

How Far Can Epidemiology Take Us in Finding the Cause of Multiple Sclerosis?

John F. Kurtzke, MD, FACP, FAAN

Figures (slides) of the presentation

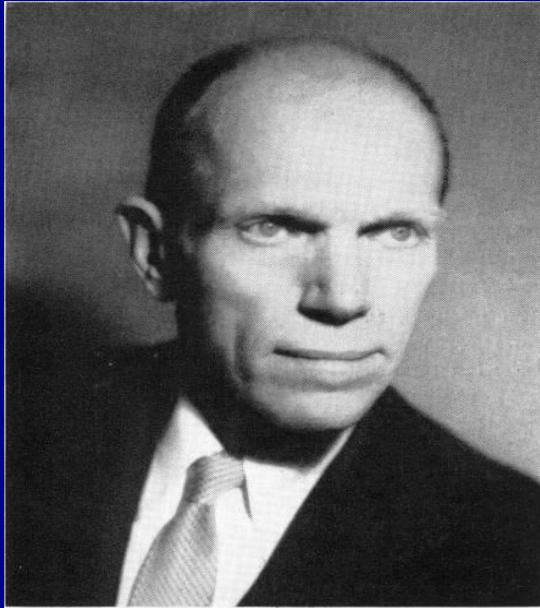
John N. Whitaker, MD
(1940-2001)

Professor & Chairman
Department of Neurology
University of Alabama at
Birmingham

President (1995-1997)
American Neurological
Association

Chairman (1994-1997)
Medical Advisory Board
National Multiple Sclerosis
Society

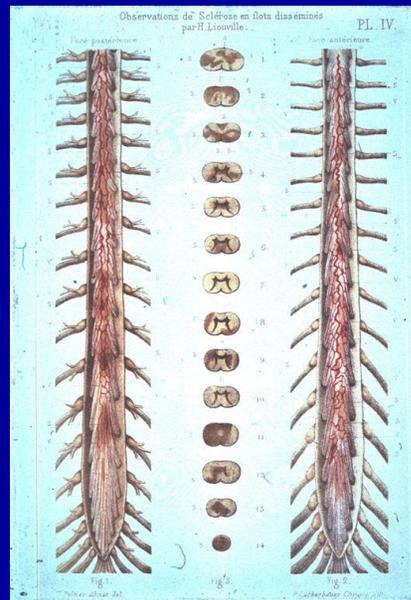
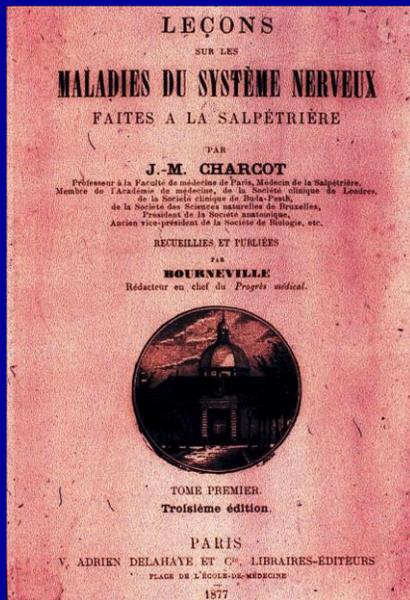




