Prostate cancer trends in Canada: Rising incidence or increased detection?

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Objectives: To analyse trends in the incidence and mortality rates of prostate cancer in Canada according to age distribution, temporal pattern and provincial variation; to determine any association with the rate of prostatectomy; and to determine whether any observed increase in the rate of prostate cancer was due to an increase in the detection rate.

Design: Descriptive epidemiologic study based on Canadian population data from 1959 to 1989 and chart review from one Canadian hospital.

Setting: The chart review was conducted at the Ottawa Civic Hospital.

Subjects: The data on prostate cancer trends were obtained from the Canadian population. Charts were reviewed for two groups of patients: (a) men discharged from inpatient care during 1976 and 1986–87 with prostate cancer first diagnosed in the same year and (b) men who underwent transurethral resection of the prostate (TURP) during 1976 and 1986.

Outcome measures: Incidence and mortality rates of prostate cancer, rates of prostatectomy and TURP, and correlations between them. From the hospital data, changes between 1976 and 1986–87 in distribution of cancer stages, distribution of cases detected incidentally after surgery for suspected benign prostatic hypertrophy and average number of slides analysed per gram of tissue obtained from prostatectomy.

Results: The epidemiologic data showed that the age-adjusted incidence rates increased by 72% overall, an increase seen in all age groups over 60 years. The mortality rates increased by 29% overall, primarily in men over 85 years old. The prostatectomy rate increased by 55%. There were significant linear correlations between the national and provincial incidence rates of prostate cancer and the TURP rates. The chart review revealed that during 1976, 53% of the cases of prostate cancer diagnosed were localized, as compared with 75% in 1986–87 (p < 0.01). The proportion of tumours diagnosed incidentally in men undergoing TURP increased by 11%, whereas the number of procedures did not increase. Significantly more slides per gram of tissue were analysed in 1986–87 than in 1976 (p < 0.01).

Conclusions: The correlations between the incidence rates of prostate cancer and those of TURP suggest that increased treatment of benign prostatic disease has led to increased detection of prostate cancer. Extrapolation of the data obtained from the chart review indicates that the increase in observed incidence rates can be attributed to an increase in the rate of localized disease and thus primarily to early detection rather than to elevated risk. However, because the rate of death from prostate cancer was elevated in elderly men, increases in exposure to unestablished risk factors cannot be ruled out.

Objectifs : Analyser l'évolution des taux d'incidence et de mortalité du cancer de la prostate au Canada en fonction de la répartition selon l'âge, le schéma temporel et la variation provinciale; déterminer tout rapprochement avec la prostatectomie; et déterminer si une augmenta-

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tion éventuellement observée du taux de cancer de la prostate est attribuable à un accroissement du taux de dépistage.

Conception : Étude épidémiologique descriptive fondée sur des données démographiques canadiennes de 1959 à 1989 et sur l'examen des dossiers d'un hôpital canadien.

Contexte : L'examen des dossiers a eu lieu à l'Hôpital Civic d'Ottawa.

Sujets : Les données sur l'évolution des cancers de la prostate ont été recueillies auprès de la population canadienne. On a examiné les dossiers de deux groupes de patients : (a) les hommes renvoyés des soins aux hospitalisés en 1976 et en 1986–1987 atteints d'un cancer de la prostate diagnostiqué pour la première fois au cours de la même année, et (b) les hommes qui ont subi une résection transurétrale de la prostate (RTUP) en 1976 et en 1986.

Mesures des résultats : Taux d'incidence et de mortalité du cancer de la prostate, taux de prostatectomie et de RTUP et corrélations entre ceux-ci. D'après les données hospitalières, les changements survenus entre 1976 et 1986–1987 dans la distribution des stades du cancer, la distribution des cas dépistés fortuitement après une chirurgie pour suspicion d'hypertrophie prostatique bénigne et le nombre moyen de lames analysées par gramme de tissus prélevés par prostatectomie.

