Epidemiology of Primary Intracranial Neoplasms in Manitoba, Canada

G.R. Sutherland, R. Florell, D. Louw, N.W. Choi and A.A.F. Sima

ABSTRACT: The incidence of primary intracranial tumors in Manitoba, Canada was reviewed. From 1980 through 1985, 657 tumors were diagnosed. The crude incidence rates were 10.2/100,000 for males and 10.8/100,000 for females. The three most common tumors were: astrocytoma 281 (43%), meningioma 145 (22%), and pituitary adenoma 111 (17%). Average annual incidence rates for all tumors showed a bimodal distribution with one peak in the 0-4 age group (4.2/100,000), and the other in the 60-69 age group (27.2/100,000). For malignant astrocytoma, the age-specific annual incidence rate increased to the seventh decade where it reached a peak of 14.3/100,000. The incidence of benign astrocytoma remained relatively constant with age at 1.1/100,000. The annual incidence of meningioma increased with age up to the eighth decade reaching 7.2/100,000. Of the 145 meningiomas, 56 (39%) were meningotheliomatous, 48 (33%) transitional, 10 (7%) malignant, 7 (5%) fibroblastic, 6 (4%) psammomatous, 3 (2%) angioblastic, and 15 (10%) lacked pathologic diagnosis. The annual incidence of pituitary adenoma showed two peaks, the first occurring in the third decade (2.6/100,000) and the second in the eighth decade (3.2/100,000). Although the incidence of meningioma was relatively high, the clinical features and pathologic patterns of these tumors were not unlike those previously reported in the literature.

RÉSUMÉ: Epidémiologie des néoplasmes primitifs intracrâniens dans la province du Manitoba, au Canada. Nous faisons une revue de l'incidence des tumeurs primitives intracrâniennes dans la province du Manitoba, au Canada. De 1980 à 1985, 657 tumeurs on été diagnostiquées. Les taux d'incidence bruts étaient de 10.2/100,000 pour les hommes et de 10.8/100,000 pour les femmes. Les trois types de tumeurs les plus fréquentes étaient: l'astrocytome, 281 (43%); le méningiome, 145 (22%) et l'adénome pituitaire, 111 (17%). L'incidence annuelle moyenne le l'ensemble des tumeurs prend la forme d'une distribution bimodale avec un pic dans le groupe d'âge 0-4 ans (4.2/100,000), et l'autre pic dans le groupe d'âge 60-69 ans (27.2/100,000). Pour l'astrocytome malin, l'incidence annuelle par âge augmentait jusqu'à la septième décennie, pour atteindre un pic de 14.3/100,000. L'incidence annuelle du méningiome augmentait avec l'âge jusqu'à la huitième décennie, pour atteindre 7.2/100,000. Parmi les 145 cas de méningiomes, 56 (39%) étaient de type méningiomateux, 48 (33%) de type transitonnel, 10 (7%) de type malin, 7 (5%) de type fibroblastique, 6 (4%) de type psammomateux, 3 (2%) de type angioblastique et 15 (10%) n'avaient pas de diagnostic anatomo-pathologique. L'incidence annuelle des adénomes pituitaires comportait deux pics, le premier dans la troisième décennie (2.6/100,000) et le second dans la huitième décennie (3.2/100,000). Même si l'incidence du méningiome était relativement haute, les manifestations cliniques et les caractéristiques pathologiques de ces tumeurs étaient semblables à celles rapportées antérieurement dans la littérature.

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The epidemiology of intracranial tumors has been studied in two ways, either as hospital-based or as community-based incidences.[1-11] In Cushing's hospital-based series of 2,186 tumors, the occurrence of the three most common tumors was 43.1% for glioma, 13.7% for meningioma, and 17.9% for pituitary adenoma. A more recent U.S. national survey of 166 hospitals found that the frequency of the same primary intracranial tumors among 17,000 patients was 37.9%, 19.5% and 14.4%, respectively. These data may not necessarily represent the true epidemiologic picture of primary intracranial neoplasms since they may be biased by the referral patterns of a particular center.

This bias is eliminated in population or community-based studies.[8,12-20] An investigation conducted in Washington, D.C., found that the frequency of glioma, meningioma, and pituitary adenoma was 68.7%, 17.5% and 9.1% respectively.[16] In contrast, the Rochester community-based study found 35% of primary intracranial tumors to be glioma, 40% meningioma, and 13% pituitary adenoma.[17] This study, however, included patients

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first diagnosed at necropsy which tended to bias the incidence of meningioma upward. When tumors diagnosed at autopsy were omitted from the study, the frequency of glioma changed to 43%, that of meningioma to 21% and pituitary adenoma to 17%.

