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Screening for Squamous Cell Carcinoma of the Cervix

SUMMARY

The author reviews the origins of screening for squamous cell carcinoma of the cervix and the question of its value. Definitions of screening and case finding are given. The natural history of carcinoma of the cervix is explored. Barriers to screening and items that facilitate the process are described. A selection of the many recommendations which have been tabled since 1976 are documented. An appropriate screening plan for Canadian family physicians is suggested. (*Can Fam Physician* 1989; 35:1365–1372.)

RÉSUMÉ

L'auteur passe en revue les origines du dépistage de l'adénocarcinome malpighien du col et remet en question sa pertinence. L'article définit le dépistage et l'identification des cas. Il explore l'histoire naturelle de l'adénocarcinome du col. On y décrit les barrières au dépistage et les éléments qui le facilitent. L'article documente un certain nombre de recommandations qui ont été présentées depuis 1976. L'auteur suggère enfin un plan de dépistage approprié aux médecins de famille canadiens.

Key words: cervical cancer, screening techniques, squamous cell carcinoma

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IN AUGUST of 1941, Drs. Papanicolaou and Traut published an article that was the culmination of more than two decades of work.[1] In 1943, the same authors published a book on the same topic, *Diagnosis of Uterine Cancer by the Vaginal Smear*.[2] The publication of these studies marked the beginning of the initiatives, which continue to this day, to eradicate death from squamous cell carcinoma of the cervix.

In 1941, cancer of the uterus caused 26 000 deaths in the United States.[1] By 1980, this figure had dropped to 7400.[3] Between 1941 and 1980 the population of the U.S. increased from 132 million to 226 million. In 1941 Canada had a population of 11 million, and the deaths from cancer of the cervix were 441.[4] By 1981, the population had increased to 24 million, but the number of deaths from cancer of the cervix was about the same: 457.[5]

Whether the fall in the number of deaths is entirely attributable to the early detection and treatment of cervical cancer may be open to question. In 1988, Skrabanek[6] forcefully questioned the effectiveness of screening for squamous cell carcinoma of the cervix and the tenet that dysplasia progresses to carcinoma in situ and then to invasive carcinoma of the cervix. The author concluded:

> the optimists who in 1960 predicted that cervical cancer would be eradicated were carried away by their wishful thinking. The incidence of cervical cancer in developed countries has been declining for decades for reasons unknown. We have no evidence that the decline has been accelerated by mass screening. Mass screening is premature and unjustifiable on scientific and ethical grounds.[6]

Miller, in an article following Skrabanek's in the same journal,[7] refuted these conclusions but conceded that deficiencies exist in the organization of screening programs. Hakama and colleagues[8] demonstrated that screening in the Nordic countries produced a significant decrease in the incidence of cervical cancer proportionate to the intensity of the screening.

In Toronto, Clarke and Anderson demonstrated the same positive cor-

relation between Pap smears and the reduction in the rate of cervical cancer in 1979.[9] The beneficial results of a well organized screening process were also substantiated in British Columbia by Anderson and colleagues in 1988.[10] The evidence to date shows that screening for cervical cancer leads to a decrease in the incidence of this disease. This is proven further if one extrapolates the curve of the decline in cervical cancer in Canada in the 1950s to the present and compares the predicted figures with the actual figures. The difference favours the screening process (personal communication from Aileen Clarke, MB, BS, Head, Division of Epidemiology and Statistics, Ontario Cancer Treatment and Research Foundation).

Despite the reduced mortality rates, women are still dying from cancer of the cervix. We can, however, generally identify the age groups at risk (Figure 1).

Comprehensive Screening

The challenge is to make the screening process more comprehensive on an organizational basis. To do this, it is necessary to examine the natural history of squamous cell carcinoma of the cervix as we understand it today. To examine the risk factors, barriers to effective screening, and items that facilitate the process, it is particularly important to develop strategies to reach women who are being missed at present.

Defining Concepts

The concepts of screening and case finding must be defined because it is the confusion between screening and case finding that makes discussion of this subject difficult.