Résultats : Les données épidémiologiques ont révélé que les taux d'incidence ajustés selon l'âge ont augmenté de 72 % dans l'ensemble, une augmentation observée dans tous les groupes d'âge au-delà de 60 ans. Les taux de mortalité ont augmenté de 29 % dans l'ensemble, principalement chez les hommes de plus de 85 ans. Le taux de prostatectomie a augmenté de 55 %. Il y avait des corrélations linéaires significatives entre les taux d'incidence national et provinciaux de cancer de la prostate et les taux de RTUP. L'examen des dossiers a révélé qu'en 1976, 53 % des cas diagnostiqués de cancer de la prostate étaient localisés, par comparaison avec 75 % en 1986–1987 (p 0,01). La proportion de tumeurs diagnostiquées fortuitement chez les hommes qui subissent une RTUP a augmenté de 11 %, alors que le nombre d'interventions n'a pas augmenté. En 1986–1987, on a analysé un nombre significativement plus élevé de lames par gramme de tissu qu'en 1976 (p 0,01).

Conclusions : Les corrélations entre les taux d'incidence du cancer de la prostate et ceux de la RTUP suggèrent qu'une intensification du traitement de l'hypertrophie prostatique bénigne a entraîné une hausse de dépistage du cancer de la prostate. L'extrapolation des données extraites de l'examen des dossiers révèle qu'on peut attribuer l'augmentation des taux d'incidence observés à un accroissement du taux d'atteintes localisées, et ils seraient donc principalement attribuables au dépistage précoce plutôt qu'à un risque élevé. Cependant, en raison du taux de mortalité élevé du cancer de la prostate chez les hommes âgés, on ne peut exclure des hausses d'exposition à des facteurs de risque qui restent à déterminer.

fter lung cancer, prostate cancer is the most common of the noncutaneous malignant neoplasms occurring in North American men; in Canada it is currently responsible for 20% of new cancers and 12% of deaths from cancer among men.¹ Over the last two decades the incidence and mortality rates have steadily increased, and the projected number of new cases in Ontario by 1995 will exceed that of new cases of lung cancer.²

Little has been established about the cause of prostate cancer. The substantial variation in rates of occurrence around the world^{3,4} and the increasing rates in groups migrating from low-risk to high-risk populations⁵⁻⁷ suggest a role for modifiable environmental factors yet to be identified. Epidemiologic studies have failed to determine a cause, although several factors for example, family history,⁸⁻¹¹ dietary fat and vitamin A,¹²⁻¹⁴ and cadmium exposure through cigarette smoke or occupation¹⁵ — have been implicated.

The rising rates of prostate cancer may be due in part to increased exposure to risk factors, or they may be an artifact of an increasing population at risk^{16,17} or of higher rates of detection.^{18,19} To further characterize this disease we examined Canadian trends in the incidence of

cedures that allow for incidental diagnosis. We analysed the charts of patients with prostate cancer in one hospital during two periods to determine whether any increase in reported incidence rates could be due to an increased rate of detection of prostate cancer.

and rate of deaths from prostate cancer as well as in pro-

Methods

Incidence and mortality rates

Data on the incidence and mortality rates of prostate cancer were obtained from the National Cancer Incidence Reporting System and the Canadian Mortality Database respectively. Population data were extracted from Statistics Canada census publications. We calculated the annual incidence and mortality rates in Canada and in each of the provinces by 5-year age groups, from age 45 years to 85 years and older. The study period was 1969 to 1988 for incidence and 1959 to 1989 for deaths.

The annual numbers of all prostatectomies as well as transurethral resection of the prostate (TURP) performed in Canada and in each of the provinces from 1970 to 1988 were obtained from the National Hospital Morbidity Statistics database at the Canadian Centre for Health Information. The annual rates of prostatectomies were calculated by 5-year age group.

Age-adjusted incidence and mortality rates and rates of prostatectomy were determined by the direct method, with the 1981 Canadian population as the standard. Linear regression of the logarithm of the rates of incidence, death and TURP on calendar year was carried out to examine the rate of change over time. Linear regression of the Canadian and provincial TURP rates on the corresponding incidence rates of prostate cancer was performed to quantify the nature of the linear relation.

Chart review

Data were collected from the charts of patients with prostate cancer diagnosed during 1976 and 1986–87 who were discharged from the Ottawa Civic Hospital during those years. From the available pool of hospital charts we selected two samples that were large enough to detect, with 80% power, a 20% increase in the incidence of early-stage disease. All charts were initially reviewed to exclude miscoded cases or those in which the diagnosis was not made during the year of the given admission. The resultant comparison groups comprised 75 cases diagnosed in 1976 and 100 diagnosed in 1986–87.