In the present report, we examined the incidence of primary intracranial neoplasms in the population of Manitoba, Canada, over a six-year period, 1980 through 1985. In Manitoba, the population has remained constant at approximately one million [$(1043.3 \pm 7.3) \times 10^3$]. The number of people emigrating and immigrating from or to Manitoba was minimal, hence providing an ideal population in which to examine the incidence of primary intracranial neoplasms. In addition, the vast majority of individuals in Manitoba suffering from neurological disease are referred to one of two teaching hospitals in Winnipeg for their investigation and treatment. Since 1980, all such patients have undergone computerized tomographic (CT) imaging as part of their investigation, providing a CT documentation of the intracranial tumors. Since the incidence of meningioma was felt to be higher than in previous reports, we also examined the clinical, radiological and pathological features of patients in whom the diagnosis of meningioma was made.

Data Sources and Methods

1. Case Material

In this study, intracranial neoplasm was defined as all benign and malignant primary tumors of the brain and cranial meninges. In view of their proximity, tumors of the pituitary gland, craniopharyngeal duct and pineal body were included. This study did not include metastatic tumors to the brain, retinoblastoma, or spinal cord tumors including those originating from the spinal meninges. Residency within Manitoba at the time of diagnosis was necessary for inclusion in the study.

In defining patients with primary intracranial tumors, we obtained all CT imaging files from both teaching hospitals. The medical charts from patients with verified intracranial neoplasms were reviewed, extracting the clinical, surgical, and histological data. In addition, the Medical Information Departments of the two teaching hospitals were accessed, in order to obtain all charts in which a discharge diagnosis of primary intracranial tumor was made. Finally, the data were cross-referenced with the Central Cancer Registry for the Province of Manitoba in order to prevent omissions.

2. General Population Information

Manitoba has a population of slightly more than 1 million. This is comprised mainly of ethnic groups from European, Ukranian, Asiatic, American Indian, and Inuit stock. The people of Manitoba have equal access to health care facilities, particularly in the past three decades, through government-sponsored universal health care systems. The age distribution of the population of Manitoba is not unlike that of Canada for the years 1980 through 1985.[21]

3. Methods

The distribution of new patients with primary intracranial neoplasms was compared by average annual incidence rates according to age, sex, and tumor type. Average annual incidence rates were computed utilizing the average population over the six year period. Overall rates for specific tumor types are crude rates.

Radiologic data from all individuals, in whom the diagnosis of meningioma was made, were obtained and reviewed. In addition, biopsy specimens from the patients were re-examined pathologically and classified according to the World Health Organization Classification.[22] Follow-up examinations of the patients with meningioma were performed in order to correlate the outcome and incidence of tumor recurrence with the initial histological features.

All values other than incidence rates and frequencies are expressed as mean ± SEM. Comparisons between groups were made using the Student's t-test with significance reported at the 0.05 level.

Results

1. Intracranial Neoplasms

Of 657 patients with primary intracranial neoplasms diagnosed during the six-year study period, 315 (48%) were males and 342 (52%) were females. Overall annual incidence rates for intracranial neoplasms were 10.2/100,000 and 10.8/100,000 for males and females, respectively. The most common type of tumor was malignant astrocytoma, which was followed by meningioma, anterior pituitary tumor and benign astrocytoma in that order of frequency (Table 1). A male predominance was noted for astrocytomas, while a female predominance was found for both meningioma and pituitary tumors.

Average annual incidence rates for all intracranial neoplasms by age and sex are shown in Figure 1. The average annual incidence rate was higher for females aged 15-29 years, whereas it was higher for males aged 40-49 and 70-79 years. The most noteworthy aspect of the incidence curves was the identification of two peaks for both sexes, one in the 0-4 year age group (4.2/100,000) and the other in the 60-69 year age group

