

Early Detection And Mass Screening For Cancer

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SUMMARY The author reviews the evidence for the efficacy of early detection and mass screening programs in reducing morbidity and mortality from cancer. In cancer of the cervix, although screening reduces morbidity, we still do not have evidence for reduction in mortality. In cancer of the breast, one study suggests a reduction in mortality in the 50-59 year age group following screening by clinical examination and mammography. In other sites, especially lung, there is no evidence at present to support the adoption of mass screening programs. It is important that such programs should be carefully evaluated in the population, preferably in controlled studies.

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FEW PEOPLE WOULD question the value of diagnosing cancer promptly if a patient reports with symptoms; the benefit to the patient in terms of easier treatment and relief from anxiety is obvious even if the hope that treatment will be given before metastases have occurred may only occasionally be realized.

The controversy over early detection, and especially mass population screening for cancer arises from doubts of the value of extending diagnostic procedures to asymptomatic, apparently fit people. And this is in terms both of the efficacy of the various procedures and their yield.

Cancer of the Cervix

At first sight, cancer of the cervix is ideal for early detection. Not only is there an identifiable precursor of invasive carcinoma (in situ carcinoma) but this can be demonstrated with a high degree of accuracy by the Pap smear, providing the smear is taken and examined with skill. No wonder the conclusion has been drawn that "... if widely and wisely applied, the present generally accepted methods of detection and treatment of preclinical carcinoma of the cervix are capable of almost eliminating death from this disease".¹

The British Columbia screening program for cancer of the cervix began in 1949, and began to reach an appreciable proportion of the population in 1955; an estimated 75 percent of the female population aged 20 or more had been screened at least once by 1966.² Even so, in 1968, it was not possible to demonstrate any impact of this program on the mortality from cancer of the cervix in B.C. compared with Ontario and the rest of Canada.³ In the meantime, screening for cancer of the cervix has been widely and increasingly used and is now available in all provinces of Canada. There seems little doubt that the incidence of cancer of the cervix decreases in populations where

screening is practiced^{2, 4, 5, 6} although even this has been disputed, at least for New Zealand.⁷ Screening programs are more likely to detect disease with a long pre-symptomatic stage than a short one, and it is likely that people with the former have a better chance of survival than those with the latter. Evidence that people with an inherently poor prognosis can indeed be missed in screening programs for cancer of the cervix appears in a recent study in Norway.⁶

Does screening really reach the people who are at highest risk for developing cancer of the cervix? Evidence that this may not be so came from a survey in British Columbia,⁸ where it was shown that the women who were least likely to have heard of the test were those in the lower household income groups living in the large urban centers and aged under 30 or over 50. Yet these are the people who are probably most at risk.

If it is difficult to persuade people to be screened once, it may be even more difficult to persuade them to be re-screened.⁶ But to eliminate a condition associated with sexual activity, it may be necessary to screen a woman periodically throughout her active sexual life. How often this should be done we do not know, though an estimate of the time taken for carcinoma in situ to progress to invasive cancer — 12 years² — suggests that an annual smear may be unnecessarily frequent and that in the absence of symptoms after one repeat normal smear (to eliminate initially false-negative smears) a follow-up smear every five years may be adequate.

Many people find it difficult to accept that it is possible to reduce the incidence of a disease in a population without reducing its death rate. One possible way out of this difficulty is to postulate two different forms of cancer of the cervix,⁹ one essentially benign tending to occur in younger women and preceded by a phase of carcinoma in situ, and the other more malignant occurring in older

women and preceded by only a very short in situ phase, if any. Whether this second group is important has been queried,² as has the method of analysis on which the occurrence of the two varieties of cancer was postulated, though there has been some support for the concept from the results of one screening program.⁶

Although a desirable object of a screening program is reduction of morbidity, it would be difficult to justify the continuation of *mass* screening programs unless reduction of mortality could be demonstrated. Although mortality reduction has been claimed for one screening program,¹⁰ the British Columbia results will be critical because of the length of time the program has been operating and the extent of population coverage achieved. The National Cancer Institute of Canada is currently collecting data to analyze in detail the changes in mortality from cancer of the cervix, bearing in mind that since comparisons have to be made between B.C. and the rest of Canada, due account must be taken of differences between the areas being compared in factors that could be related to the incidence and mortality from cancer of the cervix other than screening as well as the intensity and duration of screening itself. Although the previous attempt at such a comparison³ did not take account of these factors, it may also have been conducted too early for an effect to be demonstrable. Within a year or so we may have enough data to provide an answer to this question. That it is urgent to do so is shown by the rising prevalence of in situ carcinoma in young women,¹ so that we need to be sure we are adopting a correct approach to the detection and prevention of this disease.