As a task force reported to the Conference of Deputy Ministers of Health in 1979:

> Screening is an activity making use of procedures by which unselected general populations are classified into two groups: one with a high probability of being affected by killing or disabling conditions, unhealthy states or unhealthy behaviours, and the other with a low probability. Screening is done without an explicit or tacit ongoing relationship between the person being screened and the health worker doing the screening. In contrast, in case finding, which is detection of disease by means of various tests or procedures by a physician or other health worker who has an ongoing, explicit or tacit relationship with the person under assessment, classification is done by the health care provider. It is generally done in the course of intercurrent care. This means that the followup of high risk persons is the responsibility of the health worker who has done the initial classification, that is, the case finding.[11]

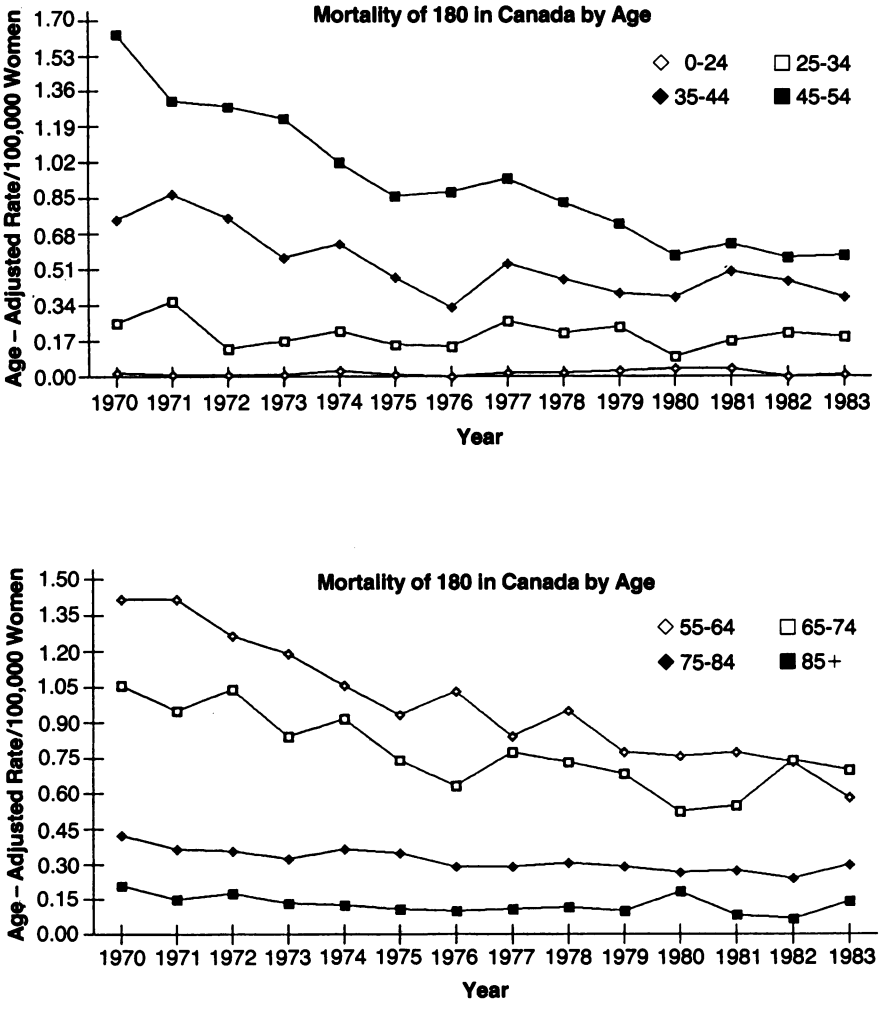
These definitions make it clear that family physicians do not, in general, screen; they case find.

Natural History

Most authorities agree that squamous cell carcinoma of the cervix progresses from normal to mild to moderate to severe dysplasia to carcinoma in situ and finally to invasive carcinoma. Different classification systems can be compared as follows: Class 1 is equivalent to a normal smear; Class 2 to mild dysplasia (also CIN 1); Class 3 to moderate or severe dysplasia (also CIN II); and Class 4 to severe dysplasia, carcinoma in situ, or invasive carcinoma (also CIS CIN III).[12]