Table 1: Distribution of Primary Intracranial Neoplasms By Tumor Type and Sex

	MALE		FEMALE	
Tumors by Sex	No.	Average Annual Incidence Rate	No.	Average Annual Incidence Rate
Astrocytoma — Malignant	129	4.17	86	2.71
— Non-Malignant	40	1.29	26	0.82
Meningioma	46	1.49	99	3.12
Anterior Pituitary Tumors	43	1.39	68	2.14
Poorly Differentiated/ Embryonal Tumor	15	0.49	8	0.25
Oligodendroglioma	11	0.36	6	0.19
Nerve Sheath Tumor	9	0.29	24	0.76
Ependymoma	7	0.23	3	0.10
Other Malformative Tumors/ Tumor-like Tissue	4	0.13	7	0.22
Primary Lymphoma	4	0.13	5	0.16
Blood Vessel Tumor	3	0.10	3	0.10
Pineal Cell Tumor	2	0.07	2	0.06
Choroid Plexus Tumor	1	0.03	2	0.06
Neuronal Cell Tumors	1	0.03	1	0.03
Germ Cell Tumor	0	—	1	0.03
Local Extension From Regional Tumors (Chordoma)	0	—	1	0.03
Total	315	10.19	342	10.84
Crude Rates: Males —	315	10.19		
Females —	342	10.84		
Total:	657	10.49		

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(27.2/100,000). Females showed a third peak in the 15-19 year age group (7.4/100,000), due mainly to the higher incidences of benign astrocytoma and pituitary adenoma (Figures 2 and 4).

A similar bimodal distribution of the incidence rates was found for combined malignant and benign astrocytomas (Figure 2a). An early peak was seen for the 0-9 year age group for both sexes. For females, another peak was seen for the 15-19 year age group, following which a male excess was observed for every age group. A second large peak occurred in the 60-69 year age group for both sexes with an incidence of 15.5/100,000. Hence, the bimodality of the incidence curve for intracranial neoplasms combined (Figure 1) appears to largely be a reflection of astrocytomas. The early peak is comprised mainly of benign astrocytomas (Figure 2b) and medulloblastoma (data not shown). The second, larger peak is due mainly to the occurrence of malignant astrocytoma (Figure 2c). For both malignant and benign astrocytomas, there was an overall male predominance in incidence, the rates being 4.2 versus 2.7/100,000 for malignant astrocytomas and 1.3 versus 0.8/100,000 for benign astrocytomas (Table 1).

In Figures 3a and 3b, average annual age-specific incidence rates are shown for all meningiomas and malignant meningiomas, respectively. For males, the incidence increased with age up to 5.1/100,000. Females showed two peaks, the first occurring in the 15-19 year age group (1.1/100,000) and a second in the 50-59 year age group (10.2/100,000) (Figure 3a). The incidence of malignant meningioma remained relatively constant with age following the fourth decade with no significant sex difference (Figure 3b). In age groups exceeding the fifth decade, a female predominance was noted. The overall incidence rates were 1.5 and 3.1/100,000 for males and females, respectively (Table 1).

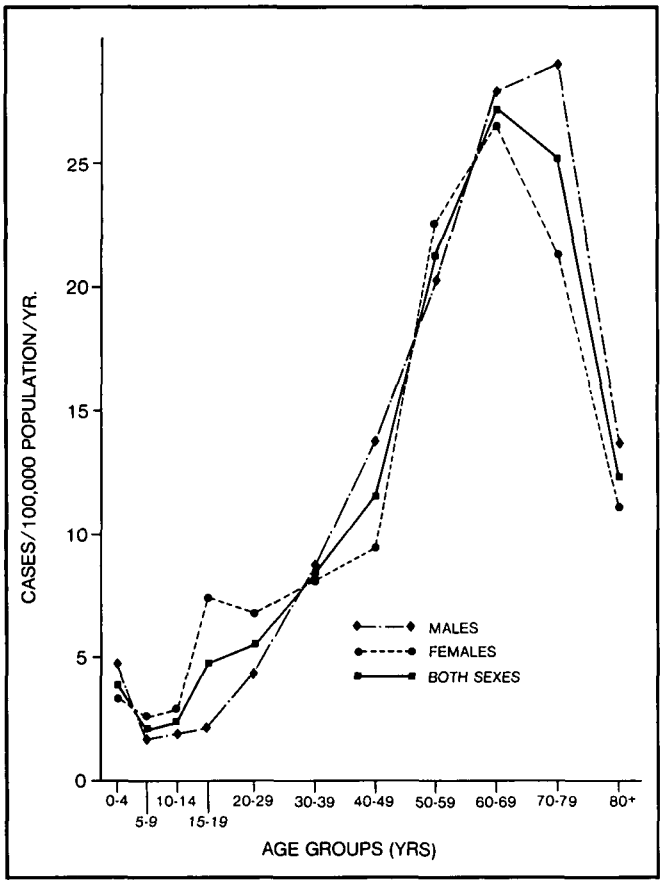

Figure 1 — Average annual incidence rates for all intracranial neoplasms by age and sex. The incidence curves show two peaks for both sexes, one in the 0-4 year age group and the other in the 60-69 year age group. Females show a third peak in the 15-19 year age group.