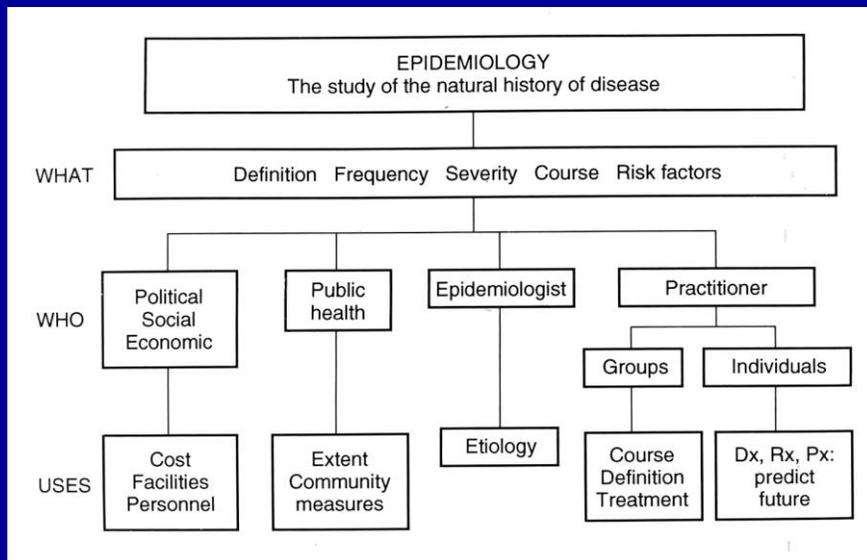
Harold G Wolff MD
1898-1962

Professor of Medicine
(Neurology)
Cornell University Medical
College

Director
Neurology Residency Training
VA Hospital, Bronx, NY



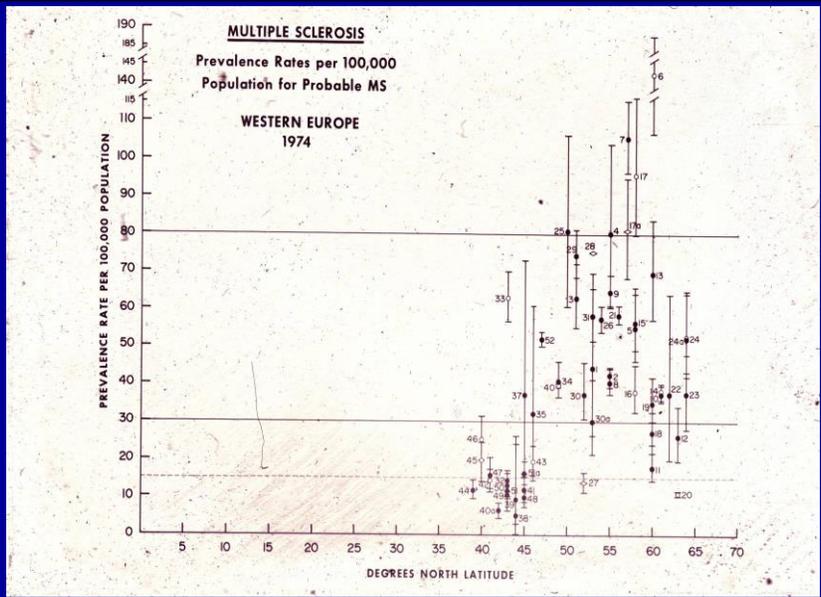
Sclérose en Plaques. Planche IV (Moelle épinière)
dans "Leçons" par J-M Charcot



Epidemiology – definition and uses

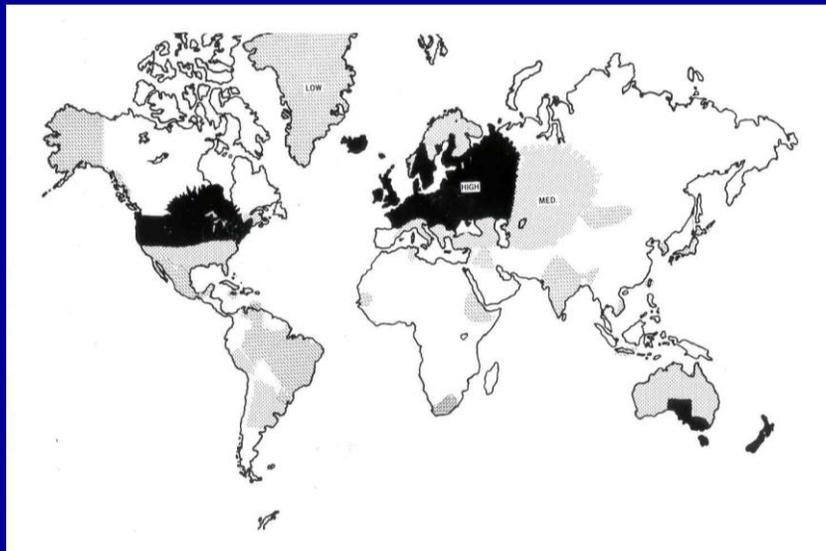
LPG – Principles of Practice

Principle	Neurology	Epidemiology
Localization	where is the lesion	where are the cases
Paranoia Don't trust anyone	do your own exam	do your own analyses
GIGO Garbage in - garbage out	wrong findings - wrong diagnosis	wrong data - wrong conclusions



