A Critical Review of Adult Health Maintenance

Part 3: Prevention of Cancer

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This is the third paper in a four-part series that presents an updated protocol for selective longitudinal health maintenance of asymptomatic adults. Selected types of cancer are reviewed with reference to six generally accepted screening criteria. A recommendation is made for each condition and compared, when appropriate, with the recommendations of the Canadian Task Force on the Periodic Health Examination and the American Cancer Society. In the fourth paper the recommendations will be combined into a practical health maintenance flow sheet for use by primary care physicians.

The purpose of this series of papers is to provide primary care physicians with an updated health maintenance protocol for asymptomatic adults that can be used in the everyday practice of medicine. The background and methods for this work were fully described in the first article of this series.[1]

This section will review the most common malignancies for compliance with regard to six generally accepted screening criteria for useful health maintenance interventions:

1. The condition must have a significant effect on the quality or quantity of life.
2. Acceptable methods of treatment must be available.
3. The condition must have an asymptomatic period during which detection and treatment significantly reduce morbidity or mortality.
4. Treatment in the asymptomatic phase must yield a therapeutic result superior to that obtained by delaying treatment until symptoms appear.
5. Tests that are acceptable to patients must be available at reasonable cost to detect the condition in the asymptomatic period.
6. The incidence of the condition must be sufficient to justify the cost of screening.

It is necessary for a disease to meet all six criteria before inclusion in the health maintenance plan. Failing a single criterion is adequate reason for exclusion.

A brief discussion of the rational for or against including each condition in a health maintenance program is presented, and a specific recommendation is compared with the most recent recommendation of the Canadian Task Force on the Periodic Health Examination[2] and that of the American Cancer Society.[3]

LUNG CANCER

Recommendation. Decreased use of tobacco is the best method of preventing lung cancer. Specific screening for lung cancer is not indicated.

American Cancer Society. Same recommendation.

Canadian Task Force. No screening for lung cancer is indicated.

Lung cancer incidence is rising so rapidly that any specific figure becomes quickly outdated. It is the leading cause of cancer death in men and is becoming the leading cancer killer of women. The disease becomes prevalent at about the age of 40 years, and the incidence rises progressively to the eighth decade. In 1984 the death rate from lung cancer was 70 per 100,000 men and 20 per 100,000 women.[4] The overall five-year survival rate is only 9 percent; it is 42 percent if the disease is localized and only 4 percent if spread has occurred.[4] Few cases are localized when diagnosed.

Since 80 percent of lung cancer is due to cigarette

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smoking,[5] it is theoretically preventable. Avoidance of cigarette smoking is the cheapest and most effective weapon in the fight against lung cancer.

Since many persons have smoked cigarettes for many years, however, and some cannot or will not quit, screening for early lung cancer detection has been attempted. Periodic chest x-ray examinations and sputum cytology testing have been the two methods used.

The American Cancer Society report on screening for lung cancer[3] reviews several early studies that failed to show any reduction in lung cancer mortality from x-ray or cytologic screening. All studies have been confined to screening high-risk cigarette smokers. No authority advocates screening the nonsmoking population for lung cancer.

One of these studies, the Philadelphia Pulmonary Neoplasm Research Project,[6] did chest x-ray examinations every six months on an uncontrolled population of smokers. Their five-year survival rate from lung cancer was only 5 to 8 percent.

Recently the National Cancer Institute's Cooperative Early Lung Cancer Detection Program has reported its early data on prevalence screening for lung cancer.[7,8] This study, started in the early 1970s, involves three centers. Two of the centers, Memorial Sloan-Kettering and Johns Hopkins University, are comparing annual chest roentgenograms with annual chest roentgenograms plus sputum cytology findings. The third center, the Mayo Clinic, is comparing chest roentgenograms and sputum cytology testing every four months with a control group getting chest x-ray examinations and sputum cytology testing annually. None of the centers has a control group receiving no screening for lung cancer.

The preliminary results of this cooperative study are interesting.[7] A great number of cancers are being detected (0.7 percent prevalence). Fifty-one percent have been stage I. Of the stage I lesions 47 percent were discovered by x-ray examination alone, 31 percent were discovered by sputum cytology testing alone, and 7 percent were discovered by both modalities. Sputum cytology testing was useful almost exclusively for detecting squamous cell carcinoma. Five-year survival rates for the study populations range from 35 to 55 percent.

These studies are intensive and expensive. At the Mayo Clinic screening is done every four months. At Sloan-Kettering three observers read each x-ray film to avoid false negatives, and 10 percent of the films require further evaluation.