As well as the age at the time of first diagnosis we collected information on each patient to characterize the process that led to the diagnosis and clinical staging of the disease. For staging purposes we used the Whitmore–Jewett staging system,²⁰ in which stage A indicates latent, incidentally discovered disease (with no evidence of any invasion on subsequent staging), stage B indicates palpable but localized disease, and stages C (regional invasion) and D (metastatic spread) indicate invasive disease. A stage was assigned to each case according to the clinical, surgical and pathological records present in the chart for the admission during which the diagnosis was first made.

We calculated the average number of slides analysed by the pathologists for each gram of prostatic tissue obtained from the patients with latent cancer in the

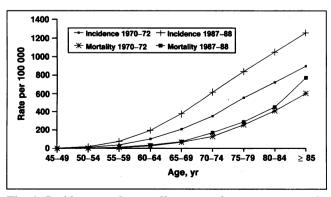


Fig. 1: Incidence and mortality rates of prostate cancer in Canada in 1970–72 and 1987–89 by 5-year age group (based on Canadian population in 1981).

two study periods. In addition, we reviewed randomly selected pathological records for 247 patients found to have benign prostatic hypertrophy (BPH) following TURP during 1976 and 1986 to obtain similar information.

The proportions of latent, localized and invasive disease were computed for each period, as were the proportions of symptomatic and asymptomatic patients and of suspected and unsuspected disease. Multiplication of these proportions by the mean age-adjusted incidence rate of prostate cancer in the Ottawa–Carleton census division during 1975–77 and 1985–87 allowed for estimates of variable-specific incidence rates in the community during the two periods. The statistical tests of significance used were the z test for comparisons of proportions and estimated rates and Student's *t*-test for comparisons of the pathological data.

Results

Age distribution

Fig. 1 shows the age-specific incidence and mortality rates of prostate cancer during 1970–72 and 1987–88. The incidence rates increased in all groups over the age of 55 years. We found an increase of 18% in the rate of death from prostate cancer among people 85 years and older but very little increase in the rate in the younger groups.

Temporal patterns

Age-standardized incidence and mortality rates are presented in Fig. 2. Between 1969 and 1989 the incidence rate of prostate cancer increased by 72%, or 3% annually; the increase was especially steep after 1976. Between 1959 and 1989 the death rate increased by 29%, or 0.8% annually. The mortality rate-incidence rate ratio decreased steadily after 1969, from 46% to 33%.

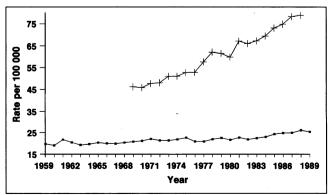


Fig. 3 shows the age-standardized incidence rates

Fig. 2: Age-standardized incidence rates (top line) and mortality rates (bottom line) of prostate cancer in Canada from 1959 to 1989 (based on Canadian population in 1981).

of prostate cancer and the rates for TURP and total prostatectomy from 1970 to 1988. There was an increase of 55% overall and 2% annually in the TURP rate. The ratio of TURPs to all prostatectomies performed in Canada during that period increased from 81% to 97%. The linear regression of the incidence rates of prostate cancer on the TURP rates yielded a direct correlation of 0.94 (p < 0.0001).

Provincial variation

Provincial incidence and mortality rates of prostate cancer during 1987–88 are presented in Fig. 4. The western provinces generally had higher incidence rates of prostate cancer, whereas the rates of death were essentially the same throughout the country. The linear regression of the age-standardized provincial incidence rates on the TURP rates yielded a direct correlation of 0.72 (p < 0.001).

Findings from the chart review

A total of 95% and 98% of the charts selected from the 1976 and 1986–87 discharges contained sufficient information from which to assess all the variables of interest. The remaining charts were used to obtain the maximum number of variables possible, and missing values were excluded from the relevant univariate analysis.

In the 1976 group 77% of the patients lived within the boundaries of the Ottawa–Carleton census division; this proportion was unchanged in the 1986–87 group. In the two periods 97% of the diagnoses were based on histopathologic reports; 99% and 97% of the cancers were adenocarcinomas during 1976 and 1986–87 respectively. The mean age at diagnosis was 71.5 years in the first period and 73.1 years in the second. The age distri-butions in the two periods were not significantly different, nor were they significantly different from those of incident cases of prostate cancer in all Ottawa–Carleton residents during 1975–77 and

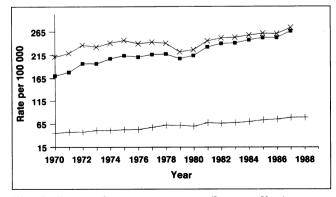


Fig. 3: Rates of prostate cancer (bottom line), transurethral resection of the prostate (TURP) (middle line) and total prostatectomies (top line) from 1970 to 1988 (based on Canadian population in 1981).