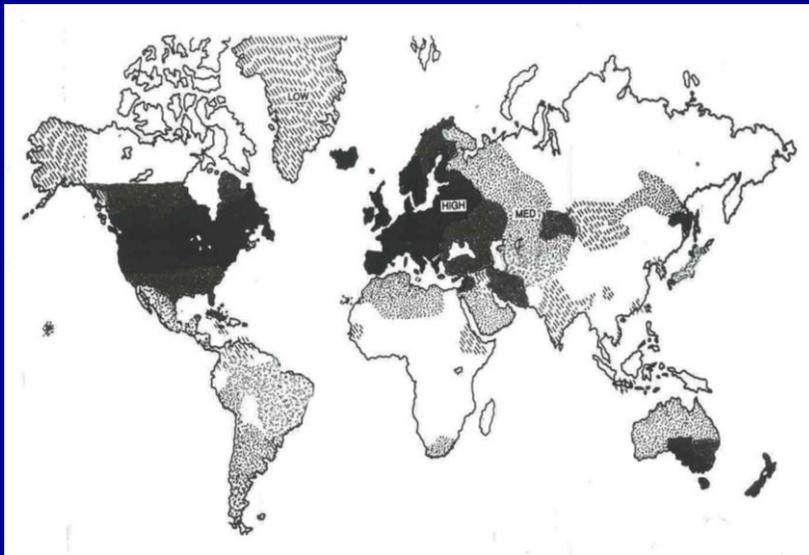
MS prevalence rates per 100,000 population with 95% CI by latitude of study site, Western Europe, 1974

Kurtzke, Acta Neurol Scand 1975; 51: 110-136

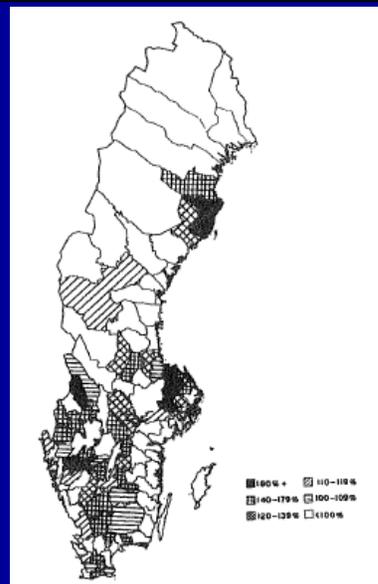
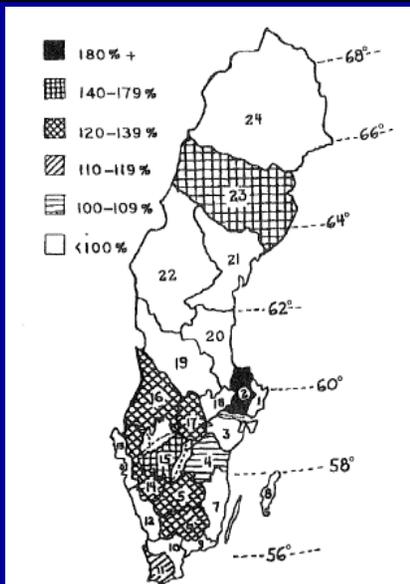


Worldwide distribution of MS into high (solid), medium (dots), and low (dashes) frequency areas, as of 1980

Kurtzke, Acta Neurol Scand 1980;62:65-80



Worldwide distribution of MS into high (solid), medium (dots), and low (dashes) frequency areas, as of 2011



Distribution of MS in Sweden, 1933, as percentiles of national rate of 21.22 per 100,000 by county (län) [left] and small units (domsagor) [right]