The authors of the cooperative study[8] note that the longer survival time of their cancer patients does not allow any conclusion about the impact of screening on mortality from lung cancer. Furthermore, it is not clear that this type of intensive screening would be feasible in the community practice setting. There is currently no evidence that screening for lung cancer even in high-risk smokers is worthwhile.

COLORECTAL CANCER

Recommendation. Patients should have a six-slide stool occult blood test biannually between the ages of 40 and 50 years and annually thereafter.

American Cancer Society. Patients over the age of 40 years should have a digital rectal examination annually. They should have a six-slide stool occult blood test annually after the age of 50 years. Sigmoidoscopy for those aged 50 years should be done annually for two years, then every three years.

Canadian Task Force. Patients should have an annual stool occult blood test starting at the age of 46 years.

Colorectal cancer is the second leading cause of cancer death. The overall incidence is 45 per 100,000 persons rising from 15 per 100,000 population for those between the ages of 40 and 50 years to over 400 per 100,000 in persons aged over 80 years. The current overall five-year survival rate is 47 percent. Early detection is important. Localized disease has a 77 percent five-year survival rate, while disease with distant spread has only a 29 percent five-year survival rate.[4]

The three methods recommended as screening tests for colorectal cancer—digital rectal examination, sigmoidoscopy, and testing stools for occult blood—have recently been reviewed by Diehl.[9]

Digital rectal examination as a screening test for colorectal cancer is a test long on tradition and short on substance. Even supporters of its use admit that "this examination is so old and time honored that no formal studies of effectiveness have been thought necessary."[3] Indeed Hertz and colleagues[10] found only 9.5 percent of 58 cancers diagnosed by sigmoidoscopy were palpable by rectal examination. One has only to consider the length of the finger compared with the colon to realize that 90 percent of colorectal cancers will be missed by rectal examination. Rectal examination may even be counterproductive in that the more uncomfortable screening tests the physician suggests, the less likely patients will be to get involved in a screening program.

Sigmoidoscopy has been shown in several studies to detect colorectal cancer at early stages. All the studies have been done using the 25-cm rigid sigmoidoscope. Gilbertsen found one cancer per 783 initial sigmoidoscopies.[9] These patients had a 64 percent five-year survival rate. On 92,000 subsequent sigmoidoscopies only 13 cancers were found, for a rate of about 1 per 7,000 examinations. Many adenomatous polyps were removed in these patients, and Gilbertsen attributes the low number of cancers found to the removal of adenomatous polyps.

A randomized controlled study of the multiphasic health examination done by the Kaiser Health Plan found decreased mortality from colorectal cancer in

the study group screened by rigid sigmoidoscopy and digital rectal examination compared with the control group.[11]

Hertz et al[10] found 58 cancers as a result of a screening program of 26,000 patients examined over nine years by sigmoidoscopy and rectal examination. He excluded seven patients with advanced disease at the time of diagnosis and claimed an 88 percent five-year survival rate in the other patients.

Flexible sigmoidoscopy is rapidly replacing rigid sigmoidoscopy for visualization of the lower bowel. The 60-cm flexible sigmoidoscope will detect two to three times as many neoplastic lesions as the rigid sigmoidoscope.[12] Flexible sigmoidoscopy is claimed to be more comfortable than rigid sigmoidoscopy but is technically more difficult to master. The procedure takes longer and costs about $100 per examination. Some experts feel the 60-cm flexible sigmoidoscope is too difficult for primary care physicians to master as a screening technique.[13] Personal experience supported by that of Rodney et al[12] is that primary care physicians can easily learn flexible sigmoidoscopy. Flexible sigmoidoscopy has not been tested in any large-scale screening program of asymptomatic patients.

Sigmoidoscopy has serious drawbacks to its use as a routine screening procedure. First, it is uncomfortable, and patient compliance is poor unless symptoms are present. In the study by Hertz et al of 26,000 patients over nine years, only 47,000 sigmoidoscopies were done (1.8 per patient).[10]

In the Kaiser Health Plan study only 60 percent of the study group showed up for testing each year, and only one third of these (20 percent of the total study group) received sigmoidoscopy.[3] Improved compliance with flexible sigmoidoscopy is being obtained at the family medicine residency of San Bernardino County Medical Center. In that program 35 percent of new asymptomatic patients had flexible sigmoidoscopy. Follow-up data on repeat examinations are not available.[14]

Second, sigmoidoscopy will miss a large number of cancers. It has been said that 70 percent of colorectal cancers were within reach of the rigid sigmoidoscope. Recently, however, the distribution of neoplasia has shifted toward the right colon, so that now perhaps 60 percent of cancers are within reach of the flexible sigmoidoscope.[15]