1985–87 (age-adjusted incidence rates 61.3 and 72.6 per 100 000 respectively).

The proportions of cases by tumour stage during the two periods is shown in Fig. 5. During 1976, 53% of the tumours diagnosed were stage A or B, as compared with 75% during 1986–87 (p < 0.01). A further subdivision of these early-stage tumours into latent and localized disease showed that the increase occurred in both groups. These changes are reflected in significant changes (p < 0.001) in the estimated stage-specific incidence rates for Ottawa–Carleton (Fig. 6).

Fig. 7 shows the proportions of patients who presented with and without signs and symptoms of malignant disease. There were three clinical pictures: (a) asymptomatic disease (evidence of prostate cancer was detected during routine physical examination or visit for unrelated medical problem); (b) symptoms of prostatism but no clinical reason to suspect cancer (BPH was suspected, and cancer was diagnosed incidentally during routine histologic examination of tissue obtained during prostatectomy); and (c) symptoms and clinically suspected cancer (patients presented with prostatism and a palpable nodule on rectal examination or with bony or perineal pain). Between the two periods the proportion of tumours diagnosed in men presenting with symptoms and signs of putatively benign disease increased by 11%,

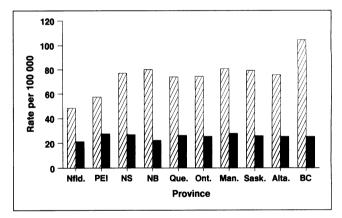


Fig. 4: Age-standardized incidence rates (striped bars) and mortality rates (black bars) of prostate cancer by province during 1987–88 (based on Canadian population in 1981).

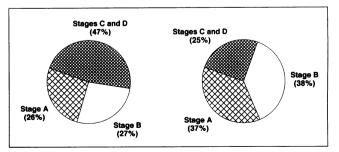


Fig. 5: Distribution of clinical stages of prostate cancer in patients at the Ottawa Civic Hospital in 1976 (left, n = 73) and 1986–87 (right, n = 100). (See text for description of stages.)

whereas that in men presenting with suspected cancer decreased by 13%.

Two procedures were used to diagnose most of the tumours: needle biopsy and TURP. A distinction was made between TURP used in the treatment of suspected BPH and TURP used in the detection of suspected cancer. The 11% increase in the rate of prostate cancer in patients with symptoms of BPH was corroborated by the observation of the same increase in the incidence of

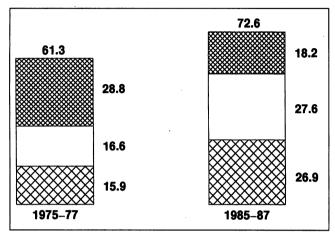


Fig. 6: Estimated age-standardized incidence rates of prostate cancer per 100 000 for Ottawa-Carleton by tumour stage at diagnosis (based on Canadian population in 1981). Bottom portion of bars represents stage A, middle portion stage B and top portion stages C and D.

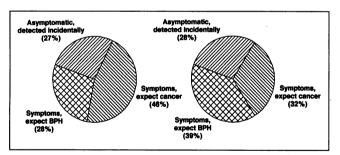


Fig. 7: Distribution of circumstances preceding diagnosis of prostate cancer in patients at the Ottawa Civic Hospital in 1976 (left, n = 71) and 1986–87 (right, n = 99). (Proportions do not total 100% because of rounding.) BPH = benign prostatic hypertrophy.

prostate cancer found incidentally following TURP carried out specifically for suspected BPH. During the two periods the number of TURPs performed at the Ottawa Civic Hospital was essentially the same (551 in 1976 and 542 in 1986–87).

Fig. 8 shows the estimated incidence rates of prostate cancer for Ottawa–Carleton according to the circumstances preceding the diagnosis. The number of patients in whom BPH was suspected and cancer diagnosed incidentally at pathological examination was significantly higher in 1985–87 than in 1975–77 (p < 0.05); there was a smaller increase in the number of asymptomatic patients in whom a suspicious lesion was found at routine clinical examination.