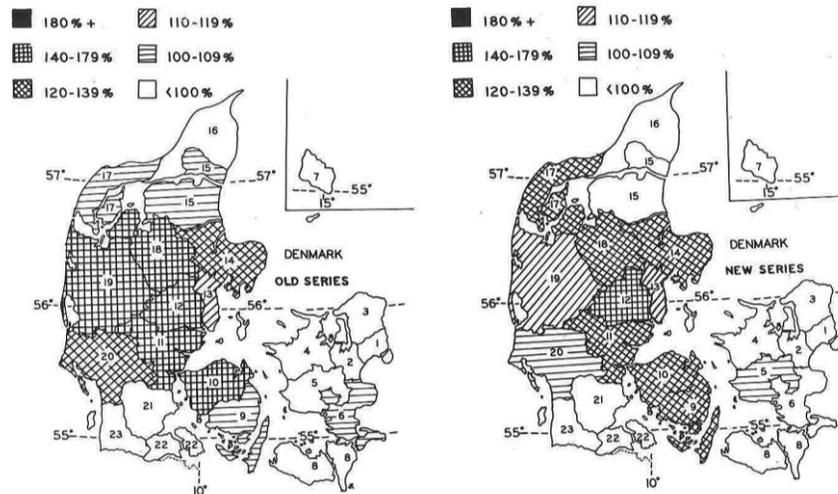
Data of Sällström, Acta Med Scand 1942; figures from Kurtzke, Arch Neurol 1966, Acta Neurol Scand 1967

Multiple sclerosis in Denmark by county of residence: (a) disability 1921-33; (b) prevalent cases 1949 by life period as percentages of the respective means: (a) Gram (1934) [col 1]; (b) Hyllested (1956) [all others]

County (Amt)	1921-1933	birth v 1906	0-15 v 1921	15-onset v 1930	Onset v 1940
01. Copenhagen	58	76	69	93	89
02. Roskilde	^	100	97	81	82
03. Frederiksborg	80	74	80	96	92
04. Holbæk	44	92	88	75	96
05. Sorø	84	99	101	84	97
06. Præstø	100	98	98	96	102
07. Bornholms	44	83	88	87	85
08. Maribo	60	88	92	88	82
09. Svendborg	104	112	121**	93	100
10. Odense	151	119**	128**	142**	133**
11. Vejle	173	128**	135**	131**	122**
12. Skanderborg	160	132**	142**	122*	130**
13. Århus	111	133**	117*	146**	143**
14. Randers	122	129**	135**	118*	118*
15. Ålborg	102	105	96	86	91
16. Hjørring	84	88	94	74	80
17. Thisted	109	116	132**	100	97
18. Viborg	147	131**	135**	115*	111
19. Ringkøbing	169	112	111	91	89
20. Ribe	138	119*	108	100	105
21. Haderslev	v	71	84	103	100
22. Åbenrå-Sønderborg	71	62	73	91	85
23. Tønder	^	56	61	65	66
Number of cases	689	2416	2426	2412	2458
Prevalence	45	87.7	74.2	67.8	63.8
Chi-square		117.51	147.91	94.13	75.83

(p = 0.00001 @ chi-square = 62.34)

** = significant (chi-square > 4.0, 1 df) * = borderline significant (chi-square 2.0-4.0)

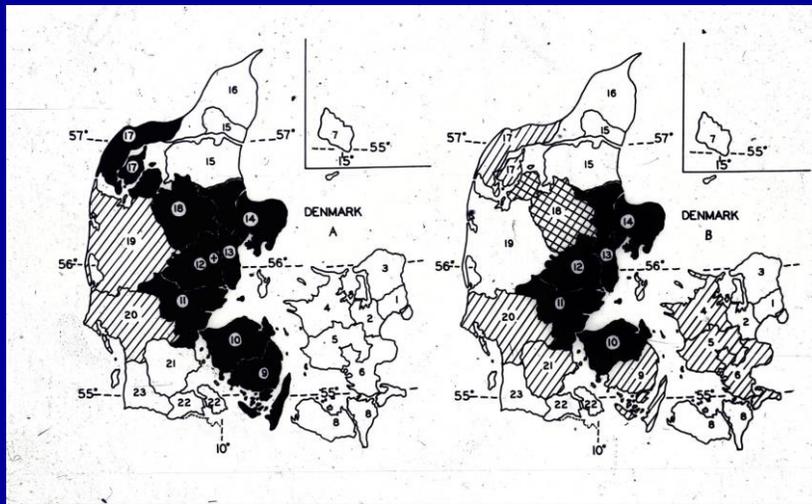


Percentile ranges of prevalence rates for MS by county in Denmark

Old series: 1921-33 disability cases (data of Gram 1934)