Third, sigmoidoscopy is expensive. The aggregate cost of screening the 60 million people aged over 50 years in the United States every three years by flexible sigmoidoscopy at $100 per examination would be $2 billion per year. A family physician with 1,000 patients aged over 50 years in his practice would do two flexible sigmoidoscopy examinations every working day just for screening. An internist with an older patient population might have to do several times that many. Finally, sigmoidoscopy is invasive, although serious complications are rare.[3]

Testing stool samples for occult blood has been promoted widely as a screening procedure for colorectal cancer since 1971. The test is usually done by testing two samples from each of three bowel movements for occult blood using one of several commercial kits while the patient is on a meat-free high-roughage diet. The test is inexpensive, costing the physician less than $1 and the patient $2 to $5. Patient compliance is about 75 percent in both the private practice and research setting.[16,17] Occult blood testing takes little physician time and theoretically detects cancer from all parts of the colon.

Numerous uncontrolled studies have shown one to two cancers detected per 1,000 persons screened. About 3 to 5 percent of slides returned will be positive for occult blood.[9]

Two controlled studies of the effectiveness of stool occult blood testing are currently in progress. A study by Winawer et al[17] at the Strang Clinic in New York is comparing sigmoidoscopy plus stool occult blood testing of the study group with sigmoidoscopy alone as a screening procedure in the control group. Preliminary results are favorable in that 74 percent of cancers are localized (Dukes A or B) in the study group compared with 33 percent localized in the control group screened by sigmoidoscopy alone. Sixty-one percent of the cancers in the study group were detected by positive stool occult blood tests, with negative rigid sigmoidoscopy findings.

A separate study in Minnesota is comparing three groups: (1) a study group receiving annual stool occult blood testing, (2) a study group receiving biannual stool occult blood testing, and (3) a control group receiving usual care.[18] Preliminary results are promising in this study also, with 74 percent of cancers detected in a localized stage. Proof that stool occult blood testing does or does not reduce mortality from colorectal cancer will not be available until these two studies are complete.

Stool occult blood testing has drawbacks. It is specific for blood, not cancer. Many of the 2 to 5 percent of patients with positive tests will not have cancer or polyps but will need to undergo an extensive workup, including colonoscopy and barium enema. In the study by Winawer et al[17] the predictive value for neoplasia was 27 percent for persons aged 40 to 49 years, which increased to 52 percent for persons aged over 70 years.

Cancers will be missed by stool occult blood testing. The exact number is not known for certain, but one study found a sensitivity of 71 percent.[9]

The recommendation of a six-slide stool occult blood test biannually between the ages of 40 and 50 years and annually thereafter is based on the feasibility of stool occult blood testing in terms of cost and patient compliance. Final proof of effectiveness is not yet available, but early results are promising. In contrast, sigmoidoscopy is not feasible as a screening test in asymptomatic patients; it is expensive and despite significant promotion, patient and physician compliance is poor.

BREAST CANCER

Recommendation. All women should (1) do monthly breast self-examination, (2) have a physician breast examination biannually to the age of 50 years and annually thereafter, and (3) have annual mammography after the age of 50 years.

American Cancer Society. All women should (1) do monthly breast self-examination, (2) have a physician breast examination every three years between the ages of 20 and 40 years and annually thereafter, and (3) have a mammogram for baseline purposes between the ages of 35 and 40 years, every one to two years between the ages of 40 and 50 years, and annually thereafter.[19]

Canadian Task Force. All women should have an annual physician breast examination and mammography between the ages of 50 and 59 years.*

Breast cancer is the leading cause of cancer death in women. The overall incidence is 89 per 100,000 women, rising from 57 per 100,000 women aged 35 to 40 years to 300 per 100,000 women over age 80 years. The overall five-year survival rate is 68 percent. Localized disease has an 88 percent five-year survival rate, which drops to 50 percent if spread has occurred at the time of diagnosis.[4]

The major controversy in screening for breast cancer is the role of mammography. The debate started following publication of the results of the Health Insurance Plan (HIP) of Greater New York study, a randomized controlled study of yearly mammography, physician examination, and patient self-examination for the detection of breast cancer.[20] The HIP results showed a 30-percent reduction in breast cancer mortality in the study group for women aged over 50 years. There was no statistically significant difference in mortality for women under the age of 50 years.