There is evidence that, at least in younger women, mild and moderate

Figure 1
Mortality from Cancer of the Cervix in Canada



Source: Aileen Clarke, M.B., B.S., M.Sc.,
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dysplasia may revert to normal and that the human papilloma virus is involved in many of the cases that revert to normal.[13] This phenomenon must be clarified because these changes are being seen more frequently in smears from younger women, because patients may suffer from emotional upset caused by knowledge of an abnormality and by repeated examination, because of possible physical trauma from some methods of management that may lead to immediate or long-term effects, and because the need for long-term follow up may have economic consequences.[14–18]

The latent period for the development of carcinoma in situ subsequent to exposure is suggested to be approximately five to six years. This period is the same for all age groups.[19] Some authorities believe that the latent period of conversion from normal to moderately severe dysplasia is much shorter.[20,21] Progression from carcinoma in situ to invasive carcinoma takes one to two decades in most women,[22] but may be appreciably faster in a small minority.

The latent periods are under intensive study. Although much of the evidence indicates that the latent period for the development of invasive carcinoma is longer in younger than in older women, some evidence also suggests that the latent period may be much shorter than that previously quoted for younger women.[20,21]

We cannot yet explain why a woman can develop invasive carcinoma within one year of a satisfactory and normal smear. Did the system fail? If so, at what point did it fail, or is this another variable?[23,24] The debate over the conflicting evidence concerning the natural history has led to most of the varying recommendations about when to start performing Pap smears and how often to repeat them. It is likely that the changing sexual mores of the 1960s led to much of the variation in the natural history. It remains to be seen whether the AIDS scare will stabilize matters.

Table 1
Risk Factors

Prime
Sexual intercourse
Other
Age at first intercourse
Number of partners
Age at first pregnancy
History of sexually transmitted disease, particularly human papilloma
Also
Less than Grade 9 education
Low socio-economic status
Older age group
The high risk male
False-negative test
Screening less often than every 3 years
Smoking

Risk Factors

The risk factors for cervical cancer have been clearly identified (Table 1). All women who have been sexually active are at risk. Those not at risk include women who have never had sexual intercourse, women older than 60 years of age whose smears have always been negative, and women who have had a hysterectomy for benign disease.[25]

The specific risk factors include age at first sexual intercourse (as opposed to chronological age),[26] numbers of partners, age at first pregnancy, and a history of sexually transmitted disease (in particular human papilloma virus infection).[27,28]

Other factors include those who have never had a Pap smear before,[9] exposure to the high risk male,[25] false-negative test results,[24] poor or no follow up of abnormal test results, screening less often than every three years,[29] less than a Grade 9 education, low socio-economic status, and increased age.[9,30] Smoking is considered a facilitator,[31] and it is likely that human papilloma virus infection is also a facilitator.

Barriers to Screening

Barriers to a comprehensive screening process include, on an individual level, objections to screening by the patient or physician and, on a societal level, the uncommitted attitudes of government and the rulings of licensing bodies (Table 2).[32,33]

Patient Barriers. Many women, understandably, do not want to have a Pap smear. This may be because of a lack of knowledge, a lack of understanding, a fear of discomfort, or a question of the privacy of the individual's body. All these items may apply at any age. Many older women who have passed through their childbearing years no longer have regular contact with their physician and may feel that this examination and test is no longer necessary.[34]

Physician Barriers. Poor attitude and disorganization are the major barriers to screening posed by physicians. Many physicians are fully involved with their day-to-day health care. Organized preventive medicine

Table 2
Factors Influencing Implementation of Screening

Influential Agent	Barriers	Facilitating Factors
Patient	Objection to the procedure Lack of knowledge	Education
Physician	Attitude Organization	Education (personal and public) Use of reminders (tickler files, file markers, continuous patient profiles, flow charts, computers)
Governments	Espouse but do not support	Formal education (primary, secondary, university) Educational inserts in mailings Dedicated funds Support of registries Posters Information pamphlets
Licensing bodies	Forbid approaching patients who have not already agreed to receiving reminders	

takes second place to healing. In those circumstances, it is difficult to remember to remind women of the need for a Pap smear when they are seen for some unrelated disease. Licensing bodies further complicate the situation by not permitting physicians to remind those at risk that a preventive measure is necessary unless the patient and the physician have previously agreed that the physician should issue periodic reminders.[33] In addition, some fee schedules are designed so that preventive services can be rendered and remunerated, but others are not.[32]

Governmental Barriers. Governments, although espousing preventive medicine as policy, do not in general facilitate prevention. The situation is complicated by the attitude of governments to the use of health services. Were physicians to promote preventive care and to recruit all the population at risk, use of health care would be increased significantly, and governments would hold the profession responsible for this increase. If physicians were to engage in a new aggressive preventive program in their practices, this would show up in their billing profile, which might lead to an investigation by the provincial paying agency and the provincial licensing body.