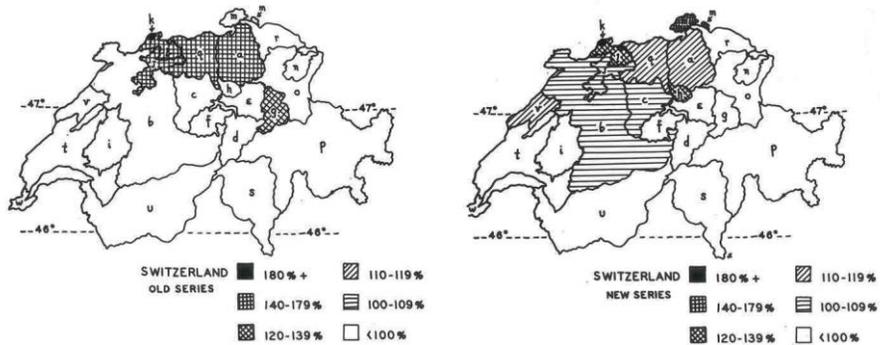
New series: age 0-15 vs 1921 population, 1949 cases (data of Hyllested 1956)

Kurtzke, Arch Neurol 1966; 14: 213-222



MS age specific prevalence by county as significance levels for rates at/above the mean, Denmark : (A) cases age 0-15 vs 1921 population age 5-24; (B) cases at onset vs 1940 population age 25-44, data of Hyllested (1956)

Kurtzke JF. Acta Neurol Scand 1967; 43: 283-298



MS prevalence rates per 100,000 population in Switzerland by Canton as percentages of the national rates

A. Old series (1922) rate 22.2 B. New series (1956-1957) rate 51.4

- A. Data of Bing & Reese, Schweiz Med Wochenschr 1926;56:30-4, Ackermann, ibid 1931;61:1245-50
 B. Data of Georgi & Hall, Acta Psychiat Neurol Scand 1960; 35 (suppl 147):75-84, and of Georgi, Hall & Müller Bibl Psychiat Neurol 1961;114:1-123

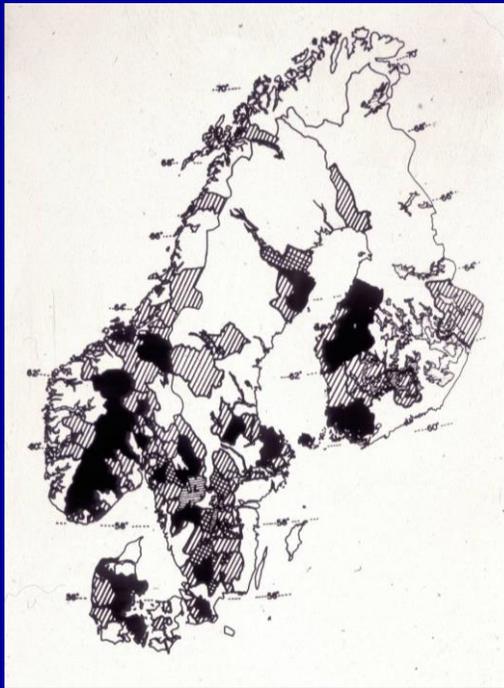
Kurtzke JF. Arch Neurol 1966; 14: 213-222.

MS in Fennoscandia from nationwide surveys.

Areas significantly high are in black; high of doubtful significance cross-hatched insignificantly high diagonal-lined; areas below the national means are unshaded. Unit boundaries are omitted.