The Breast Cancer Detection Demonstration Projects (BCDDP) have shown a large number of early cancers detected by mammography.[21] Fewer than 20 percent of cancers detected in the BCDDP centers had lymph node spread. Forty-one percent of cancers were detected by mammography alone. Thirty-five percent of cancers found in women aged between 40 and 49 years were found by mammography alone.[21] Unfortunately, the BCDDP was designed to study the feasibility rather than the value of screening for breast cancer. There was no control group, and mortality data were not reported.

A recent randomized controlled trial of mammography screening for breast cancer in Sweden[22] showed a 40 percent reduction in breast cancer mortality among screened women aged between 50 and 74 years. No significant reduction in mortality was demonstrated in screened women aged less than 50 years. In this study mammography done every two to three years was compared with no screening for breast cancer.

Two case control studies from the Netherlands also show a reduced risk of dying from breast cancer in a population screened by mammography. The Utrecht study reports the relative risk of dying from breast cancer among women screened by mammography compared with those never screened to be 0.30.[23] A study from Nijmegen reports a relative risk of dying from breast cancer of 0.48 for women screened by mammography compared with controls who did not get mammograms.[24] Neither of these studies was able to show decreased mortality from breast cancer in screened women aged less than 55 years.

The radiation risk of a mammogram done with modern equipment is very small, equivalent to the radiation exposure from riding 400 miles in an airplane.

Opponents of routine mammography point out that none of the studies has separated out the incremental effect of mammography from that of physician breast examination and patient self-examination. Uncontrolled studies have shown both physician examination and self-examination to detect breast cancer earlier than found in unscreened populations.[25-27] Eddy[28] estimates the incremental value of mammography to be about 10 percent. That mammography detects some lesions before they are palpable does not necessarily mean survival time is better if mammography is included in a screening program.

The question of the incremental value of mammography is especially important since the cost is enormous. The average mammogram in the United States cost about $100 in 1982.[29] If 33 million women over the age of 50 years in the United States were to receive annual mammograms, the total cost would be $3.3 billion per year. A typical family physician would refer four or more patients for mammography every working day.

The cost of mammography should not be so high as it is. State-of-the-art mammography equipment could be bought for under $50,000 in 1985, which is not expensive when compared with other x-ray equipment. There is no reason mammograms could not be done profitably for under $40.

The Canadian government has established a National Breast Screening Study to address some of the unanswered questions about mammography.[30] This controlled study will specifically compare screening women aged over 50 years by mammography plus physician and self-examination with screening by physician and self-examination of the breasts alone. In women aged under 50 years it will compare screening

*The 1985 update recommends annual mammography and physician breast examination for all women aged over 50 years. Canadian Task Force on the Periodic Health Examination. The Periodic Health Examination: 2. 1985 Update. *Can Med Assoc J 1986; 134:724-727.*

by all three modalities with no organized screening. Unfortunately, the results of this study will not be available until the 1990s.

Cost is the crux of the mammography issue. If a mammogram cost no more than a stool occult blood test, physicians would be ordering them while waiting for the final proof of efficacy. Reducing the cost of mammography should be a major priority.

The appropriate interval for doing mammography is not known. The Swedish and Netherlands studies used less frequent than annual screening and still achieved good results. Quite possibly mammograms every two years would be just as good as annual examinations.

In spite of these unanswered questions, the accumulation of data from the HIP, BCDDP, Swedish, and Netherlands studies shows impressive evidence that mammography is effective in women aged over 50 years. There is little evidence of reduced mortality from breast cancer screening in younger women. Despite the cost of mammography, therefore, it is recommended annually for women aged over 50 years.

PROSTATE CANCER

Recommendation. No screening for prostate cancer is indicated.

American Cancer Society. Digital rectal examination is recommended annually for men aged over 40 years. (Prostate cancer is not specifically discussed.)

Canadian Task Force. No screening for prostate cancer is indicated.

Prostate cancer is the third leading cause of cancer death in men. The overall evidence is 56.3 per 100,000 men. Significant risk starts between ages 55 and 60 years with an incidence of 68 per 100,000. It rises progressively to the impressive rate of 1,000 per 100,000 men aged over 80 years.[31] The overall five-year survival rate from the cancer itself is reported to be 63 percent, 77 percent for localized disease, and 39 percent for advanced disease.[4] Five-year survival rates may not represent cure, but merely the slower progression of the disease.

The variable and incompletely understood natural history of prostate cancer makes determining whether a given screening procedure is effective very difficult. Prostate cancer is staged as follows:[32] Stage A is occult disease not clinically detectable, which is diagnosed only by biopsy, transurethral resection of the prostate for benign disease, or at autopsy. Stage B is disease clinically detectable by rectal examination but confined to the prostate gland. Stage C is disease spread to the seminal vesicles but not the pelvic lymph nodes. Stage D means distant spread to pelvic nodes or other sites, especially bone.