An analysis of the subgroup of asymptomatic patients and of those who had presented with symptoms and signs of cancer is presented in Table 1. In the two subgroups the proportion of localized disease increased from 1976 to 1986–87, with a concomitant decrease in the proportion of invasive disease; however, neither change was statistically significant.

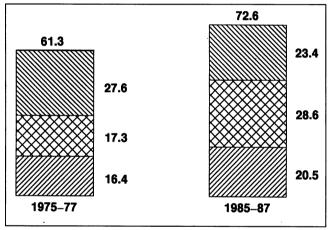


Fig. 8: Estimated age-standardized incidence rates of prostate cancer per 100 000 for Ottawa–Carleton by circumstance of diagnosis. Bottom portion of bars represents asymptomatic disease detected during routine physical examination, middle portion represents cases in which BPH was suspected but cancer was diagnosed incidentally following TURP, and top portion represents cases in which symptoms were present and cancer was suspected.

Table 1: Distribution of prostate cancer by disease stage in patients at the Ottawa Civic Hospital in whom cancer was detected after routine examination (asymptomatic) and in those in whom it was suspected a priori (symptomatic)

Stage	Group; no. (and %) of patients			
	Asymptomatic		Symptomatic	
	1976 (n = 18)	1986–87 (n = 27)	1976 (n = 31)	1986–87 (n = 32)
A and B (localized)	12 (67)	22 (81)	8 (26)	16 (50)
C and D (invasive)	6 (33)	5 (19)	23 (74)	16 (50)

Pathological findings

The mean number of slides per gram of prostatic tissue analysed by the pathologists was significantly greater in 1986–87 than in 1976, both in patients found to have BPH (0.29 v. 0.17, p < 0.01) and in those whose cancer was diagnosed incidentally (0.38 v. 0.23, p < 0.01).

Discussion

Although the incidence and mortality rates of prostate cancer have increased over the past several decades in Canada, the incidence rates have increased much more rapidly. Some researchers believe that the increased use of TURP to treat BPH has led to an artifactual increase in the incidence of prostate cancer.^{19,21} TURP now accounts for more than 95% of all prostatectomies performed in Canada, and since the use of other types of prostatectomy is often restricted to patients with unusually large glands²² or known cancer we used the TURP rates rather than the total prostatectomy rates in our analysis.

Both the national and the provincial data showed evidence of a direct correlation between the incidence rate of prostate cancer and the TURP rate. The weaker correlation in the case of the provincial data may have resulted because the linear regression was performed on only 10 data points; this may have led to an increase in the variance of the estimate and thus a decrease in the magnitude of the correlation. Nevertheless, the strong positive correlations between the increasing incidence rates of prostate cancer and the TURP rates suggest increased case finding. These associations are ecological, however, and cannot be construed as causal.

Potosky and associates¹⁹ used data from the Surveillance Epidemiology and End Results Program for four areas in the United States and found equally strong linear correlations between the incidence rates of both total and localized prostate cancer and the TURP rates. They concluded that the rising incidence rates were due primarily to increased detection of formerly undiagnosed tumours as a result of the greater number of TURPs being undertaken to treat BPH. The proportion of all cases of prostate cancer diagnosed by TURP in Canada is not known, nor is it known whether rates of other methods of diagnosis, such as digital rectal examination and needle biopsy, have increased during the study period. However, US data have indicated that more than 50% of prostate tumours are diagnosed by TURP.23 Our data from the Ottawa Civic Hospital showed that about 40% of the tumours were diagnosed by TURP in 1976, a proportion that increased to 49% by 1986-87.

The data from the chart review provided descriptions of change over time in the process leading to a diagnosis of prostate cancer and descriptions of the clinical manifestations of the disease. Patients could not be selected from a population-based registry and were restricted to those discharged from a local teaching hospital. We assumed that the characteristics of these patients were generalizable to the population in the main catchment area of the hospital and thus extrapolated from them to estimate population rates.

The increase observed in the incidence rates between the mid-1970s and the mid-1980s can be attributed to increases in the rates of latent and localized disease. The greatest change was in the rate of cancer discovered incidentally; there was a smaller increase in the rate of disease detected through routine examination. As more tumours are detected earlier the pool of men who will develop symptomatic, clinically evident disease may shrink.