Cancer of the Breast

Quantitatively, cancer of the breast is a more important problem than cancer of the cervix, both in terms of morbidity and mortality from the disease and because the problems of early detection are often greater. The most important reason for this is that there is no readily diagnosed precursor, so that the *cancer* must be diagnosed in its presymptomatic stage. This introduces a new dimension into assessment of the results of programs for the early detection of cancer of the breast because if, for example, a cancer is diagnosed one year earlier than it would have been if the program was not in operation, the apparent survival will inevitably be increased by one year even if the natural history of the disease is not influenced. Moreover, screening may only increase the period of awareness of the cancer and have no effect on the patient's lifespan. This factor, which has been called the 'lead time' gained through screening, is still not always appreciated.

There are three options open to us for early detection of breast cancer: examination of the breasts, either by a doctor or by the patient herself, mammography and thermography. For years the only method of detecting breast cancer was by clinical examination and a natural extension of this is breast self-examination. But it has never been clear what proportion of breast cancers were discovered by *regular* breast self-examination (as distinct from an accidental discovery by the patient or her husband), and it has recently been suggested that the yield may be less than was supposed.¹¹ As ancillary methods of diagnosis became more common, the deficiencies of clinical examination alone became obvious. Mammography has its devotees but concern over the exposure of the breast to radiation has led to the advocacy of xeroradiography which involves less

radiation and may also have some advantages over mammography in diagnostic accuracy.¹² Thermography, which avoids the need to expose the breast to any radiation, stood up well compared with other diagnostic methods in an American study,¹³ but appeared less satisfactory in two recent British studies.^{14, 15} It is probably capable of further development.

It is becoming increasingly clear that all these methods will diagnose cases not detected by the others (even though there is a considerable overlap) and probably none is acceptable as an isolated procedure. This has led to suggestions that different modalities should be combined for screening, and even that patients should have clinical examination, mammography (or xeroradiography) and thermography, together with a questionnaire at the same session.

To date, there has been only one study that sought to evaluate mass screening for cancer of the breast in a population. This is still ongoing, though preliminary results have been published.¹⁶ The study, being conducted among the membership of the Health Insurance Plan in New York, takes two systematic random samples, each of 31,000 women aged 40 to 64 who had belonged to the HIP for at least a year. One group was offered screening by clinical examination and mammography, with an initial response rate of 65 percent; the other served as the control population. Follow-up is through claims to the HIP, from hospitals, through matching of death records on file in various health departments and through a mail survey five years after entry into the study. It is critical to the study design that follow-up should be adequate and equal in both the group offered screening and in the controls, and the data so far presented is reassuring about this. The preliminary results show a lower mortality from breast cancer in the group offered screening, the reported rates being 2.2 compared with 3.7 deaths per 10,000 person-years. The benefit appears to be almost restricted to the 50-59 year age group, and is not noticeable until two years after entry to the study. As the authors of the study emphasize, these results are based on only a short period, and ten years of observation will be necessary to determine whether the effect on mortality will be maintained.

Implications

What are the implications of this, particularly for Canada? Most will agree that the time is not ripe for indiscriminate mass screening, but perhaps we should be moving towards selective screening in high risk groups. People at high risk of breast cancer are women older than 40 who are single or if married have had few if any children, especially if they were first pregnant after the age of 25, who are Caucasian, with an early age of menarche, who have had benign breast disease, have a family history of breast cancer or belong to a higher socio-economic stratum. But even this is not the complete picture and other risk factors remain to be determined. More work is needed on developing predictive factors for the development of breast cancer. If screening for breast cancer is to be introduced in Canada, then a strong plea must be entered for evaluating programs carefully in relation to the population, and if possible in a controlled study. In the meantime the family physician needs to be aware of the diagnostic facilities for detecting breast cancer in his area, and he should be prepared to refer women who seem likely to be at risk whenever this seems appropriate.