Autopsy studies have shown that fully 46 percent of men aged over 70 years have prostate cancer, mainly stage A.[33] Of these, the disease is suspected clinically in only 8 percent. Klein[34] states that 7 to 40 percent of stage A tumors will progress. Many men, perhaps the majority with prostate cancer, will have asymptomatic occult disease, never be aware of it, and die of other causes. Once progression occurs, it is often insidious, so that a large number of patients initially thought to have stage B disease will actually be stage C or D.[34] In several series only 7 to 20 percent of cases detected were stage B.[32,34,35]

Treatment of localized prostate cancer (stage A or B) for cure is effective but is expensive and intensive, involving pelvic lymphadenectomy for staging and either radical prostatectomy or radiation therapy.[32] There is not full agreement among urologists as to which stage A lesions should be treated and how aggressively.[32,34] Murphy et al,[35] reporting a series of 426 cases treated at Roswell Park Memorial Institute, showed that only 13 percent of patients diagnosed as stage B progressed to stage D. In this series, however, only 43 percent of patients died of prostate cancer. Mean survival time from all causes was 3.8 years for stage A patients, 3.7 years for stage B, 3.4 years for stage C, and 2.0 years for stage D. The mean difference in survival time from all causes between stage B and D patients was only 1.7 years.

Among the possible screening tests for prostate cancer, digital rectal examination is the best. Guinan and colleagues[36] compared rectal examination with several methods of acid phosphatase determination and cytologic methods in a population of men with symptoms of urinary tract obstruction. This population had a 23 percent prevalence of cancer as determined by biopsy. Rectal examination had a positive predictive value of 67 percent, a negative predictive value of 91 percent, and an 85 percent efficiency in this symptomatic population. None of the other tests was as good. Of course, in an asymptomatic population with a lower prevalence of cancer, the efficiency of rectal examination would not be so good.

Gilbertsen[37] reported a study in 1971 in which 75 patients were found to have prostate cancer on periodic rectal examination. These patients were aggressively treated and had a five-year survival rate of 77.3 percent. No information was given about the stage of the cancers detected or whether any cancers were missed by screening. The men undergoing curative resection were young (aged between 48 and 72 years) and probably not representative of the population at risk for prostate cancer. Chodak and Schoenberg[38] also found a large number of early cancers in an uncontrolled screening program. Recently Thompson et al[39] reported a urologic screening program of 2,005 men that detected 17 prostate cancers. Only three of these were localized stage B cancers. He concludes that the rectal examination is an insensitive screening procedure for early prostate cancer.

It is not known that periodic rectal examination will

detect early prostate cancer in a significant number of cases. Even if such examination does, the variable natural history of the disease and its occurrence in a population prone to death from other causes make uncertain the benefit of curative treatment.

A properly controlled study of screening for prostate cancer should be high priority.

CANCER OF THE UTERINE CERVIX

Recommendation. A Papanicolaou smear should be done every two years after two annual smears on all sexually active women aged less than 70 years.

American Cancer Society. Women 20 years of age and over and those aged under 20 years who are sexually active should have a Papanicolaou test at least every three years after two initial negative tests one year apart.

Canadian Task Force. Women aged between 18 and 35 years should have a Papanicolaou smear annually. A Papanicolaou smear should be done every five years between ages 35 and 60. No Papanicolaou smears are necessary after the age of 60 years.[40]

When discussing the natural history of cervical cancer, it is necessary to distinguish between invasive cancer and carcinoma in situ. Invasive cervical cancer has an incidence of 13.0 per 100,000 population. It is uncommon in women aged under 40 years but rises to an incidence of about 28 per 100,000 women aged over 50 years.[31] The incidence remains at this level in older women, even those aged over 75 years. The incidence of invasive cervical cancer in the United States has declined steadily since the 1950s.[41] Stage I invasive cervical cancer has a five-year survival rate of 80 percent. Stage III has only a 30 percent five-year survival rate.[4] There has been no improvement in survival time by stage in the past 25 years.[42] The overall five-year survival rate is 68 percent.[4]

Carcinoma in situ was rarely diagnosed before the introduction of the Papanicolaou smear in the 1940s. The reported incidence has increased markedly since then, and carcinoma in situ is now three times more common than invasive cancer.[4] It is a disease of young women. The incidence peaks at age 34 years and falls rapidly after the age of 40 years.[41] Carcinoma in situ is uncommon in women aged over 60 years.

