The Incidence and Prevalence of Multiple Sclerosis in Newfoundland and Labrador, 1960--1984

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A ,tidy of the incidence and pKvaleamof multiple sclerosis on the lstood of Newfoundland between 1960 and 1984 *loo* yielded a current overall ptsvatence rate of 111 per 100,000, bur wide rasiarion is ooeed in the rhea for different p ates ofthe Island (range, 1S-9 to 10S.0 Pat 100,000). *The* anoual incidence seta for St, JohWraad the Avalonragionof Newfoundland show cyclical variation on an appmodmare five- or six-yearcrele. Suggestive evidence for a temporal llAk between vayfng incidence rare in these areas and recurrent local outbreaks of canine distemper *was* obtained.

Prym-Philips WED: The incidence sad prevalence of multiple sclerosis in NeRfoundland and lsbaador, 1960--1994, Ann Neurol 20:113-328, 199

Epidemiological data have influenced much of the research into the causes of multiple sclerosis (US) [l21. ;.The geogtaphital pattern of the disease And the !identification of time-clusters of DAS have ptooopted ,the opinion that MS is an acquired etmgenous (envi-Conmental) disease, Areas studied with special interest have included a number of islands in which the population ;i relatively homogeneous and uncheoging and in ***which NIS leas occurred*** either with high prevalence *or* in point-sourm outbreaks. No data have so far been reported from the Largest island adjacent to the American continent, namely Newfoundland. This study was lilastgned to remedy this deficiency, by derenminigg the prevalence and incidence of i)dS in Nesfouncitand and to establish art MS registry to follow funtre incidence trends.

i Sources And Methods

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; 1Le Castadun P#CwinCt of Newfoundland amt ***Labrador*** comprises she island of Newfaundbrtd, lying between latitudes 46 and 52 N and Longitudes 12 and 19 W, and the ' mtinlatd section, labrador, situated bemeen 12 and 61 N '. NJ $6 and 61 W. The island has been ietded since 1613, far the most part by people of southern English and Irish stock; the erortoiny is Largely bated upon the fishing and lumber Wumies. Half of cite present population of }67,681 is diridai equally between the city of St. Juhn'r and the rim of the Avalon Penimsutw. The remainder of the inhabitants live is A few small towns (less than 25,000 population) and numetous, often isaLsted uurpnnr (srm1L Ctt4SW cercLements) ringing the island.

The population bit ihowo a decelerating inrrmw ao s current opproaimote figure of 6% increase every S ywss in the analysis of data, appropriate correction has been made. In labradnj, a popuWan of similar origin inbabitr coon teams; An equal number of Amerindian or Inuit (populady koc ao As Eskimo) people live mainly (n coastal regions. The province is divided into seven census divisions that were used to monitor local point-source outbreaks tFjg l1.

The islrna't climate *u* tempetae, with January And July mean tempermtres ranging around 0 to - la'C and 15 to 20°C, respectively. Precipitation is modest at 100 to 130 cm per year.

Provision of health care services Altered subararufalLy is 1969 with the establishment of a faculty of medicine a Memorial University, due consecra or recruitment of numerous specialist physkum, and the subsequent training of Newfoundland physicists willing to locate throughout the province. Whereas high-queliry medical core had been available but sparse before 1961, the subsequent years have seen on Augmentation of %be esosbluhnserrc of services to levels generally comparable to the national storms.

On Prevalence Day (March 3L, 1985), five nrumlagssts (2.3 fait-time equivalents in adult ocurotm) practiced from the npital city of St. John's, giving An effective ratio of 1:146000 population, 71te first neurologist in Newfoundlutd commenced practice in 1960. wad was joined by aherv in 19K 1967, and 1972, and mare subsequently. The overall number practicing on the island has been wahle since 1977 but was dighnly, higher in the preceding S years Trsveting clinics to the four general hospitals elsewhere an the island have been conducted since 1974. Advanced elertradiiSnoaic and biochemical techniques far the dlignosts of W5 have been available locally since 1980.

The diagnosis of MS was made following the criteria of the

t gram due Fuultr of medicine. lletmrid Univeniy of Nawfauod-Lr4l. *St. John's, Newfoundland. Canals A* l B 1V6.

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Schumacher cmomiuee (191 as adapted by Hades (8I: clamikadon into the Clinically Deinim, Clinically Probable, and Clinically, possible categories oat based upon established criteria.