Age-specific average incidence rates for anterior pituitary adenomas are depicted in Figure 4. While male rates gradually increased with age from the 15-19 year age group and peaked at the 70-79 (5.3/100,000) year age group, female rates showed a bimodal distribution with one peak at 20-29 (4.7/100,000) and a second at the 50-59 (2.6/100,000) year age groups. Of the 40 female pituitary tumors occurring in age groups 20-29 (26) and 30-39 (14) years, 32 were prolactinomas. The overall incidence rates for anterior pituitary tumors were 1.4 and 2.1/100,000 for males and females, respectively (Table 1).

2. Meningioma (Clinico-Pathological Features)

The history and physical findings obtained from the meningioma patients are presented in Table 2. Headaches, confusion, focal weakness, and seizures were the most common symptoms, and paresis was the most frequently found sign. Twenty-five percent of the patients had a history of seizures only, and had a normal neurologic examination. The distribution of meningiomas according to location as defined by CT imaging is shown in Table 3. Parasellar meningiomas were included in the tuberculum sella group. In 48 patients (33%) the tumors were located over the cerebral convexities, while 36 (25%) were parasagittal, and 23 (16%) were located along the sphenoid wing. The remaining tumors were distributed throughout the cranial compartments, with 10 (7%) found within the lateral ventricle. Among patients with parasagittal tumors, the majority, (49%), were located along the anterior one-third portion of the falx cerebri, 29% were located within the middle third, and the remaining 22% were located along the posterior third of the falx. Medial sphenoid ridge tumors were more common than middle or laterally situated tumors.

Computerized tomographic data from 145 patients with meningioma are presented in Table 4. One hundred and one (70%) showed homogeneous enhancement following the injection of contrast, 38 (26%) had a non-homogeneous enhancement pattern, and in 8 cases (6%), the tumor was totally calcified without enhancement. Mean tumor size, as defined by the CT image, was 4.3 ± 1.7 cm. Midline and/or ventricular displacement were seen in 111 (77%) meningiomas. Peritumor hypolucency was found in 100 (69%) and these data are presented as mild, moderate or severe. Tumor calcification and/or associated hyperostosis were less consistently observed, although these findings were present in over 20% of the patients. Angiographic evaluation revealed a tumor blush in 77 (80%) patients. The vascular supply to the tumor was derived mainly from the external carotid artery, with a lesser component arising from branches of the internal carotid artery.

One hundred and twenty-seven meningioma patients underwent surgical intervention. Complete gross excision of the tumor was obtained in 92 (72%) patients. In 33 (26%) patients, the tumor was subtotally resected and 2 (2%) patients underwent a cerebrospinal fluid diversion procedure only, for control of elevated intracranial pressure. The most common perioperative complication was postoperative paresis associated with progressive cerebral edema, occurring in 21 (17%) patients. This complication did not correlate with the degree of preoperatively-defined peritumoral hypodensity.

