MEDICAL PRACTICE

*Contemporary Themes***Organisation and results of the cervical cytology screening programme in British Columbia, 1955-85**

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Abstract

A screening programme to detect preinvasive carcinoma of the cervix was started in British Columbia in 1949. Since 1970 the number of women who have been screened at least once has been maintained at about 85% of the population at risk. More than 500 000 cervical smears are being examined each year in the central laboratory. There has been an appreciable increase in the number of cases and rates of carcinoma in situ seen since 1970, particularly in women between 20 and 30 years of age. Since the programme started over 26 000 cases of squamous carcinoma in situ have been detected and treated. The incidence of clinically invasive squamous carcinoma of the cervix has fallen by 78% during the period under review, and mortality from squamous carcinoma of the cervix has fallen by 72%. A colposcopy programme, introduced throughout British Columbia over the past 12 years, has been important in reducing the problems of managing preinvasive lesions, particularly in younger women.

It is concluded that the reduction in morbidity and mortality

from invasive squamous cancer of the cervix in British Columbia over the past 30 years is directly attributable to the province wide screening programme and that a large potential increase in invasive cervical cancer rates among younger women is being prevented.

Introduction

A centralised gynaecological cytology screening programme has been in effect in British Columbia over the past 30 years. A pilot project was established in 1949 by the late Dr H K Fidler, who was joined shortly thereafter by Dr D A Boyes, to determine the efficacy of the cervical smear technique in detecting preclinical cancer of the cervix. By 1955 it was thought that the value of the technique had been established, and a decision was made to determine whether taking cervical smears would appreciably reduce the incidence and mortality of invasive squamous carcinoma of the cervix by screening all women over the age of 20 in the province yearly. Since 1955 when approximately 12 000 cases were screened the programme has grown: 536 800 smears from 465 676 women were examined in the laboratory in 1985, and since 1980 there has been a yearly increase of about 1.5%, roughly equivalent to the yearly increase in the female population of the province.

British Columbia has a population of 2.8 million people, about half of whom live in the greater Vancouver area, the remainder being scattered around the province, which has an area of 366 000 square miles (948 000 km²), stretching 1500 miles (2414 km) from north to south and 800 miles (1287 km) from east to west.

The laboratory employs 42 cytotechnologists, 10 technical aides, and 29 clerical staff. Up to 2500 cervical smears are processed by the laboratory each day. The computerised patient file now contains records on 1.4 million patients.

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Methods

COLLECTING AND PROCESSING SMEARS

Most of the cervical smears are obtained by the 3000 general practitioners and 200 gynaecologists in the province, and a few are also received from health clinics, outpatient departments, and correctional institutions. The smears are delivered by mail or courier service to the laboratory, which supplies requisitions, slides, Ayre's spatulas, and mailing containers to all physicians who are participating in the programme. A Cytology Office Manual is also supplied, which describes the optimal method for collecting the smear, with the aim of obtaining a representative sample from the transformation zone of the uterine cervix. Because of problems associated with inadequate fixation of smears in the past we now recommend that the smears should be air dried in the physician's office. The slides are then rehydrated in the laboratory before staining, using a modified Papanicolaou technique.¹ The preparation, staining, and coverslipping of the slides is performed by assistant technologists. We have used this method for the past 10 years, and it results in very acceptable cell preservation of squamous cells, although glandular cells are less well preserved. The requisition that accompanies the smear is designed to provide clinical information to help to interpret the smear. Preprinted, sequentially numbered paired adhesive labels are fixed to each smear and requisition when they are received in the laboratory as the first step in processing.

ENTERING AND REPORTING DATA ON CYTOLOGY

The cytology patient file is maintained on a Honeywell DPS 6/96 32 byte mainframe computer with a data base of approximately 1000 megabytes. The computer system is an interactive on line system which allows patient data to be displayed, added to, altered, or deleted using video display terminals, so that the information in the system is always current.

In the cytology clerical area the data from each requisition is entered into the cytology file by a staff of 11 clerks using the video display terminals. Patients are identified primarily by their name, birthdate, and name at birth. In addition, if the patient has been seen in the laboratory previously she will have been assigned a unique laboratory identification number which we ask the physician to include on the cytology requisition together with the previous cytology smear number; compliance with this request is extremely high and helps to avoid duplication of patients. New patients are allocated a unique laboratory identification number and are then added to the file. Most of the patients have been screened previously; for these patients the record is scanned and if any important previous histological or cytological history is found a copy of the patient's history is printed out and attached to the requisition. After screening, the cytology results are returned to the clerical area and are entered into the system. The computer generated reports are printed overnight and mailed out the next day.