Cancer of the Lung

The finding of a number of unsuspected cases of lung cancer as a by-product of mass X-ray surveys for tuberculosis led to the hope that repeated annual, or more frequent, X-rays of populations of men believed to be at risk of developing lung cancer would be rewarding. Disillusionment, however, is now the order of the day. For example, the Philadelphia Pulmonary Neoplasm Project in which 6,137 men aged 45 or older were enrolled and followed for 10 years by semi-annual X-rays, revealed 68 cases of lung cancer on entry to the study and 105 during follow-up. Although valuable information on the natural history of lung cancer was obtained there was no evidence of any improvement in survival of those cases detected by regular X-ray.¹⁷ Although some community X-ray surveys appeared to show a better prognosis for patients detected by X-ray than would have been expected, others did not; while the yield was low and most failed to consider the statistical pitfalls in evaluating screening programs discussed above. The only controlled evaluation of X-rays in lung cancer screening was conducted in London, England,¹⁸ where factories were allocated at random to six-monthly X-rays compared with X-rays only on entry to the study and after three years. This yielded two groups of men aged 40 or over; 29,416 who had six-monthly X-rays and 25,044 controls shown to be comparable with regard to age and smoking habits. Over three years the average annual mortality rate from lung cancer was 0.7 per 1,000 in the X-ray group and 0.8 in the control, a negligible difference.

Not surprisingly, attention has recently concentrated on sputum cytology. Here, the yield of community surveys is low, and even when lung cancer is found, it is not always amenable to treatment.¹⁹ A new problem has been the detection of cytological abnormalities without any detectable lesion in the lungs.¹⁹ Even though the yield is increased by conducting both X-rays and cytology together,²⁰ a lot of work remains to be done in this area. It is possible that with the development of automated cytological methods, still probably some years away, with concentration on high risk groups, especially on men over 45 who are heavy smokers, and with attention being given to finding identifiable precursors of lung cancer, mass screening might have a future if it could identify people at special risk, who could reduce that risk by stopping smoking. At the moment, however, this is a distant possibility.

Cancer of the Colon and Rectum

Early detection by regular proctoscopic and sigmoidoscopic examinations was first advocated many years ago, yet we still do not have evidence that they have an effect, although the constancy of mortality rates for colo-rectal cancer in the United States, where such examinations probably have been most widely practiced, suggests that they may not. The description of a test for carcino-embryonic antigen (CEA) in colorectal cancer, and its apparent high sensitivity and specificity,²¹ led to the hope that a blood test for this disease that could be of enormous value in early detection was just around the corner. Faced with the results of a number of studies, and especially of a joint Canadian/U.S. study²² which showed a sensitivity of the test of approximately 65 percent in colo-rectal cancer and a specificity of the same order in a hospital population with other, mainly gastrointestinal diseases, we have to recognize that we are still a long way from a blood test for

colo-rectal cancer that can be evaluated as a mass screening tool. Nevertheless, a lot of work remains to be done in this field, and perhaps, in a few years, we may yet reap the benefits of the Canadian discovery of CEA, not only in relation to colo-rectal cancer but possibly in relation to tests for other cancers as well.

Other Cancers

Although cytology has been advocated for oral cancer and found valuable in diagnosis in a Canadian study,²³ and urine cytology is being used in occupationally exposed groups at risk for bladder cancer, no studies have so far been reported on the impact of such procedures on mortality in the population. In other countries there may be a different order of priorities than in Canada (for example, in Japan, exfoliative cytology and radiology are used for the early diagnosis of stomach cancer) but for each site the same problems have to be faced: will the patients who are at risk attend for screening? Will the procedures used have any effect on the natural history of the disease?

What Can Family Physicians Do?

Faced with conflicting claims and rebuttals, what should the family physician do? First, as always, he must maintain a high index of suspicion for cancer. Second, if he believes in screening, he should try and identify the patients in his practice who fall into the high risk groups and arrange for them to have the appropriate tests regularly. If, on the other hand, he does not find the arguments for screening compelling, he should be prepared to change his position if suitable evidence is produced. Finally, he should use the opportunities open to him in his practice to encourage patients to abandon habits that may result in cancer, particularly smoking. ◀

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QUOTE

A rose by any other name is just as sweet, and there has been in common English usage for the past 400 years what the doctor has known as prophylactic (to keep guard before) meaning precautionary, medicine. And it would be a slur on the students' intelligence for a surgeon, let us say, to point out, as he has been urged to do, that he wears rubber gloves to 'prevent' infecting the patient, gives the anesthetic to 'prevent' pain, removes the appendix to 'prevent' peritonitis, and so on, ad infinitum. For his part, he sits down and has a cup of tea to 'prevent' fatigue, and then to 'prevent' irritation keeps away from the faculty meeting where the great importance of preventive medicine will again be pointed out to him. Like many another catchword, — 'reconstruction', for example, which was on everyone's lips after the war, — 'prevention' can be very much overworked. There is only one ultimate and effectual preventive for the maladies to which flesh is heir, and that is death.

— Harvey Cushing, *The Medical Career and Other Papers*