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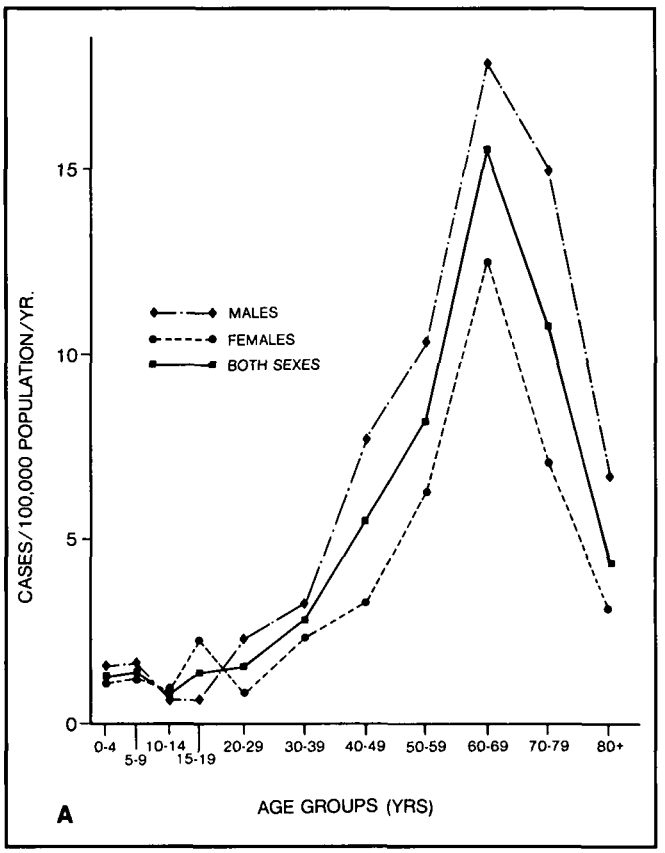
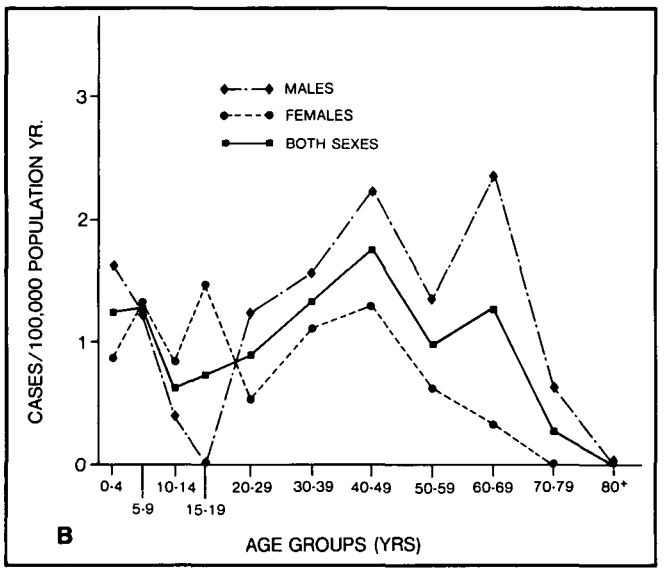
The frequency of histological subtypes of meningioma patients is shown in Table 5. Meningotheliomatous and transitional types comprised the majority of meningiomas (72%). Ten (7%) tumors had histological features of malignant meningioma demonstrating increased mitotic rate, pleomorphism, hypercellularity, focal necrosis, and invasion of brain parenchyma. Although eighteen (12%) patients did not undergo operative intervention, only 15 (10%) tumors lacked histopathological examination. Three patients with CT-defined meningiomas died, allowing for autopsy confirmation of their presumed diagnosis.





Similar to the meningioma group as a whole, the number of malignant meningiomas diagnosed in any given year remained relatively constant at 1.7 ± .4 tumors/year. The mean age at diagnosis for patients with malignant meningioma was 58 ± 15 years which was identical to that seen in patients with non-malignant meningioma (58 ± 15).

During the study interval, 15 patients with diagnosed meningiomas had tumor recurrence. This was significantly ($p<0.05$) more frequent in patients with malignant meningioma (6/10) compared to those with benign meningioma (9/117).

Discussion

1. Limitations of the Data

We estimate that more than 90% of all intracranial tumors diagnosed pre-mortem in Manitoba during the years 1980 through 1985 have been identified in this study. It is possible that some tumors would have been diagnosed outside Manitoba and, therefore, would not be included in this study. The number would, however, be small since most patients are initially reviewed in Winnipeg prior to possible referral elsewhere and would thus have undergone CT imaging and/or have been registered with the Central Tumor Registry of Manitoba. As obligatory postmortem examination is not the practice in Manitoba,