Data are cumulative death rates by small units in Norway 1951-65, prevalence rates for hospital cases by small units in Sweden 1925-34, disability prevalence rates by hospital districts in Finland 1964, and childhood distribution of prevalence rates by county in Denmark 1949

Acta Neurol Scand 1974;50:478-502



THE THIRTY YEARS WAR
1618-1648

Campaigns of 1630-1639

Campaigns of Gustav II Adolf of Sweden

Map 3. Germany During the Thirty Years War, 1630-39, p 44

John Childs. Warfare in the Seventeenth Century. Cassell & Co, London, 2001



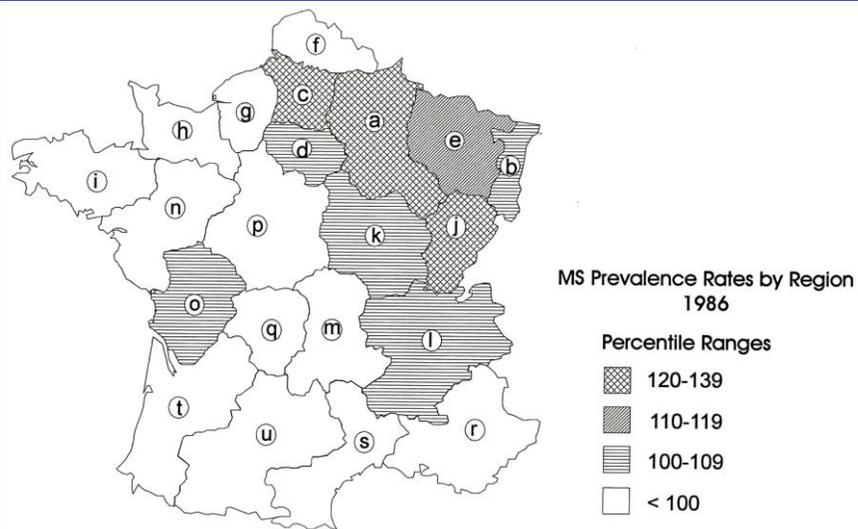
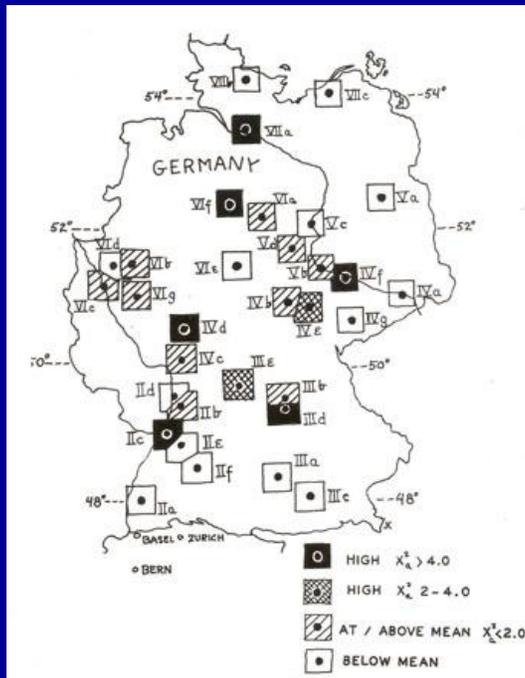
Multiple Sclerosis

Rates per 1000 autopsies
in 32 Pathological Institutes

Germany 1906-1950

shading shows levels of statistical
significance at/above mean, as
shown in the figure

Data of Maretschek et al. Deutsche
Zeitschr Nervenheilk 1954;172:287-308



Multiple sclerosis in France

Prevalence rates by region from nationwide questionnaire returns in 1986
as percentile ranges of a national reported rate of 13.8 per 100,000

Kurtzke & Delasnerie-Lauprêtre, Acta Neurol Scand 1996;93:110-7

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The Baltic States
in the
17th Century