SCREENING AND INTERPRETATION

Up to 2500 smears are screened a day, using a hierarchical system, with grade I and grade II screeners each examining 85 smears a day. Their only responsibility is to screen these slides. There are comprehensive signout rules for each level of screening, with notable degrees of cellular atypia being referred to more experienced cytotechnologists, each of whom supervises a group of four or five grade I and grade II cytotechnologists. Approximately 100 (4%) of the cases screened each day are referred to a cytopathologist.

The report form, which is used for all cases apart from those that are negative, was designed to be as comprehensive as possible in terms of the cellular abnormalities seen, the expected histological appearance, and recommendations for repeat smears and investigations as suggested by the Canadian Task Force Report.² Each person in the laboratory with signout authority is assigned a unique number which appears on the cytology record and is an important part of the laboratory quality control programme.³ If the interpretation of a particular smear cannot be encompassed in the standard report form the cytopathologists may add a comment.

FOLLOW UP

An essential component of the screening programme is the follow up and recall system for patients in whom appreciable cellular abnormalities are found. There is no laboratory recall for patients whose smears are negative or show only benign atypia, this decision being the responsibility of the referring physician. The most important function of the follow up system is to ensure that a cytological abnormality is dealt with. If a recommendation for a repeat smear, a colposcopic examination, or a biopsy is made and the

result does not appear on the computer within four months of the recommended date a follow up letter of inquiry is generated by the computer and sent to the referring physician. This sometimes acts as a timely reminder of the need for a particular investigation. Because of the enthusiastic compliance of the physicians in the province the follow up rate is virtually 100%. If the whereabouts of the patient is not known to the physician a district nurse in the area is asked to locate the patient to attempt to persuade her to return for further investigation.

Patients who are found to have severe dysplasia or carcinoma in situ are deemed to require long term follow up even after their disease is treated since it has been shown that these patients are at a high risk of developing either recurrent or new disease. The computer automatically generates an annual reminder letter to the physician for these patients.

COLPOSCOPY

A colposcopy programme was started in 1973 to complement the cytology screening service,⁴ and there are now 24 regional colposcopy clinics throughout the province. This programme was started mainly because of a pronounced increase in the rate of preclinical cervical intraepithelial neoplasia in younger women. Each of the gynaecologists who performs colposcopy undergoes one month of instruction, which includes cytology and histology in addition to training in colposcopy.

A record of all colposcopic examinations from these clinics on a standardised colposcopy report form is sent to the central cytology laboratory, and these data are entered into the cytology file with the results of any colposcopic biopsy or relevant surgery. This helps the interpretation of subsequent cervical smears and also allows for centralised quality control of the colposcopy programme.

Results

In 1955 approximately 12 000 cervical smears were screened. Table I shows the increase in screening over the subsequent 30 years. By 1965 roughly a third of the population of women at risk was being screened yearly, and since the early 1970s about 40% of this population have been screened each year. It is estimated that by 1970 85% of the population at risk had been screened at least once, and this coverage has been maintained.

Table II shows the pattern of screening during 1985, which has been consistent since the mid 1970s. Over three quarters (82%) of the screening is carried out in women between the ages of 20 and 59 years. Just under two thirds of the population between the ages of 20 and 34 is screened yearly, whereas the proportion in the population over 60 is much smaller.

Table I and the figure show the increasing numbers of cases of carcinoma in situ detected over three decades. Since 1980 the detection rate has fallen, possibly as a result of the treatment of many patients with moderate and severe dysplasia. Over 26 000 cases of squamous carcinoma in situ have been detected and treated since the beginning of the programme. As might be expected with increasing rescreening the number of cases of microinvasive

TABLE I—Number of women screened and number of cases of squamous carcinoma in situ of the cervix in British Columbia

Year	Population over age 20 (000s)	No of women screened	No of cases detected	Rate per 100 000
1955	422.9	11 707	52	12.3
1960	486.4	59 844	221	45.4
1965	543.2	161 556	504	92.8
1970	664.4	297 407	761	114.5
1975	805.5	355 917	1 239	153.8
1980	926.2	433 329	1 545	166.8
1985	1 063.1	465 676	1 420	133.6