The five-year survival rate for carcinoma in situ is virtually 100 percent. Risk factors for cervical cancer include sexual frequency, multiple sex partners, age of first intercourse, and low socioeconomic class. Black women have twice the incidence of cervical cancer found in white women.

It is generally agreed that cervical cancer develops progressively from an early focus of dysplasia to carcinoma in situ to invasive cancer. The time necessary for this progression to occur is variable and a subject of great controversy. Richart and Barron[43] report a mean transit time from mild dysplasia to carcinoma in situ of 5.8 years. They report a mean duration of carcinoma in situ of 10 years but state 5 percent will become invasive in less than three years. Others have reported a 22-year duration of carcinoma in situ.[3] The consensus is that it takes eight to 30 years for most carcinoma in situ to become invasive cancer.[3,43]

Not all carcinoma in situ will become invasive cancer. Between 30 and 60 percent of carcinoma in situ cases will spontaneously regress without treatment. It is not known whether invasive cancer can occur in the absence of previous carcinoma in situ.

The Papanicolaou smear is the only test seriously considered as a screening procedure for cervical cancer. Although some controversy remains,[41] there is a large body of evidence that Papanicolaou smear screening does reduce the incidence and mortality from invasive cervical cancer. The evidence comes mainly from comparing areas without screening programs, such as Norway, with areas that have screening programs, such as Denmark and Sweden.[42] In Iceland[44] the mortality from cervical cancer was rising until a screening program was initiated. Following initiation of a Papanicolaou smear screening program, a twofold reduction in cervical cancer mortality was achieved.

The Papanicolaou smear has a reasonable cost and is accepted by patients and physicians. It is not perfect. False-negative results can occur as a result of inadequate sampling or misreading the slides, even with good technique and interpretation. Estimates of the false-negative rate for Papanicolaou smears vary from 5 to 50 percent.[43] Thirty percent seems to be a commonly agreed average false-negative rate under normal conditions.[3,43]

With most of the evidence supporting Papanicolaou smear screening for cervical cancer, the major controversy is how often should Papanicolaou smears be done. Only two variables affect the decision of how often Papanicolaou smears are indicated: the sensitivity of the screening test and the rate of progression of the disease. Knox[45] calculated the effectiveness of varying screening intervals assuming 80 percent sensitivity of the Papanicolaou smear and a mean interval between detectability and the development of invasive disease of six years. Eddy[28] did a similar analysis assuming a 50 percent sensitivity of the Papanicolaou smear and an eight-year duration of disease before becoming invasive. Both analyses support a three-year interval between Papanicolaou smears to be cost effective.

Although critics, including the reconvened Canadian Task Force,[40] have argued that high-risk groups need to be screened more often, there is no evidence that cervical cancer progresses more rapidly in high-risk persons.[42] Even if a disease has a 100 percent incidence in a given population, if it has a ten-year detect-

able and curable period and the screening test is 70 percent sensitive, virtually all cases will be detected with a three-year screening interval. It is true and very important that more intensive efforts need to be made to get high-risk patients involved in the screening program. They do not, however, need to be screened more often.

Recently several articles have demonstrated that Papanicolaou smear screening is not perfect. Brown and Barker[46] analyzed 63 cases of invasive cervical cancer diagnosed over ten years in a screened population. Fifty-three percent of these cases had not had a Papanicolaou smear within two years. Thirty percent had abnormal smears but inadequate follow-up. Only 17 percent of the cases were due to false-negative Papanicolaou smear results. Bain and Crocker,[47] arguing for annual Papanicolaou smear screening, reported a series of 130 cases of in situ or invasive carcinoma diagnosed at a large hospital over a 13-year period. Thirty-three of these cases had had one or more Papanicolaou smears in the past three years. Six cases were invasive, the rest were carcinoma in situ. They downplayed 11 cases that had had negative smears within one year (five cases within 2.5 months) and used the remaining 19 cases to argue that annual screening was needed. They failed to appreciate that the diagnosis of curable carcinoma in situ is a triumph of screening, not a failure.

In 1975 the recommendation of biannual Papanicolaou smears after two negative smears was a compromise between the traditional practice of annual Papanicolaou smears and evidence indicating an every three-year interval was sufficient.[48] The evidence has not changed, and the American Cancer Society's recommendation remains appropriate. However, that people scheduled every three years may actually be screened less often is a concern. Furthermore, the author is uncomfortable stopping screening at age 60 or 65 years given the fact that the incidence of invasive cervical cancer does not decline in older women. Therefore, and considering the current controversy, biannual Papanicolaou smear screening continues to be the favored recommendation.