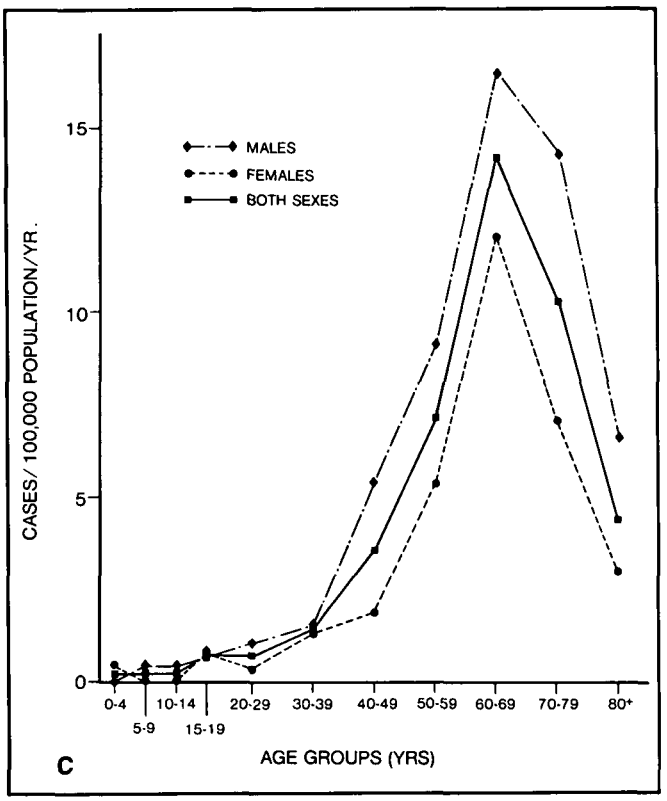


Figure 2A — Average annual incidence rates for all astrocytomas by age and sex. The incidence curves show an early peak for the 0-9 year age group for both sexes. For females, another peak is seen for the 15-19 year age group. A second large peak occurs in the 60-69 year age group for both sexes. Following the second decade, a male excess is seen for every age group. 2B - Average annual incidence rates for benign astrocytoma by age and sex. The combined incidence remains relatively constant with age at 1.1/100,000 population per year. 2C - Average annual incidence rates for malignant astrocytoma by age and sex. The incidence curves show a single peak for both sexes occurring in the 60-69 year age group. After the fourth decade, a male excess is seen for all age groups.

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patients in whom tumor diagnosis would have been established first at the time of death would not be available for analysis.

2. Incidence of Primary Intracranial Neoplasms

Intracranial tumor incidence rates have been estimated to range from 4/100,000 population (Iowa)[23] to 15/100,000 (Rochester).[17] These variations may be due to discrepancies in case definition and ascertainment. Walker et al.,[9] compared incidence rates of intracranial neoplasms for the United States during 1973 and 1974 with those reported for Carlisle, England, Connecticut, Iceland and Rochester, Minnesota. The age-adjusted rates for brain and pituitary neoplasms ranged from 6.6/100,000 population in the Connecticut and Iceland studies to an average incidence rate of 14.7/100,000 population in Rochester. Both the Rochester and Connecticut studies contained post-mortem tumor statistics. If intracranial tumors diagnosed at post-mortem examination are excluded from these studies, the incidence rates become 8.2 and 4.9/100,000 population, respectively.

In the present study, the average incidence rate for intracranial neoplasms was 10.5/100,000. This figure approaches that obtained in the Rochester combined clinical post-mortem study and is attributed to the introduction of CT brain imaging that provides greater diagnostic accuracy. Similar to both the Rochester and U.S. studies, we found that the annual incidence rates by age for intracranial neoplasms diagnosed pre-mortem increased to the seventh decade and then declined. This may reflect a less aggressive investigative approach to patients in this age group due to accompanying chronic diseases rather than to intrinsic biological differences. Age-specific annual incidence rates for all tumors in our study revealed a bimodal distribution with the first small peak reflecting mainly the occurrence of benign astrocytoma and medulloblastoma in children and the second much larger one reflecting the progressive increase with age of malignant astrocytoma, meningioma and pituitary adenoma.

The bimodal distribution of glioma observed in the present and previous studies may indicate different risk factors and natural histories of childhood and adult tumors. Male excess in the crude incidence for all astrocytomas is consistent with the findings in previous studies.[9,16,17]

In this study, the incidence of meningioma (22%) was higher than that commonly reported.[1,7,9,16] This may be due to the fact that previous studies were conducted prior to the increased diagnostic accuracy provided by CT brain imaging. In support of this suggestion, the Rochester study found an incidence of meningioma of 39%.[17] In this pre-CT era study, 55 of 88 meningiomas were incidental findings at necropsy and measured 1 to 2 cm in size. Speculatively, many of these tumors would now be diagnosed premortem. As has been repeatedly shown in previous studies, we found a significant female excess in meningioma incidence of roughly 2:1.[16,17]