Facilitating Factors

The most effective facilitator of appropriate screening would be a consensus statement supported by such authorities as the Canadian Cancer Association, the Society of Obstetricians and Gynecologists, and the College of Family Physicians of Canada.

Patient Facilitators. Patients can be sensitized to the need for regular Pap smears in the formal educational process and subsequently by exposure to appropriate information (Table 2). Governments, physicians, and the various associations must work in concert and broadcast the same message if patients are to be sensitized to the need for screening.

Physician Facilitators. There are adequate numbers of family physicians, as shown by the manpower studies of the federal government[35] and The College of Family Physicians of Canada. These family physicians have the facilities to provide a preventive service to their patients, but the inclusion of comprehensive preventive measures depends on attitude and organization. Attitude and organization will develop as a result of exposure to continuing medical education[36,37] and response to the pressures of patients. (The pressures from patients would arise as a result of their education in the formal educational setting and by the enclosures in the regular mailings from federal and provincial governments. These would be reinforced by releases through the media.) Family physicians have a responsibility to educate their patients about the value of Pap smears and particularly when they should be taken.

Family physicians can organize follow-up strategy by identifying patients at risk in their practice, either at the time of contact or in advance. The charts of those at risk can be identified at the time of contact, either by a coloured marker on the front of the chart or by the appropriate notation in a patient profile on the inside of the first page of the chart.[38] Flow charts may help to identify patients in advance, and come in several five-year packages encompassing childhood, adolescence, or adulthood, or that cover the patient's lifetime.[39,40]

Age and sex registers help, but are cumbersome and rapidly outdated if compiled by hand. Information retrieval is arduous.[41] Reminder, or tickler, files are of benefit, but only for patients who have been examined previously. For example, if a patient presents for a Pap smear in a given month and year, a file card can be made out for that patient noting test results. The file card can be recovered at the appropriate time for recall. In any month, the appropriate file cards can be retrieved. If a patient has not made arrangements for a further contact, she is reminded by phone or mail, provided physician and patient have agreed on the need for a reminder.

Computerization will make the identification of those at risk easier, provided the appropriate software is used (Table 2).[42,43]

I have heard it quoted that 78% of patients visit their family physicians in a given year. According to one authority, individuals visited their physician approximately five times a year.[43] Whether either or both of these figures is correct, today it is realistic to assume that the number of contacts between family physician and family members, whether in traditional practice settings, through emergency departments, or walk-in clinics, encompasses a major percentage of the population in a given year.

Provided there is a system for identifying the files of patients at risk, protecting these patients should become a simpler matter. Case finding could be expanded readily to provide comprehensive screening. Patient information sheets, alone or incorporated in a practice newsletter, will help, as will posters displayed in waiting rooms and examining rooms. Patients who use emergency departments at their local hospital for their primary care need to be reminded when attending these facilities of their need for preventive medical manoeuvres, such as Pap smears.

Many walk-in clinics provide comprehensive care, but others apparently do not. Those that do not perform Pap smears should be encouraged to do so or should direct patients to facilities where screening can and will be done. There is an urgent need for attractive, simple patient information sheets and posters of various sizes to display in physician's waiting rooms and examining rooms, public buildings, offices, bus shelters, and public lavatories to help educate those at risk of cervical cancer.[30,41]

Federal Government. The federal government could allocate funds for specific preventive programs. The Conference of Deputy Ministers of Health must be encouraged to continue sponsoring such task forces as The Walton Task Force on Cervical Screening[22] and the Task Force on The Periodic Health Examination,[11] which made recommendations over a wider spectrum of conditions. They must also ensure that the information generated by these task forces is available to physicians in an easily understood form. These task forces must have committed long-term funding to ensure continuity and thus the timeliness of their recommendations.[32]

The information generated must also be shared with all Canadians. This responsibility could be discharged by appropriate inclusions, such as pamphlets, in regular government mailings. The health of the pop-

ulation has been shown to be dependent on socio-economic conditions.[44] It is possible that the observed decline in carcinoma of the cervix prior to the introduction of screening programs was due to improved socio-economic conditions and better hygiene. To ensure good socio-economic conditions is a major responsibility of the federal government.