ENDOMETRIAL CANCER

Recommendation. Women should be taught to report postmenopausal bleeding.

American Cancer Society. Women should report postmenopausal bleeding. High-risk women should have an endometrial tissue sample at menopause.

Canadian Task Force. Not reviewed.

The incidence of endometrial cancer has increased dramatically in the past few decades to a current rate of 30.0 per 100,000 women in the United States,[31] with significantly higher rates in some areas such as San Francisco.[49] A disease of perimenopausal and postmenopausal women, endometrial cancer has an age-specific incidence of 30 per 100,000 women aged between 45 and 50 years, which rises to 114 per 100,000 women aged between 65 and 69 years.[31] Risk factors include obesity, infertility, and estrogen use.

The natural history of endometrial cancer is important to the discussion of screening and prevention. Although progression rates vary, endometrial cancer is usually felt to be the end stage of changes of endometrial hyperplasia.[50] It is estimated that early cystic adenomatous hyperplasia progresses to cancer 5 percent of the time. Twelve percent of cases of adenomatous hyperplasia progresses to cancer in five to 15 years, and 30 percent of atypical adenomatous hyperplasia will progress to cancer.[51] Thus many cases of adenomatous hyperplasia do not become cancer.

Endometrial cancer is a highly curable disease. Currently 75 percent of cases are detected in stage I even without widespread screening.[51] The overall five-year survival rate is 79 percent, 90 percent for localized disease, and 40 percent once distant spread has occurred.[4] Eighty percent of women with endometrial cancer have abnormal bleeding.[51]

The Papanicolaou smear is not a good screening test for endometrial cancer. A number of histologic and cytologic sampling techniques are available with up to 90 percent sensitivity.[51] Histologic sampling with a Novak curette, Vabra aspirator, or other products is most accurate, but it can cost $50 to $100 and causes significant patient discomfort, especially in older women.[51] Cytologic techniques using such devices as the Gravlee Jet Washer or Mi-Mark are less expensive (cost $10 to $15 plus office visit) and more comfortable but do not easily distinguish grades of adenomatous hyperplasia.[51]

In one study of an initial screening program of asymptomatic women by cytologic techniques, eight cancers and eight cases of adenomatous hyperplasia were found in 1,280 women.[50] Seventeen percent of women aged over 70 years could not be sampled. No analysis of compliance with repeat screening or effect on mortality was made.

Endometrial cancer is a highly curable disease without screening. Eighty percent of women will have abnormal bleeding. In a large study of periodic health examinations using no specific screening protocol for endometrial cancer, seven cases were detected. All were symptomatic. The five-year survival rate was 100 percent.[52] In view of these facts it is doubtful that screening by any endometrial sampling technique would significantly improve survival time in asymptomatic women, and it is probable that many unnecessary hysterectomies would be done for adenomatous hyperplasia. There is no direct evidence that a single sample of high-risk women at menopause is beneficial.

Women should be instructed to report

postmenopausal bleeding. No other screening test for endometrial cancer is indicated.

OVARIAN CANCER

Recommendation. There is no evidence that screening for ovarian cancer is worthwhile.

American Cancer Society. Screening for ovarian cancer is not specifically discussed. Women aged over 40 years should have an annual pelvic examination.

Canadian Task Force. Not reviewed.

Ovarian cancer is less common than either cervical or endometrial cancer but is the most lethal gynecologic malignancy. The overall incidence is 14.4 per 100,000 women. It becomes a problem at about the age of 35 years and rises to an incidence between 40 and 50 per 100,000 women aged over 60 years.[31] Risk factors for ovarian cancer include infertility or increasing years of ovulation. Use of oral contraceptives may be protective.[53]

The natural history of ovarian cancer is incompletely understood, but ovarian cancer is felt to be a rapidly growing cancer with few signs or symptoms of early disease.[54] Early metastasis is common. Two thirds of women have advanced stage III or IV disease when diagnosed.[53]

Survival rates are directly related to the stage at diagnosis. The overall five-year survival rate is 35 percent, 81 percent for localized disease, and only 20 percent for advanced disease.[4] There is some evidence that treatment has improved in recent years, although the vast majority of women with ovarian cancer die of the disease. Young[53] reports a 10 percent decrease in the overall death rate between 1970 and 1980 and a 33 percent improvement for women aged less than 50 years. He attributes this improvement to better staging, total abdominal radiation, and combination chemotherapy, not to earlier diagnosis.