The increased incidence rate of early cancer suggests that improvements in case ascertainment may have contributed to the observed rise in overall incidence. It is well known that there are latent and active forms of prostate cancer. Latent cancer is common in middle-aged and elderly men and often never becomes active.²⁴ Autopsy studies have shown that the prevalence of unsuspected cancer that has no negative health effects is about 40% in men over 60 years;²⁵ this estimate is supported by data from surgical series in live patients.²⁶ An estimated 90% of cases of prostate cancer may remain clinically unimportant for decades.²⁷ When these cancers are detected incidentally they are recorded as stage A disease and contribute to the numerator of the incidence rate.

There have been numerous advances in the detection of prostate cancer in recent years. Immunologic markers (prostate-specific antigen), transrectal ultrasound probes and spring biopsy guns have been developed.^{24,27–29} Our study specifically eliminates the potential impact of these influences, since none of the techniques was in use at the Ottawa Civic Hospital during the study period.

Earlier detection could also be a function of heightened health awareness and a greater tendency for patients to visit general practitioners either for routine examination or for investigation earlier in the natural history of obstructive prostatic symptoms. Or, general practitioners could be performing more digital rectal examinations, possibly looking for cancer. The contribution of these factors is suggested by the apparent shift, seen in the subgroup analyses, to earlier stage disease detected in patients routinely examined or in those who presented with suspicious signs and symptoms; however, further studies are required to test these hypotheses. Finally, more TURPs or more scrutiny in the pathological examination of surgical specimens obtained from TURP would contribute to earlier detection.

In many countries, including Canada, TURP is the treatment of choice to relieve obstructive symptoms due to BPH.²² We have shown that the rate of this procedure has increased in Canada; the greater availability of surgi-

cal specimens from TURP may have resulted in the increased detection of previously undiagnosed cancer, especially in asymptomatic patients with localized disease. TURP is known to be the commonest method of obtaining tissue for the diagnosis of prostate cancer,^{18,30} but it is usually impossible to know whether the diagnosis after surgery for putative BPH was a surprise to the physician or whether cancer had already been diagnosed or considered. We have shown an increase over time in the rate of cancer diagnosed in men who had undergone TURP specifically for BPH. However, at the Ottawa Civic Hospital there were no more TURPs performed in 1986 than in 1976, which suggests that this finding was not attributable to an increase in the number of specimens reaching the laboratory. Rather, our results indicate that the source of the artifact may be in the pathology laboratory itself.

Although the number of slides required for optimum examination has not been established, no doubt the number of cases of latent cancer is directly proportional to the amount of tissue examined.²⁰ More slides were analysed per gram of tissue submitted after TURP in 1986–87 than in 1976, regardless of whether BPH or prostate cancer was ultimately diagnosed.

Early-stage prostate cancer is often found as a result of routine screening or is detected unexpectedly in TURP specimens. Our data showed that earlier detection of the disease was a major factor in the observed increase in incidence and was due predominantly to increased scrutiny in the laboratory of specimens of supposedly benign prostatic lesions.

An increase in the diagnosis of early-stage prostate cancer will presumably lead to an increase in survival rates. In fact, data from Canada^{1,31} and the United States³² have shown that such survival rates did increase between 1970 and 1980. Byar³² noted that a general shift toward earlier diagnosis could account for the observed increase in survival.

Nevertheless, the rate of death from prostate cancer has increased over time, most notably in older patients. This suggests that increased detection alone may not be responsible for the rise in incidence rates. The lower rates of death from other, "competing" conditions, such as cardiovascular disease, and the greater number of men aged 85 years and over may explain the increased rates of death from prostate cancer.¹⁹ However, it remains possible that the rise in the incidence and mortality rates is due, in part, to increased exposure to unknown etiologic agents. Analysis of stage-specific survival over time will help to elucidate further the role of early detection of this important public health problem.