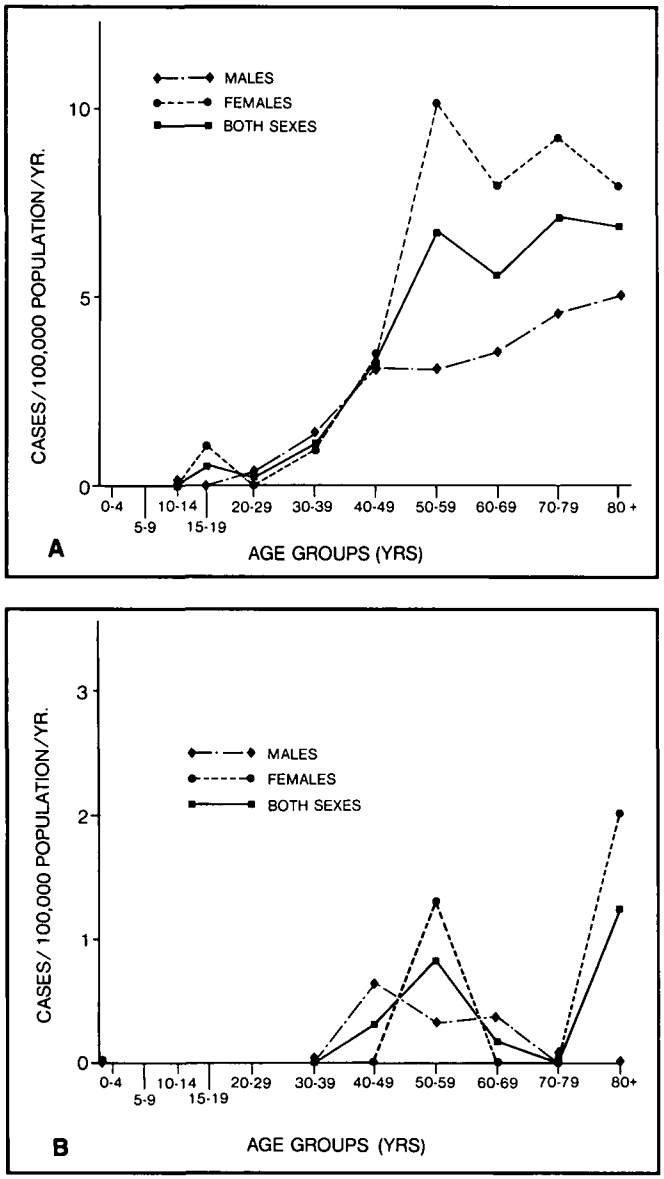

Figure 3A — Average annual incidence rates for all meningiomas by age and sex. For males, the incidence increases with age. Females show an early peak in the 15-19 year age group and a second in the 50-59 year age group. In age groups exceeding the fifth decade, a female predominance is noted. 3B - Average annual incidence rates for malignant meningioma by age and sex. No malignant meningiomas occurred prior to the fifth decade. Thereafter, their incidence remained relatively constant with no sex difference.

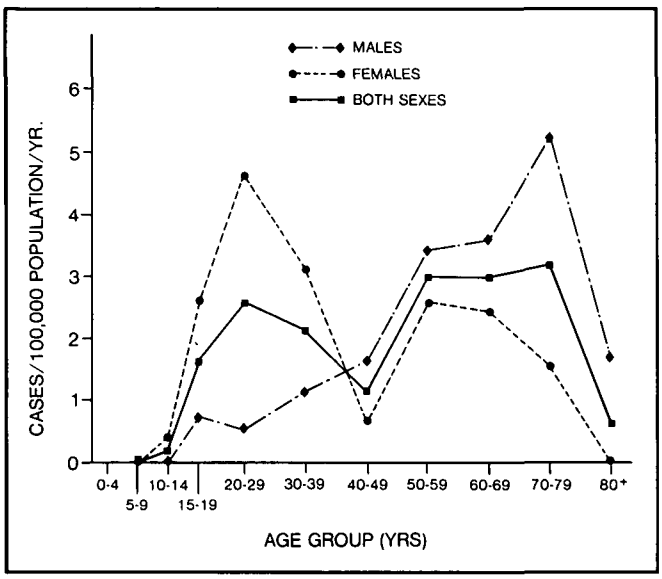

Figure 4 — Average annual incidence rates for pituitary adenomas by age and sex. For males, the incidence increases with age up to the eighth decade where it peaks. Females show a bimodal distribution with one peak occurring at the 20-29 year age group, and a second at the 50-59 year age group.