Cast Findiovg

Inpatient rnedicd records were examined from the throe general hospitals in St. Jaho's and from those of the ocher lour towns in the province. All hospitals were able to pca-side rmords back to 1959; recorJs fmm the General Hospital in Sc Johns went back to 195 5. Diagnoses of optic neuri-us, transverse myeGtik Arud MS were sought.

Outpatient records have one been entered into a dlag-**IWSOr** index in any of the hospitals In al(cases of doubt, the original attending neurologist was naked m review the diak sosis.

Ali neurologists, general inccrnist4 ophthalsoologisis, and general practitioners on the island were mailed a question-sate requesting names and ocher identifying data on all patients in their practices wlwm they knew to have INS. 10 addition, the private office him ofneurologisu were individually examined.

Data were requested horn all members of the Multiple Sclerosis Society in the region. All padeors whose data were imamplete or in whom the diagnosis ran uncertain mere exandned individually or contacted by mail as telephone to permit completion of the nussiog information.

In 1969, universal government-funded insurance for physiciaroservices was established in Newfssandtaral. Compwer-atored physician claims, necessarily specifying a diagatrais, and data oa all services rendered to paticou with the diagnosis of IRIS back to January 1, 1983. were made available-Government mortality statistics were also released far saudy. Every patient who had required arty physician service in the preceding 2 years And who had been coded as haying MS could tbercfose be detected.

Data concerning the incidence of canine distemper (CD) in the Stjobn•t and Avalan regions were compiled from five wturesr (1) the Avalon Animal Hospital records of dap° seen with CD, 1973 to 1982; (2) rcmds of all dogs with Cb examined as the St. John's city dM pound and deattok 1973 to 1982; (3) records of CD vaccine used u the Av Animal Hospital, 196) to 1972; (4) records of diagttow CD made n the other two more recently established an hospitals in St. John's, 1971 to 1982; and ()) repnru of C6 incidence two the clinical recntds and personal cecdteaG of vete rkadsru practicing in the region, 1967 oo 1982. these mearu, all available data on CD incidence were all mitred, And it was posslbfe to aaslgn a yeatly more lot the imideoce of CD in the St. John's and Avalon regions se scale from 0 (no CD reported) to 3 (CD epidcmfc).

Results

On Prevalence Day, 320 patients with einicaltj definite or probable 1O were known to be alive acrd residing in (he province, yielding a etude ptevaleaor race of $5.2 per 100,000. Two hundred forty-three': patients had clinically definite and 77 patients had clinically probable h18- Because of limited data available concerning 99 other patients with optic neuritis, scans-verse rn*it(s, or clinically possible NIS, these patients were excluded from consideration.

The mean and range of age at onset for all patients in Newfoundland (females, 3 l.4 year; tange, 17 to 61 years; males, 32.7 years; range, 1) to 61 years) wise sirnitar to those reported in other studies [2, 8, 15), The mean age at onset in male and female patients in the seven regions defined (Fig I) also showed nv ; significant differences.

Area-specific- prevalence races (Table 1) showed wide disparities among regions, the highest rates pre,4m; vailing in St. Johris 1105 per 100,0001 and in the cen• asst part of the province, Area 4 (75.8 pet 100000); the lowest rates were found on the southern sbare (15.9 per 100,000), When the prevalence rate was cal. culated as tbough all patients had continued to tier a -

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Area	Population	No. DIS Padena	Prevalence Roes per 10 Populations. (95% fimirs)
1	121,024	127 (121)	105.1(86-126)
2	1 l8,381	61(19)	11-T (38-61)
3	36,180	900)	11.9(4-27)
4	42,20	32(32)	75.8 (49-10))
5	74,645	3909)	12-2 (35-69)
6	123,725	37(35)	27.8(18-33)
7	31,311	1107)	47.9 (23-T3)
Torahs	567,879	320 (317)°	16.4 (50-631

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	Population (Eseimased)	No. ofCaur	Prrvalersu per LOs Population
L-20	124,000	2	1.6
1-30	99,1100	41	41.4
1-40	78,000	90	11).4
-~1-50	54,000	91	168.3
1-60	43,000	16	134.2
61-70	36004	3 L	86, t
I1+	N1A	9	?

their onset addresses, similar figures were found, thus excluding an overall effect of migmaon to the main anedicul center.