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- 1. National Cancer Institute of Canada: Canadian Cancer Statistics, 1991, NCIC, Toronto, 1991
- 2. McLaughlin JR: Cancer trends in Ontario. In Marret LD (ed): *Proceedings of the Cancer Epidemiology Seminar*, Ontario Cancer Treatment and Research Foundation, Toronto, 1990: 3–10
- 3. International Agency for Research on Cancer: Cancer Incidence in Five Continents, vol 5, IARC, Lyon, 1987: 170–766
- Armstrong B, Doll R: Environmental factors and cancer incidence and mortality in different countries, with special reference to dietary practices. *Int J Cancer* 1975; 15: 617–631
- 5. Haenszel W: Cancer mortality among the foreign-born in the United States. J Natl Cancer Inst 1961; 26: 37–132
- Staszewski J, Haenszel W: Cancer mortality among the Polishborn in the United States. J Natl Cancer Inst 1965; 35: 291–297
- Haenszel W, Kurihara M: Studies of Japanese migrants. I. Mortality from cancer and other diseases among Japanese in the United States. J Natl Cancer Inst 1968; 40: 43–68
- Ghadirian P, Cadotte M, Lacroix A et al: Family aggregation of cancer of the prostate in Quebec: the tip of the iceberg. *Prostate* 1991; 19: 43-52
- 9. Fincham SM, Hill GB, Hanson J et al: Epidemiology of prostatic cancer: a case-control study. *Prostate* 1990; 17: 189-206
- Steinberg GD, Carter BS, Beaty TH et al: Family history and the risk of prostate cancer. Ibid: 337–347
- 11. Spitz MR, Currier RD, Fueger JJ et al: Familial pattern of prostate cancer: a case-control analysis. *J Urol* 1991; 146: 1305–1307
- Kolonel LN, Yoshizawa CN, Hankin JH: Diet and prostatic cancer: a case-control study in Hawaii. Am J Epidemiol 1988; 127: 999-1012
- Heshmat MY, Kaul L, Kovi J et al: Nutrition and prostate cancer: a case-control study. *Prostate* 1985; 6: 7–17
- Graham S, Haughey B, Marshall J et al: Diet in the epidemiology of carcinoma of the prostate gland. J Natl Cancer Inst 1983; 70: 687-692
- Elghany NA, Schumacher MC, Slattery ML et al: Occupation, cadmium exposure, and prostate cancer. *Epidemiology* 1990; 1: 107–115
- Ayiomamitis A: Epidemiology of cancer of the prostate in Canada. Br J Urol 1987; 60: 157–161
- Carter HB, Coffey DS: The prostate: an increasing medical problem. *Prostate* 1990; 16: 39–48
- Murphy GP, Natarajan N, Pontes J et al: The national survey of prostate cancer in the United States by the American College of Surgeons. J Urol 1982; 127: 928–934
- Potosky AL, Kessler L, Gridley G et al: Rise in prostatic cancer incidence associated with increased use of transurethral resection. *J Natl Cancer Inst* 1990; 82: 1624–1628
- Murphy WM: Urological Pathology, Saunders, Philadelphia, 1989: 174–184
- Severson RK: Have transurethral resections contributed to the increasing incidence of prostatic cancer? J Natl Cancer Inst 1990; 82: 1597–1598
- Roos NP, Wennberg JE, Malenka DJ et al: Mortality and reoperation after open and transurethral resection of the prostate for benign prostatic hyperplasia. N Engl J Med 1989; 320: 1120–1124
- Schmidt JD, Mettlin CJ, Natarajan N et al: Trends in patterns of care for prostatic cancer, 1974–1983: results of surveys by the American College of Surgeons. J Urol 1986; 136: 416–421
- 24. Dohm G: Epidemiologic aspects of latent and clinically manifest carcinoma of the prostate. *J Cancer Res Clin Oncol* 1983; 106: 210-218
- Donn AS, Muir CS: Prostatic cancer: some epidemiological features. Bull Cancer (Paris) 1985; 72: 381–390
- 26. Montie JE, Wood DP Jr, Pontes JE et al: Adenocarcinoma of the prostate in cystoprostatectomy specimens removed for bladder cancer. *Cancer* 1989; 63: 381–385
- 27. Gittes RF: Carcinoma of the prostate. N Engl J Med 1991; 324: 236-245

- Catalona WJ, Smith DS, Ratliff TL et al: Measurement of prostate-specific antigen in serum as a screening test for prostate cancer. Ibid: 1156–1161
- Murphy GP: The current and potential status of screening for prostatic cancer in asymptomatic populations. *Prog Clin Biol Res* 1989; 303: 19–25
- 30. Humphrey P, Vollmer RT: The ratio of prostate chips with cancer: a new measure of tumor extent and its relationship to grade

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Nov. 27–28, 1993: Memorial University School of Pharmacy 2nd Annual Symposium — Update on Drug Use: the Rational Use of Antibiotics (in collaboration with the Faculty of Medicine and the Provincial Quality Assurance Committee)