Given that the five-year survival rate for stage I disease is 80 percent, an accurate method of early detection would be expected to lead to a major improvement in survival time. Unfortunately, no adequate screening test is available. The annual pelvic examination is frequently mentioned as the best screening test for ovarian cancer and is advocated by many groups including the American Cancer Society.[3,55,56] However, there is no evidence that annual pelvic examinations significantly increase the detection of early cancer or improve survival rates.[4,54,55] Jenson et al[52] reported only a 12.5 percent five-year survival rate for women with ovarian cancer diagnosed as part of an annual screening program.

Because of the failure of the pelvic examination to detect early ovarian cancer, a large number of other modalities have been investigated including cervical and peritoneal cytology, ultrasound, tumor-associated antigens, and biochemical markers. Smith and Oi[55] have published an exhaustive review of this work. Unfortunately, no adequate screening test for ovarian cancer has been found.

Without evidence of effectiveness, the annual pelvic examination should not be recommended just because there is nothing better.

BLADDER CANCER

Recommendation. No specific screening is indicated. Avoidance of cigarette smoking is the most effective prevention.

American Cancer Society. No recommendation.

Canadian Task Force. No screening tests are recommended for the general population. Cytology studies might be considered for high-risk groups.

The incidence of bladder cancer has risen 51 percent since 1939.[57] The overall incidence in men is 22 per 100,000, and in women is 7.6 per 100,000.[31] A significant problem in persons aged over 50 years, bladder cancer is more common in urban areas. Dyestuff workers, rubber workers, and leather workers are at increased risk.[57] Cigarette smoking doubles a person's risk of developing bladder cancer and is now a more important cause than occupational exposure.[57]

The natural history of bladder cancer is variable.[58,59] Most cases are slow-growing papillary tumors; however, a few progress quite rapidly. Eighty-two percent of cases are detected when localized, but the effectiveness of treating localized disease is uncertain.[57] The overall five-year survival rate is 54 percent, 60 percent for localized disease, and only 12 percent if spread has occurred.[4]

No authorities have recommended screening the general population for bladder cancer because of its low incidence.[60] Screening has been studied for workers in high-risk industries. Initially examination for hematuria was used as the screening test; however, urinary cytology studies have been shown to be more sensitive and specific than has examination for hematuria.[61] Cytologic testing tends to detect more aggressive, unfavorable cases of cancer and not detect slower growing, more treatable cases.[57,58] It is not clear whether the survival rate of patients with bladder cancer detected by screening is better than that of patients who had symptomatic cases.[57]

Reduction of cigarette smoking is the best way of preventing bladder cancer. Even in high-risk groups it is not certain that screening by urinary cytology testing yields a significant improvement in survival time.

SELF-EXAMINATION FOR CANCER OF THE SKIN, ORAL CAVITY, AND TESTES

Recommendation. Patients should be taught self-examination of the mouth, neck, skin, and testes.

American Cancer Society. No recommendation.

Canadian Task Force. No recommendation.

Testicular cancer has an overall incidence of 3.5 per 100,000 men.[31] In contrast to many other cancers, the peak incidence is between 25 and 40 years. White men are at higher risk than black men. Cryptorchidism and higher social class are also risk factors. Five-year survival rates depend on the cell type. Seminoma, the most common type, has the best prognosis. The overall five-year survival rate is 82 percent.[4] Testicular cancer is amenable to detection by palpation, and early detection improves survival. No studies of screening effectiveness have been done.

Cancer of the oral cavity includes several tumors including cancer of the lip, which is slow growing and has a 90 percent five-year survival rate, and cancer of the mouth and tongue, which is more rapidly progressive and has a 50 percent five-year survival rate.[62] The overall incidence in the United States is about 10.2 per 100,000 men and 3.3 per 100,000 women.[62] Smoking or chewing tobacco is the major risk factor. Ninety percent of cases occur in patients aged over 45 years.

Skin cancer, including basal cell and squamous cell carcinomas, are the most common of all cancers; however, they do not often metastasize and even without screening are rarely a cause of severe morbidity or mortality. Thus, they do not warrant screening. Melanoma, however, does cause significant mortality if not detected early and treated aggressively. Melanoma is mostly diagnosed in patients aged over 35 years and has an overall incidence of about 6.1 per 100,000 population.[31] The overall five-year survival rate is 79 percent.[4] Melanoma is more common in persons living closer to the equator and those involved in nonmanual labor.[63]

Each of these cancers, testicular cancer, cancers of the oral cavity, and melanoma, is theoretically detectable by palpation or examination. No organized screening has been shown to be effective for any of them. Because of their low incidence it is not likely that screening for them would be cost effective. It does seem prudent, however, to educate patients to examine themselves and report any new lesions of the mouth, skin, and testes.

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