P~: A,.~-specific prevalence rates frabie 2) reached a ~~YsnsxuHum of 16&5 pet 100,000 overall in patients fr` aged 41 to 30 years.

Study of]early MS incidence (Table 3, Fig 2) revested an increasing yearly ease than could not plaured by an increase in population. The mart, incidence was not constant but showed peaks in 19e_ 1970, 1976, and 198 [, which mainly involved festules. Study of the crude average annual incideme lace for each 3-you period from 1960 to 1984 (Table 4) showed that in Areas 1 .and 2, rates had **been stable** since 1965, except for a virtual outbreak among le-nules in the most rewat period, When the data **from** all other areas of the province were **pooled, ntei im** metes were seen to have been treble dtuiog the period of this study, except for increased rates between 1975 and 1979, whereas rates for females showed an impressive and continuing increase. (In both sexes, figures since 1980 arts anifuialty low because patients with, for example, **only** optic neuritis have been ex. eluded from consideration, and doubtless other pa dents have nor yet been referred to a neurologist.)

The CD statistics identified three outbreaks in the Sr. JohnVAvalon region, in 1967, 1973, and 1978 (Fig 3). There was no visible correlation between these

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	Area																			
	1		2		3		4		5		6		7		Total					
d yes	F	hl	F	Ill	F	It	F	RE	F	M	F	AI	F	M	F	M	Popu4efon it 10)	Incidence$ 10s
1960	1	0	0	0	0	0	1	0	1	L	0	1	0	D	3	1	440	1.14
1961	2	1	0	0	0	0	t	0	2	1	0	0	0	0	1	2	4117	1.13
1962	1	1	1	0	0	0	0	0	0	0	0	a	0	0	2	1	462	0.63
1963	1	0	2	0	0	0	0	0	0	a	1	1	0	0	4	1	470	1.06
1964	2	1	0	0	0	0	0	I	0	0	0	1	0	0	2	3	477	1.04
1961	4	3	1	0	0	0	0	0	3	0	1	0	0	1	10	4	484	2.89
1966	3	3	0	1	0	0	0	0	1	1	1	0	0	0	1	5	493	2.03
196'	3	1	1	0	0	0	0	1	1	0	0	1	0	1	5	4	499	1.80
196b	3	0	1	0	0	0	0	1	1	2	0	2	0	0	5	5	506	1.98
1969	3	0	1	0	0	0	0	1	0	0	0	0	0	0	4	1	113	0,98
1970	6	4	1	1	0	0	0	I	L	0	1	0	1	0	10	6	518	3.19
1971	2	2	0	0	0	0	0	0	0	0	3	0	2	0	7	2	122	1.72
1972	1	0	3	2	1	1	1	0	1	1	0	0	0	0	7	4	529	2.27
1973	1	1	0	2	0	1	2	0	0	0	1	0	0	0	4	4	536	1.49
1474	4	1	2	1	0	0	3	2	1	0	2	1	0	1	12	6	543	3.11
1975	5	3	3	1	0	0	1	2	0	2	3	2	0	1	12	11	550	4.18
197fs	3	1	2	2	0	0	1	2	2	0	3	1	2	0	13	6	516	3AI
	4	2	1	a	a	2	3	a	1	1	1	0	0	0	to	)	560	2-68
1973	3	1	1	2	1	0	0	1	0	0	1	0	0	1	6	1	562	1.96
1979	1	0	1	0	1	0	0	o	L	0	1	1	1	1	6	2	564	1.92
980	4	1	0	1	0	0	2	0	2	0	0	1	1	0	9	3	566	1-12
981	4	3	7	1	1	0	2	0	3	0	0	0	1	1	is	)	16B	4.05
1962	3	2	1	0	1	D	I	1	I	1	1	0	1	1	12	5	170	2-98
1983	3	L	0	1	0	0	0	0	1	0	0	0	0	0	4	1		
19114	3	1	2	1	0	D	0	0	3	0	0	0	0	D	8	2		

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Tabfr 4. Alma Imideaot of A1+rl44 Sdow4 for Feewlr and Alan Spbferu from strew I m d 2 f aid Areri 3-7, Erpmmd ear ifv Atwa for EaA S-Year Per* 1960--19194