TABLE II—Number of women screened in British Columbia during 1985 by age group

Age group (years)	Female population	No (%) screened	% Age of each age group screened
15-19	103 000	25 571 (6)	25
20-34	380 800	224 970 (49)	59
35-59	415 800	168 186 (36)	40
60 and over	266 600	44 179 (9)	16
Total	1 166 200	462 906 (100)	40

and early invasive carcinoma has fallen from about 10% of the yearly total in 1955 to 2% in 1985.

Table III shows the appreciable increase in the rates of carcinoma in situ that has occurred in recent years in women in the age group 20-30 years. Although the rate has also increased dramatically in the 15 to 19 year age group, these cases represent only about 2% of the number detected up to age 35.

The incidence of clinically invasive squamous carcinoma of the cervix fell by 78% between 1955 and 1985 (table IV; figure) if the disease rates between 1980 and 1985 inclusive are averaged. Ten per cent of the new cases between 1980 and 1985 occurred in women under age 35, 50% in women between 35 and 65, and 40% in women over 65. Table IV and the figure show a similar fall in mortality of 72% between 1958 and 1985 if the mortality rates for 1980-5 inclusive are averaged.

Discussion

There has been an impressive reduction in the incidence and mortality from invasive squamous carcinoma of the cervix in British Columbia over the past 30 years, which we believe is a direct result of the cytology screening programme. Similar evidence was recently summarised by Laara *et al*, who concluded that "organized

screening programs have had a major impact on the reduction of mortality from cervical cancer in the Nordic countries."⁵

We agree with the view expressed by Draper and Cook and by Wolfendale *et al* on the substantial increase in the rates of carcinoma in situ among younger women in Britain.^{6,7} This increase is closely similar to that observed in British Columbia. These papers suggest that screening prevents a large potential increase in invasive cervical cancer among younger women. A recent well documented report on premarital sexual activity among teenage women in the United States over the past three decades concluded that the sexual revolution of the late 1960s is continuing among older teenagers, with an apparent slowing of the rate of increase in this group.⁸ Younger teenagers, however, continue to engage in intercourse at earlier ages and in increasing numbers. Undoubtedly, similar behaviour patterns have occurred in Canada, and indeed throughout the Western world, so that these later cohorts are likely to continue to be at high risk.

The regional colposcopy programme carried out in the province over the past 12 years has been important in managing preinvasive lesions, particularly in younger women, many of whom can be treated with cryotherapy or laser treatment, thus avoiding the potential problems of cone biopsy. In 1985 8188 new patients were referred for colposcopic examination in the province, approximately 3000 with severe dysplasia or carcinoma in situ and the remainder with persistent mild or moderate dysplasia. This represents 1.7% of the women screened during that year. The colposcopy programme has resulted in the transfer of much of the responsibility for the diagnosis of preinvasive lesions of the cervix from the pathologist to the colposcopist. Because the experience of performing colposcopy is concentrated in a few gynaecologists, who therefore see a relatively large number of cases regularly, it has been possible to maintain a high standard of colposcopic practice. We believe that this reduces the possibility of diagnostic errors, now well documented,^{9,10} particularly in early invasive disease. Early invasive disease now represents only 2% of the total number of in situ and preclinical invasive lesions that occur in the province. Our experience with 180 patients with preclinical invasive disease who were seen between 1973 and 1982 suggests that colposcopy can be very useful in diagnosis and management.¹¹

A widely discussed aspect of screening programmes for cervical cancer is the age at which screening should start and the frequency with which it should be performed. Key factors are the proportion of cases of carcinoma in situ that will become invasive and the estimated time from preinvasive lesions to the development of invasive carcinoma. Richart and Barron calculated that of 1000 patients with undetected carcinoma in situ, about a fourth will undergo transition to invasion within five years.¹²