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Dr. Gerald R. Duncan, director and professor of pharmacy, School of Pharmacy, Memorial University of Newfoundland, St. John's, NF A1B 3V6; tel (709) 737-6571, fax (709) 737-7044

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Tiberias (on the Sea of Galilee), Israel

Gil-Kenes, 946–1617 J.F.K. Blvd., Philadelphia, PA 19103, tel (800) 223-3855, fax (215) 568-0696; or Secretariat, 2nd Dead Sea Conference, PO Box 50006, Tel Aviv 61500, Israel, tel 011-972-3-517-4571, fax 011-972-3-660-325

Nov. 29–Dec. 3, 1993: Neonatal Course for Senior Paediatricians (sponsored by the Royal Postgraduate Medical School [RPMS] Institute of Obstetrics and Gynaecology)

London, England

Symposium Secretary, RPMS Institute of Obstetrics and Gynaecology, Queen Charlotte's and Chelsea Hospital, Goldhawk Road, London, England W6 0XG; tel 011-44-81-740-3904, fax 011-44-81-741-1838

Dec. 2–3, 1993: 26th Annual Symposium of the Society of Toxicology of Canada

Montreal

- Gordon Krip, executive director, Society of Toxicology of Canada, PO Box 517, Beaconsfield, PQ H9W 5V1
- Dec. 3–4, 1993: 2nd Montreal–Cleveland Cerebrovascular Symposium

Montreal

- Aneurysms Secretariat, Conference Office, McGill University, West Tower, 490–550 Sherbrooke St. W, Montreal, PQ H3A 1B9; tel (514) 398-3770, fax (514) 398-4854
- **Apr. 24, 1994:** Association of Canadian Medical Colleges 6th Conference on Physician Manpower Vancouver

Deadline for abstracts: Dec. 3, 1993

and prognosis. Hum Pathol 1988; 19: 411-418

- 31. Mao Y, Robson D, Semenciw RM et al: Long term survival rates among patients with cancer in Saskatchewan. *Can J Public Health* 1991; 82: 413–420
- 32. Byar DP: Incidence, mortality and survival statistics for prostatic cancer. In Coffey DS, Bruchovsky N, Gardner WA (eds): *Current Concepts and Approaches to the Study of Prostate Cancer*, Liss, New York, 1987: 785–796

Eva Ryten, Association of Canadian Medical Colleges, 1006–151 Slater St., Ottawa, ON K1P 5N1; fax (613) 594-3364

Le 24 avr. 1994 : Association des facultés de médecine du Canada 6^e conférence sur la main-d'oeuvre médicale canadienne

Vancouver

Date d'échéance pour les résumés : le 3 déc. 1993

Eva Ryten, l'Association des facultés de médecine du Canada, 1006–151, rue Slater, Ottawa, ON K1P 5N1; fax (613) 594-3364

May 12–15, 1994: Communication, Aging and Health — International Conference

Hamilton, Ont.

Office of Public Relations, McMaster University, 1280 Main St. W, Hamilton, ON L8S 4L8; tel (416) 525-9140, ext. 2959, fax (416) 521-1504

July 24–30, 1994: 14th Federative International Congress on Anatomy (includes presentation of the Sobotta Prize [US \$10 000])

Lisbon, Portugal

Sobotta Prize competition rules may be obtained from the address below. Deadline for manuscripts: Sept. 1, 1993.

- Dr. Wolfgang Kühnel, Institut für Anatomie, Medizinische Universität zu Lübeck, Ratzeburger Allee 160, D–2400 Lübeck, Germany; tel 011-49-0451-500-40-30-1, fax 011-49-0451-500-40-34
- Sept. 18–23, 1994: XIIth International Congress of Neuropathology (in conjunction with the annual meetings of the Canadian Association of Neuropathologists and the American Association of Neuropathologists)

Toronto

Dr. J.J. Gilbert, Department of Pathology, Victoria Hospital Corporation, PO Box 5375, London, ON N6A 4G5; tel (519) 667-6649, fax (519) 667-6749

Oct. 2–7, 1994: World Congresses of Gastroenterology 10th Quadrennial Celebration

Los Angeles

Secretariat, World Congresses of Gastroenterology, Ste. 300, 655–15th St. NW, Washington, DC 20005; tel (202) 639-4626, fax (202) 347-6109