	Areas 1 + 2		Areas 3-7	
Yearn	Female	Mile	Female	Male
1960-1964	2.0	0.6	1.2	1.2
1965-1969	4.2	LA	1.6	L8
1970-1974	4-0	2.8	1-6	1.2
1975-1979	4.8	2.6	4.6	3.4
1984-1984	6.2	2.4	3.4	1.0

peaks and peals of 1118 incidence in those years. However, when the annul case-number curves were rhifced to obcsin a best fir, a passible 3-year lag from peak CD to peak MS incidence was suggested. As a result of one-way analyses of variance, significant differer1CC! were found and are noted in Table 5. no, arsons females, the annual number of MS cases 3 years after CD outbreaks was two to three times higher than the number of cases occurring 3 years after a year of low CD incidence A similar trend, which did not atom significance, wan detected among male piatieors. In comparing averages for significance, Tukey's %v- pro-cedure [21] was used in place of Studenes t rest to compeau sce for multiple comparisons and to retain on overall 95% CODfltlente revel.

Discussion

The geographical distribution of 1118 worldwide has been subject to extensive study [2, 15]. The results have shown in general that increasing latitude results in increasing risk, although high- and medium-prevalence zones may exist within similar ladmiles (3]. High-risk cones with prevalence rates over 30 per 100,000 in. ;Jute Nonhem Europe, the northern United States vtd southern Canada, and New Zealand and southern :Australia [I, 2, 7, Q 13-15,'19, 20,12].

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Fed **3. Tiiuafpear raA.7iAg ...MEW,rrma wa;aftiPb nletp(4 M) iaridratsnarls, 1960 to 1982, is Arms 1 mod 2 rfNrla fean&eAFstiawerofprmAerr(a – aerates; 3'= «r rail a)'raaim dntseeprr (CD.), St. Jo.+rai aAd Aialon Periatala, 1966 in 1980, an pmeamd o6wir on a limp «,s4 that iawrParaki a 3-?ear lag p"W meth star lbe AIS/1PM for, n.d„ 1980. an oligwd wiA ldv CD sewirr rrtiAwyrfar 1977.**

To* J. Awroger sAd I m& of Cam of **Af altiplr** Srbrwir par **Yror wirb Rerpws to Snrrt** eJ **Caaim Didwprr 3 Yon Prerioar1y is S4. J&5AYAsa1ax Area i**

a	5	6	2
Mean (femaleil	2.ff	5.7'h	Us
Mean (males)	2.0'	2.&	4.0'

"Meant in each sex with disdmilar suprnnipu are sirnifiandj Weveot u p – c0.05.

CD s canine diuemiper.

The demographic features of NIS in NewfoundW *differ lisle from* those described elsewhere for otbd geographical locations (8, 11, 13-17],

The major fusdings of this study are the presence of high overall incidence Lad prevalence rates in thg province, with great regional differences in MS preyF fence; also noted has been the suggestion of a cortelt-Lion between a high MS incidence and a high CD iottl deuce 3 years before

The overall prevalence of MS in Newfoundland sand labrador makes this area a high-risk tone fill. '11th "I MS rate in Newfoundland is lover than th at reported; for Saskatoon, Canada [8], but higher than due in most oct" Cuadian studies reported to dare [20, 22], most'" of which were conducted at least 20 years rte. T1se present study concerns a population with subsumial common origin in southwest England and heland, cad among whom population mobility is slight. This may make the results more reliable than those from else• where in Canada, where changing populations bar led to considerable variability. Because of geographical f-on and undersupply of physicians in the province; p9di about 1970, previous underreporting of MS is poely.

neither prevalence nor incidence can be usocisted Ih the mull latitude differences in this province; I, with *the* highest prevalence, is ac a lower latitude than all others apart from Area 3.