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Table 2: History and Physical Findings in Patients With Meningioma (n = 145)

Patient History	No. of Patients	%
Headaches	53	37
Personality Change/Confusion	36	26
Paresis	32	22
Generalized Seizures	25	17
Visual Impairment	23	16
Focal Seizure	21	15
Ataxia	20	13
Aphasia	12	8
Decreasing Level of Consciousness	7	5
Paresthesia	6	4
Diplopia	4	3
Vertigo	2	1
Decreased Hearing	2	1
Physical Findings		
Paresis	41	28
Normal Exam	40	28
Memory Impairment	21	15
Visual Field Deficit	15	10
Papilledema	14	10
Paresthesia	12	8
Decreased Visual Acuity	12	8
Other Cranial Nerve Deficit	11	8
Aphasia	9	6
Altered Level of Consciousness	7	5
Decreased Hearing	4	3
Nystagmus	2	1
Other	1	1

Table 3: Frequency of Meningiomas at Various Tumor Sites

Location	Total Tumors No.	%
Convexity	48	33
Parasagittal	36	25
Sphenoid Ridge	23	16
Lateral Ventricle	10	7
Tentorial	5	4
Cerebellar Convexity	5	4
Tuberculum Sella	4	3
Intraorbital	4	3
C-P Angle	4	3
Olfactory Groove	3	2
Foramen Magnum	1	1
Clivus	1	1
Other	1	1
TOTAL	145	

Table 4: CT Scan Findings In Meningioma Patients (n = 145)

Findings	No. of Patients	%
Shift	111	77
Homogenous Enhancement	101	70
Nonhomogenous Enhancement	38	26
Calcification	36	25
Hyperostosis	28	19
Peritumor Hypolucency		
— Mild	38	26
— Moderate	36	25
— Severe	26	18

The incidence of anterior pituitary adenomas increased in males from the 15-19 year age group to a peak in the 70-79 group. Female incidence rates, which were higher than the male rates, were noted to have two peaks, at 20-29 and 50-59 years. This bimodality reflects the higher incidence of prolactinoma in the younger age group and non-secreting pituitary adenoma in the older age group, suggesting that different etiological factors are responsible for these types of tumors.

Table 5: Histological Subtypes of Meningiomas (n = 145)

Pathology	No.	%
Meningotheliomatous	56	39
Transitional	48	33
Unknown	15	10
Malignant	10	7
Fibroblastic	7	5
Psammomatous	6	4
Angioblastic	3	2

3. Clinico-Pathological Features of Meningioma

Compared to several reports, the incidence of meningioma in this study was relatively high.[9,16] The symptom-sign complex in these patients, however, was not unusual.[24,25,26] Tumor distribution was at some variance with the established overall incidence in cases of intraventricular and convexity tumor. We located 10 lateral ventricular meningiomas (7%) which contrasts with the overall incidence of 1% to 4%.[27,28] However, it should be noted that in studies of intraventricular meningioma, the incidence rate varies from 1% to 14.3%.[24,29] It is believed that intraventricular tumors are being detected more frequently in recent years. This fact may be a reflection of the increasing sophistication in diagnostic technology as well as the availability of safe surgical approaches to the lesions. Thirty-three percent of the meningiomas in our study were found to be located on the cerebral convexities. This figure contrasts markedly with the 13% established by the Mayo Clinic[25] and is more in keeping with the series of Shuangshoti and Panyathanya.[26]

We failed to demonstrate a relationship between peritumoral hypodensity on CT imaging and perioperative complications as has been previously reported.[30] Peritumoral hypodensity was noted in all our malignant meningiomas, an association that has been previously documented.[31] The incidence of malignant meningioma has been reported to range from 1 to 9%.[24,32,33] Our result of 7% is, therefore, similar to previous findings. The recurrence of meningioma in this study was 10%, which is not unlike that previously reported.[32,34,35,36] As would be expected, the recurrence of malignant meningioma was higher (60%) compared to that of benign menignioma (8%). Overall, the clinical features, pathology, and tumor recurrence among meningioma in Manitoba were not unlike those previously reported. The relatively high incidence of meningioma in this study probably reflects the improved diagnostic capability subsequent to the introduction of CT imaging.

In summary, this study has demonstrated the epidemiology of intracranial neoplasms in a stable population that is representative of the population of Canada.

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