Provincial Governments. The major contribution of provincial governments could be the funding of registries, so that those at risk may be identified and appropriately followed, and the setting of educational standards, which should include mandatory health classes in primary and secondary schools, universities, and community colleges. Provincial governments could also enclose informative pamphlets with their regular mailings to constituents.

Local Governments. At a local level, health departments, through the provision and support of birth control clinics, sexually transmitted disease clinics, and other public health programs, can fill the gaps and provide the facilities for those at risk who, for whatever reason, do not have a family physician or do not wish to see their own family physician for internal examinations and Pap smears.

Screening Recommendations

The Walton Report in 1976[22] recommends that those who are sexually active when they are younger than 18 should have a Pap smear at 18 (Table 3).[11,22,32,45-51] If that smear is satisfactory and normal, another smear should be taken in one year. If that smear is likewise satisfactory and normal, further smears should be taken at three-year intervals until the age of 35. If these smears are satisfactory and normal, the patient should be examined at five-year intervals until she is 60. Women older than 60 who have had repeated satisfactory and normal smears may be dropped from the screening program.

The Task Force on The Periodic Health Examination[11] endorses these recommendations, giving them a "B" rating. (There is fair evidence to support the recommendation that the cervical cancer be specifically considered in a periodic health examination.)

The Consensus Development Conference on Cervical Screening[45] recommended that screening should begin at the onset of sexual activity. If the first smear is satisfactory and normal, it should be repeated in one year. If the second smear is satisfactory and normal, rescreening should occur at one- to three-year intervals. The woman and her medical care provider should jointly decide precisely how often screening should be repeated. If two smears are satisfactory and normal after the age of 60, further screening appears to be unrewarding.

The American College of Obstetricians and Gynecologists[46] in 1980 recommended annual screening for most

Table 3
Task Force Recommendations For Papanicolaou Test (1976-1988)

Year	Task Force	Initiation of Screening	Follow-up Examinations	Termination of Screening
1976	The Walton Task Force[22]	Age 18 if sexually active	If 2 normal at annual intervals, then every 3 years to age 35, every 5 years to age 60	Age 60
1979	Task Force on Periodic[11] Health Examination	Same	Same	Same
1980	Consensus Development[45] Conference	Onset of sexual activity	If 2 normal at annual intervals, then every 1–3 years at the discretion of patient and physician	If 2 annual tests are normal after 60, stop
1980	American College of Obstetricians and Gynecologists[46]	Annual screening for most women	If low risk, frequency at discretion of patient and physician	
1980	International Academy of Cytology[47]	Annual screening for all women	Annual intervals	
1982	Shun-Zhang, Miller, and Sherman[48]	Age 25	Triennially to age 52 or age 40, quinquennial to age 50	Age 60
1982	Walton Task Force Update[49]	Onset of sexual activity of age 18	Annually to age 35, every 5 years to 60	Age 60
1986	International Agency for Research on Cancer[50]	Age 25	Every 3 years	Age 60
1988	*CA—A Cancer Journal for Clinicians*[51]	Onset of sexual activity or age 18	If 3 normals at annual intervals, then less frequently at discretion of physician	

women in the U.S. They added that, because the choice of any screening interval is arbitrary and the factors dictating such a choice are complex, extending the screening interval in the low risk group should be an informed choice of the patient and her physician.

The International Academy of Cytology[47] in 1980 recommended annual screening for all women.

Shun-Zhang, Miller, and Sherman,[48] using a computer-simulated model, recommended that, with a 75% test sensitivity and an 80% population acceptance, a program designed to reduce mortality by 90% would commence screening at age 25, would screen every three years to age 52 or to age 40, and would screen every five years to age 60, a total of 10 tests in a lifetime. A repeat test at 26 did not decrease mortality. They added that additional modifications to the natural history specifications to accommodate high risk younger women would require a more frequent schedule of examinations under the age of 35, though at substantial cost in terms of the total number of examinations required in a population.