Growth of the Swedish Empire
1600-1699

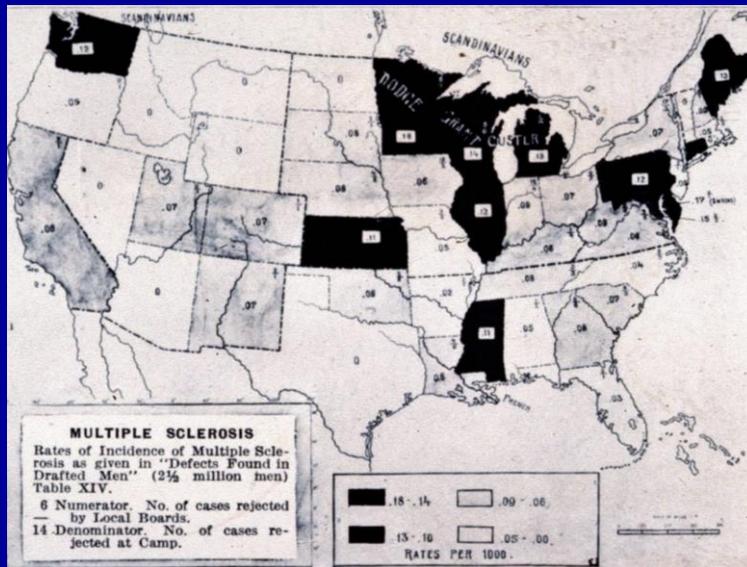
John Childs.
Warfare in the Seventeenth Century
Cassell & Co, London, 2001
Map 4, p. 51



THE CONCLUSIONS OF THE COMMISSION

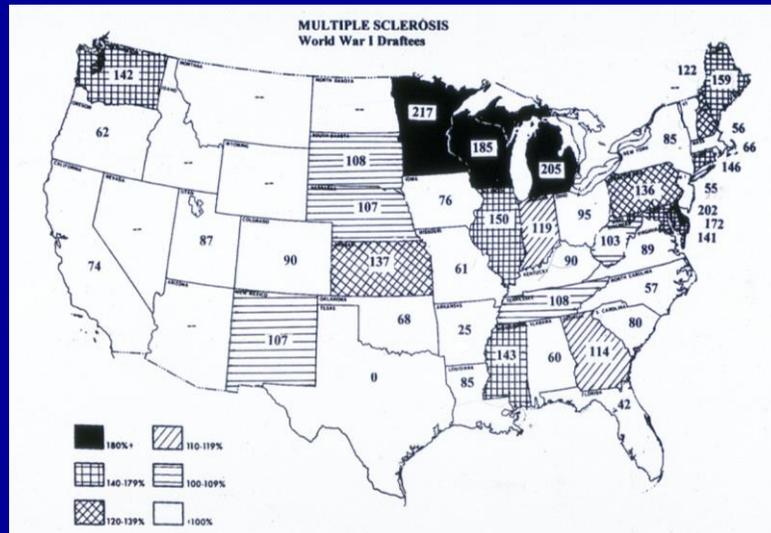
1. The age of persons suffering from multiple sclerosis ranges chiefly from twenty to forty, but the disease may occur as early as the tenth or as late as the sixtieth year.
2. The disease occurs more often in males than females in the ratio of about 3 to 2; and makes up about 1 to 2 per cent of the organic diseases of the nervous system including those due to syphilis.
3. The duration of the disease averages about eight years but may run less than a year or more than thirty years.
4. It occurs in persons doing skilled manual work more often than in ordinary laborers or in brain workers.
5. In the United States it seems to occur more in the region of the Great Lakes—at least among young males, while in Europe it prevails more in Northern parts than in Italy and about the Mediterranean Sea.
6. It is not a familial disease, and is not inherited, there being rare and doubtful exceptions; but in the ancestry there is often evidence of a neuropathic stock.

