stage of the cancer and gestational age at diagnosis. The traditional approach has been to recommend immediate therapy appropriate for the disease stage when the cancer is diagnosed before fetal maturity; if the cancer is detected after twenty weeks of gestation, treatment may be delayed until fetal maturity, at which time a Caesarian Section may be performed followed by definitive treatment.

5.3.2 Treatment by Stage

Stage 0 Cervical Cancer

- Properly treated, the cure rate of in-situ cervical carcinoma or HSIL (CIN II or III) should be nearly 100%. Unrecognized invasive disease, treated with inadequate ablative therapy, may be the most common cause of failure. The choice of treatment will also depend on several patient factors including age, desire to preserve fertility, and medical condition.

- Methods to treat squamous exocervical lesions include:
  1. Cryotherapy
  2. Loop electrosurgical excision procedure (LEEP)
  3. Laser therapy
  4. Conization or ablation

- When the neoplastic process extends to the endocervical cone margin, invasive cancer must be ruled out.

- For adenocarcinoma in situ (ACIS) of the cervix
  1. Conization (with previous cone-negative margins)
  2. Abdominal or vaginal hysterectomy (with previous cone-negative margins)
  3. Positive cone margins require evaluation to exclude invasive adenocarcinoma

Invasive Cervical Cancer

Stage IA and Stage IA_1

1. Conization: If the depth of invasion is less 3.0 mm, no vascular or lymphatic channel invasion is noted, and the margins of the cone are negative, conization alone may be appropriate in patients wishing to preserve fertility.

2. Total hysterectomy: If the depth of invasion is less than 3.0 mm as proven by cone biopsy with clear margins and no vascular or lymphatic channel invasion is noted, the frequency of lymph node involvement is sufficiently low that lymph node dissection is not required. Oophorectomy is optional and should be deferred in younger women.

3. Intracavitary radiation therapy: In stage IA1 and where no capillary or lymphatic space invasion is noted, the frequency of lymph node involvement is low enough that external beam is not required. If the vascular space is involved, treat as stage IA2.

Stage IA_2, IB and IIA

1. Radical hysterectomy with pelvic lymphadenectomy: Radical hysterectomy with node dissection may also be considered for patients where the depth of tumor invasion was uncertain due to invasive tumor at the surgical cone margin.

2. Intracavitary and external radiation.

3. Trachelectomy and radical parametrectomy with pelvic lymphadenectomy: For patients who wish to preserve their fertility potential and have a small lesion, this is a new alternative treatment that could be considered. Long term outcomes of this procedure are yet to be documented.

- For invasive adenocarcinoma

The treatment options for invasive adenocarcinoma are the same as above.

Stage IIB

Usually, stage II cancers of the cervix are treated by radiotherapy.

1. Radiation therapy: Intracavitary radiation combined with external-beam pelvic irradiation.

2. Clinical trials including radiation and chemotherapy (sequential or concurrent) are ongoing.

Stage III

- The treatment of choice is external beam therapy including intracavitary radiation application. Patients with unilateral pelvic side wall involvement have a better outcome than patients with bilateral involvement or when the lower third of the vagina is involved.

1. External and internal radiotherapy.
2. Clinical trials of combined modality therapy using radiation therapy and chemotherapy concurrently or in sequence are ongoing.

Stage IV

- The treatment of choice is radiation therapy. In the presence of rectovaginal or vesicovaginal fistula or lack of response to radiation therapy and where no regional or distant disease is present, pelvic exenteration may be an option.

- No standard chemotherapy treatment for stage IV cancer of the cervix provides substantial palliation. Such patients could be candidates for new anticancer treatments of phase I and II clinical trials.

1. External and internal radiation therapy.

2. Ongoing protocols for combined modality therapy using radiation therapy and chemotherapy.

3. Hypofractionated irradiation therapy may be used to palliate central disease.

4. Chemotherapy

5. Pelvic exenteration.

5.4 Recurrent Cervical Cancer

There is no standard treatment for recurrent cervical cancer that has spread regionally or distally. Some patients may be appropriate candidates for clinical trials testing drug combinations or new anticancer agents. For local central recurrent disease, pelvic exenteration can lead to a five year survival of 50%-60% in selected patients.

1. Pelvic exenteration.

2. For recurrence in the pelvis only, when the patient had primary treatment by surgery, radiotherapy alone or radiation and chemotherapy may cure 40%-50% of patients.

3. Chemotherapy can be used for palliation.

4. Palliation only

5.5 Follow-up

Patients with invasive cancer of the cervix, who have completed their treatment by either surgery or radiotherapy, can develop recurrence. If this happens, in 80% of cases it will occur within the first two years of follow-up and in 98% within the first five years.

At each visit, a gynecological examination, palpation of lymph nodes (supraclavicular, inguinal) and cytology should be done. The patient should be informed how to keep the vagina patent.

5.5.1 Frequency of Follow-up

- Once every three months during the first year.
- Once every four months during the second year.
- Once every six months during the third year to the fifth year.
- Once a year from between the sixth to the tenth year of follow-up and then when needed.

For the first five years, follow-up of the patient should be done by a tertiary care cancer unit.

5.6 Hormone Replacement Therapy

In treated cervical cancer patients, there is no contra-indication for using hormone replacement (if uterus is in place) except where there are medical contraindications.

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