In 1982, the reconvened Walton Task Force[49] recommended the following:

- that there be no attempt to categorize high risk women;
- that women have Pap smears annually from the onset of sexual activity or age 18 until they are 35, and every five years between the ages of 35 and 60;
- that women older than 60 who have had repeated satisfactory smears that were normal be dropped from the screening program for squamous cell carcinoma; and
- that women older than 35 whose contact with the health care system is through venereal disease clinics or penal institutions and who, in their own judgement or that of their physician, are at high risk should not be discouraged from having smears more frequently than every five years if they request them.

In 1986, the International Agency for Research on Cancer published a book[50] titled *Screening for Cancer of the Uterine Cervix*, which suggested that triennial screening from age 25 provides close to maximal protection in most populations at present. The agency adds that it seems desirable to rescreen at the same frequency irrespective of age and to stop rescreening women older than 60, provided the woman has had at least two consecutive negative smears at appropriate intervals in the previous 10 years and no positive smears in that period.

The agency suggests that screening in a new program should aim at women between the ages of 35 and 60 to have the greatest immediate effects. Screening women 25 and older, with repeat smears every three years, should reduce the incidence of invasive disease by about 90%; screening women 25 and older, with repeat smears every five years, should reduce the incidence of invasive disease by about 80%.

The agency further comments that more intensive screening is unlikely

Figure 2
Recommended Screening Procedures

TIP
The introduction of prevention in primary care

TARGET
Squamous cell cancer of the cervix

MANOEUVRE
Papanicolaou smear

THE CHALLENGE
To ensure that all women who are at risk (who have been sexually active) have regular Papanicolaou smears

RECOMMENDATION
A Pap smear should be taken soon after the onset of sexual activity. If the first Pap smear is satisfactory and normal and is followed by at least one and preferably two further satisfactory and normal smears at annual intervals, testing should be repeated at least every three years to age 60. At 60, if there have been a series of satisfactory and normal smears, the woman may be dropped from further screening.

FACILITATORS

Pamphlets for patients	Patient profile inserts
Posters	Flow charts
Tickler files	Age and sex registers
Chart identifiers	Computer programs

to provide more than marginal improvement. Screening less often than every five years is likely to lead to a considerably smaller reduction in incidence. Screenings every 10 years after the age of 30, however, may reduce the incidence by two thirds. Some developing countries may now be able to apply this policy.

In 1988, *CA—A Cancer Journal for Clinicians*[51] published the following recommendation.

> All women who are or who have been sexually active or who are older than 18 should have an annual Pap test and pelvic examination. After a woman has had three or more consecutive satisfactory and normal annual examinations, the Pap smear may be performed less frequently at the discretion of her physician.[51]

This recommendation is endorsed by The American Cancer Society, The National Cancer Institute, The American College of Obstetricians and Gynecologists, The American Medical Association, The American Nurses Association, The American Academy of Family Physicians, and The American Medical Women's Association.

Many of these recommendations state in their preliminaries that the Pap smear is a drawing card and a memory jogger. It is recognized that presentation for a Pap smear is an opportunity for the physician to cover other areas of disease, and concern is expressed that if this drawing card is removed it will have a deleterious effect on patients individually and collectively.

Further, though screening for carcinoma of the ovary is not recommended for the individual patient, regular examinations may be indicated if the woman still has her ovaries (they may have been removed at hysterectomy for other than neoplastic disease) and as a means of monitoring the need for hormonal replacement. It is relatively easy for a woman to remember she needs a Pap smear every year, but remembering to have a Pap smear every third year is more difficult. This challenge must be met. It is difficult, and in my opinion, inappropriate, to neglect these factors when faced with the individual.

In the light of all that has been said and considering the patterns of practice in Canada, I suggest the following.

> A Pap smear should be taken soon after the onset of sexual activity. If the first Pap smear is satisfactory and normal, and this is followed by at least one (and preferably two) further satisfactory and normal smears at annual intervals, the smears should be repeated at least every three years until the patient is 60. At age 60, the woman may be dropped from further screening if there have been a series of satisfactory and normal smears (Figure 2).

We are challenged to see that all women who have been sexually active have Pap smears. ■

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