The 1976 Canadian Task Force report recommended that sexually active women should have a cervical smear every three years after two negative smears once sexual activity has started.² There is an important proviso to this recommendation, however—namely, that women at high risk should continue to have yearly smears. High risk is defined as the early onset of sexual activity or exposure to multiple sexual partners. This was acknowledged in the report of the reconvened Canadian Task Force in 1982, which recognised that most young women in Canada now fall into the high risk group.¹³ The task force therefore modified its recommendation to a yearly smear after the onset of sexual activity until age 35, at which time the frequency could be reduced to every three years if the patient had never had an abnormal smear. In practice, when all women who participate in the screening programme in British Columbia are considered, approximately 45% of women are screened yearly; the average interval for rescreening in the province is once every two years. The recent report of the IARC Working Group on Evaluation of Cervical Cancer Screening Programmes shows that there is only a minimal gain in the reduction of invasive cervical cancer from screening yearly as opposed to every two years, or even every three years.¹⁴

Despite the success of the programme in British Columbia an average of 65 new cases of invasive squamous carcinoma of the cervix is found each year. In addition, we are seeing many cases of adenocarcinoma of the cervix—about 15% of our new cases of

TABLE III—Rates for carcinoma in situ per 1000 women screened in British Columbia

Age group (years)	1972	1975	1980	1985
15-19	0.1	0.2	0.8	0.7
20-24	1.1	2.2	4.5	3.3
25-29	2.7	4.3	7.1	4.9
30-34	3.0	4.8	6.2	4.8
35-39	2.4	3.3	4.2	3.8
40-44	1.9	2.2	2.8	2.3
45-49	1.1	2.1	1.6	1.8
50-54	1.3	1.2	1.9	0.9
55-59	1.0	1.5	0.9	0.7
60-64	1.3	0.8	1.2	0.7
65-69	1.2	1.3	1.4	0.8
70-74	2.4	0.8	1.1	0.6
75 and over	1.0	0.8	1.2	0.9

TABLE IV—Incidence of clinical invasive squamous carcinoma of the cervix and refined mortality

Year	Population over age 20 (000s)	Total No of cases	Incidence per 100 000	No of deaths	Rate per 100 000
1955	422.9	120	28.4	*	*
1958	473.0	112	23.7	54	11.4
1960	486.4	96	19.7	48	9.9
1965	543.2	80	14.7	42	7.7
1970	664.4	82	12.3	46	6.9
1975	805.5	70	8.7	42	5.2
1980	912.9	63	6.9	24	2.6
1985	1 063.9	68	6.4	33	3.1

*Refined mortality was not calculated until 1958.

The incidence of clinical invasive squamous carcinoma of the cervix and squamous carcinoma in situ 1955-85 and mortality from squamous carcinoma of the cervix 1958-85 in British Columbia (age standardised rates per 100 000 women over age 20).

invasive cancer of the cervix. Of the women who presented with invasive cervical cancer in British Columbia over the past 10 years, 69% were over age 50 and three fourths had not had a cytological examination before developing clinical symptoms. A small proportion of these patients had consulted their physicians for non-gynaecological problems before developing symptoms and had never had a cervical smear, which might have detected the disease at an earlier stage. If morbidity and mortality from cancer of the cervix are to be further reduced it is this segment of the population that must be reached and persuaded to participate in the screening programme.

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References

- 1 Anderson GH. Cervical cytology. In: Miller AB, ed. *Screening for cancer*. London: Academic Press, 1985:87-102.