The remarkable differences in prevalence rears pared from region to region (Table 1), foe eumple between Areas 3. 4, and 5, deserve comnLCOL Area 3 is isolated, with low population density, although medW coverage is available in all cearert with over 2,00D population. Area 4 is served by mo small general hospids, but no neurologists are based there and naveling neurology clinics we held with less frequency than in Area 5 (weir coast), where the rare is approxinutely 'into thirds that in Area 4, Mote iarernisn practice in Area S and basic neurodiagnostic services are available do.. but are nor in Area 4. Diagnostic Facilities in other provinces might have been used by residents of Ateu S and 7, but those in St. John's would always Lave been far more accessible from all other atm. In any event, government hearth care records would have identified all cases diagnosed outside of the province (mace the provincial government would have been re- tponsible for payment), as would family practice records. In Area 7 tUbmdor). there are no neurrodirg- nost . facilities, no neurology clinics, and a low physitian supply in comparison with Area 5. local increases Jn incidence rates and vuuble prevalence rates thus cannot be ascribed ca better diagnostic facilities or to Aeteer physician coverage, and certainly not since 1972 wben the number of neurologists in the province increased. Furthermore, if improved case aicertaintnent had been the reason far the differences between areas, this finding should have applied to both sexes, but such it ac: the case, as is shown in Figure 2 and Tible 3.

Population growth has slowed, and the proportion of immigrants has not increased, according to government statistics.

In this contest, the incidence and prevalence rats by Lien of residence at onset are relevant. If the prov- ice is considered to be stable as regards population, and if the differing races in different areas are considered merely to reflect the density of medical coverage, then Srost undemeporting has occurred, as all areas dtauhi have rues equal ro tbat of the highest area, snmely St, Johns. In this event some 300 cases have "ban missed-almost as many as were actually recorded. This would make Newfoundland Sri Area of ataaitrW MS occurrence in Canada, with a prevalence rate of well over 100 per 10'. Alternatively, local fac- ton relating to the acquisition of lclS cvouU have to be operative. Similar finding: have been reported from rudand (91 and from weiwrn Norway [161. It is also of 1. incest that in the regions of relatively less population stability (Areas 1 and 4), the prevalences at absolutely high, while in those of least intermixture and greatest population stability (Areas 3 and 6), rsR unusually (ow for these latitudes. The copective y suppm the concept of an acquired, perhaps wrumu. able factor being of relevance in the genesis of MS.

Four point-source AIS epidemics have been described; in the Farce Islands (141, Iceland (4, 6,1,13}, and Sitha, Alaska (3). Three of these occurred after World War 11 cad causal hypotheses have incriminated the occupation of these islands by the military dudgg the tear. However, Cook and co-worker [3-1] proposed that regional epidemic of CD could have been related to these outbretdts. In this context, the pieced. irtg outbreaks of CD in Newfoundland may be of importance, but the analysis of the relationship between MS and CD on the Avalon Peninsula is based upon historical and incomplere date, which dhemselvei are not free of subjectivity. Nevertheless, the fodigg of a 3-year W period between peaks of MS and CD incidence was unexpected and appears to have snrisrisd significance. Further testing of any hypothesis concern ing an association between the two diseases will have to be ~ means of a prospective study, in which cases of CD u well as of MS can be recorded accurately.

A 1951 outbreak of parvovirus infection in dogs coincided with the most recent peak of MS incidence in SL JOWL lc has been shown that CD may occur u higher-than-expected tares in association with paivovirus infections [10), but such is not yet the care In Newfoundland, where no CD has been. reported since 1982 [G. Jones, unpublished tan, 1985]. A continu- !% study of incidence trends in Newfoundland will therefore be important to auertain any relationship between MS and CD, and following the present survey should be perfectly feasible, ear the island now has an awarepopulation wish a location that rerneiosrelatively stable, excellent communications, increasing neurological manpower, and reliable dam on ISIS incidence over the Ima 2D year. Newfoundhrtd row provides the setriag for a natural experiment because CD has for the last 3 yeah been extinct in a region where MS demtlgraphy is well docuneared.

1 also acknowledge with gndtudc a donation faaa the Sr. John's Cb4aer of the Multiple Sdemais 8oeiety of Cansda is summ of shu wdy and the anisrance of the Government of Ne4modlaoi and Lbndor and Di G.1-all is permicang acres; ors duo Dr at. DrAYomiu-Ascmarek verified tlhe do respecting prsnlrme adiik holding a pouadoaonl feltowship• provided by the Medic.) Research Council of Canada. Dr David Hryant of Memorial 1)aiversiq Faulty of Sfelkinn provided iovaGwble soeiuiral advice. Dr Gnlmen Jones of the Avaka Aniaul Hospiml. Se. Jlvn A researched oaf made pvrit&e dam on cite inridcnce of CD in the Anion Peninsula tea, 1961 to 1984.

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