- 2 Canadian Task Force. Cervical cancer screening programs, 1976. *Can Med Assoc J* 1976;114:1003-33.
- 3 Anderson GH, Flynn KJ, Hickey LA, Le Riche JC, Matisic JP, Suen KC. A comprehensive internal quality control system for a large cytology laboratory. *Acta Cytol* 1987;31:895-9.
- 4 Benedet JL, Anderson GH. Cervical intra-epithelial neoplasia in British Columbia: a comprehensive program for detection, diagnosis, and treatment. *Gynecol Oncol* 1981;12:S280-S91.
- 5 Laara E, Day NE, Hakama M. Trends in mortality from cervical cancer in the Nordic countries: association with organised screening programs. *Lancet* 1987;i:1247-9.
- 6 Draper GJ, Cook GA. Changing patterns of cervical cancer rates. *Br Med J* 1983;287:510-2.
- 7 Wolfendale, MR, King S, Usherwood MM. Abnormal cervical smears: are we in for an epidemic? *Br Med J* 1983;287:526-8.
- 8 Hofferth SL, Kahn JR, Baldwin W. Premarital sexual activity among US teenage women over the past three decades. *Family Planning Perspectives* 1987;19:46-53.
- 9 Townsend DE, Richart RM, Marks E, Nielsen J. Invasive cancer following outpatient evaluation and therapy for cervical disease. *Obstet Gynecol* 1981;57:145-9.
- 10 Townsend DE, Richart RM. Diagnostic errors in colposcopy. *Gynecol Oncol* 1981;12:S259-64.
- 11 Benedet JL, Anderson GH, Boyes DA. Colposcopic accuracy in the diagnosis of microinvasive and occult invasive carcinoma of the cervix. *Obstet Gynecol* 1985;65:557-62.
- 12 Richart RM, Barron BA. Screening strategies for cervical cancer and cervical intraepithelial neoplasia. *Cancer* 1981;47:1176-81.
- 13 Canadian Task Force. Cervical cancer screening programs: summary of the 1982 Canadian Task Force report. *Can Med Assoc J* 1982;127:581-9.
- 14 IARC Working Group on Evaluation of Cervical Cancer Screening Programmes. Screening for squamous cervical cancer: duration of low risk after negative results of cervical cytology and its implication for screening policies. *Br Med J* 1986;293:659-64.

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Changes in maternal age distribution and their possible impact on demand for prenatal diagnostic services

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Abstract

Between 1977 and 1985 there was a 65% increase in births to women aged 35 or more in England and Wales, but only a 15% increase in all births. Two factors of roughly equal importance were responsible for this differential increase. Firstly, the proportion of older women (35-44) among all women of reproductive age (15-44) increased from 28% in 1977 to 31% in 1985; and, secondly, in the same period the fertility rate for women aged 35-39 increased from 18.2 to 24.1 per 1000 and for women aged 40-44 from 4.1 to 4.6 per 1000.

The increased fertility rate among older women is not due to an extension of the reproductive period but to a delay in childbearing. This delay was seen in women married only once and also in those who had remarried.

As prenatal diagnosis for the exclusion of chromosome abnormalities is customarily offered to older mothers the increased numbers of women aged 35 or more and their increased fertility rate have important implications for the provision of obstetric and laboratory services. There were 51 859 live births to women aged 35 and over in 1985; the projected figure for 2001 is 85 000. If the use of prenatal diagnosis continues to increase facilities for about 70 000 prenatal cytogenetic analyses will be needed in 2001.

Introduction

The incidence of trisomy 21, as well as of other autosomal trisomies and sex chromosome aneuploidies, increases with maternal age. The effect becomes quite striking in mothers aged 35 or older.

There is a 0.26% risk of a woman aged 35 having a liveborn child with trisomy 21 and a 0.49% risk of her having a child with any chromosome abnormality. At age 45 these risks are 3.3% and 5.6%, respectively.¹

In many parts of the United Kingdom older mothers are offered amniocentesis or chorionic villus biopsy for exclusion of fetal chromosome abnormalities. Data relating to the rate of use of chorionic villus biopsy are not yet available, but those for amniocentesis show steady increases over the past decade. Ferguson-Smith reported that in the west of Scotland the use of amniocentesis by mothers aged 35 or over rose from 8% in 1976 to 28% in 1981.² Similarly, Walker and Howard recorded an increase from 27% in 1978 to 44% in 1983 in Liverpool.³ In Edinburgh in 1986 we estimate that about half the population of mothers aged 35 or over underwent amniocentesis.

An important factor to consider in estimating future requirements for prenatal diagnosis is the maternal age distribution of the population. This study was undertaken to investigate changes in the number of births among women 35 years or older in England and Wales between 1946 and 1985 and to identify factors influencing these changes that might affect the provision of prenatal diagnostic services in the future.

Subjects and methods

The data used in this study were obtained from the yearly publications entitled *Birth Statistics*, published by the Office of Population Censuses and Surveys.⁴ From these we obtained, for England and Wales, the number of births in each year of the study period to women in different age groups, with different numbers of marriages and different numbers of previous liveborn children. We also obtained fertility rates (mean number of live births per woman) and the estimated total numbers of women of different age groups in the population.

From these data we calculated the percentages of live births to women aged 35 or over for all women, women married only once, and women in their second or later marriage. Both for women married only once and for remarried women we calculated separately the percentages of first live births (live births to women who had had no liveborn children in their present or

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