ARNMD 1921 meeting conclusions (1)



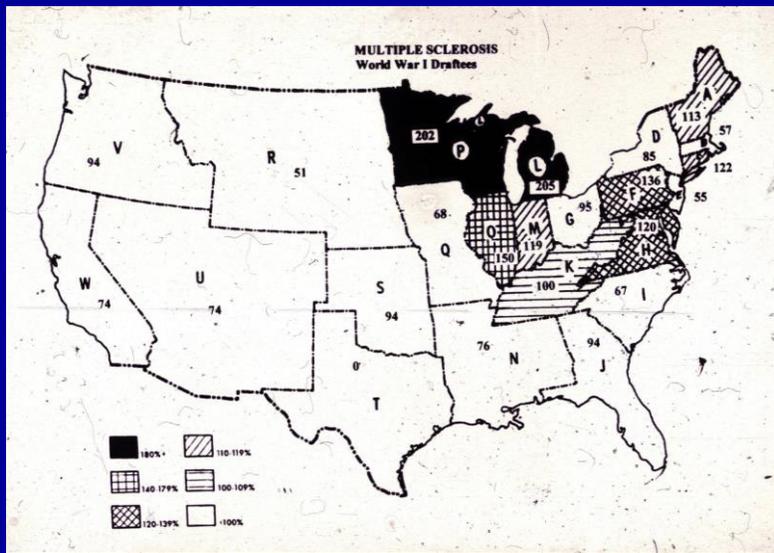
MS prevalence rates per 1000 for draftees of World War I

Davenport CB. Multiple sclerosis from the standpoint of geographic distribution and race. Proc ARNMD 1922; 2: 8-19



Percentages of national (mean) prevalence rate of 10.67 per 100,000 for MS in draftees in World War I by state of residence in the United States

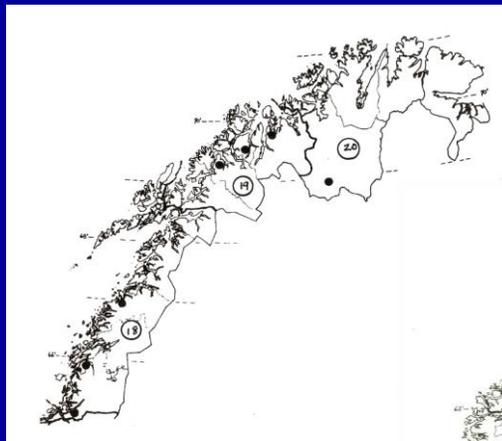
Data in Love AG, Davenport CB: Defects Found in Drafted Men. War Department, Government Printing Office, Washington, DC, 1920



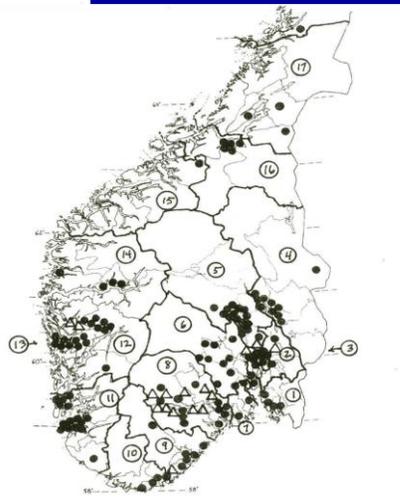
Percentages of national prevalence rate of 10.67 per 100,000 for MS in drafttees of World War I by residence in 23 areas of the United States

Data of Love and Davenport, 1920

23



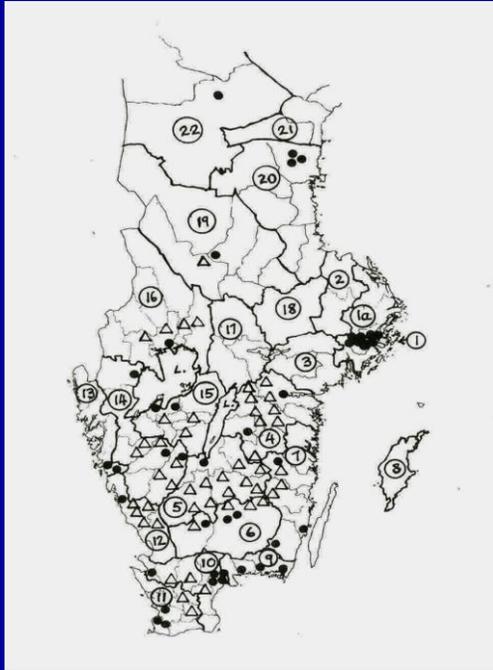
Homes of Norwegian immigrants to Wisconsin and Minnesota in mid-19th century



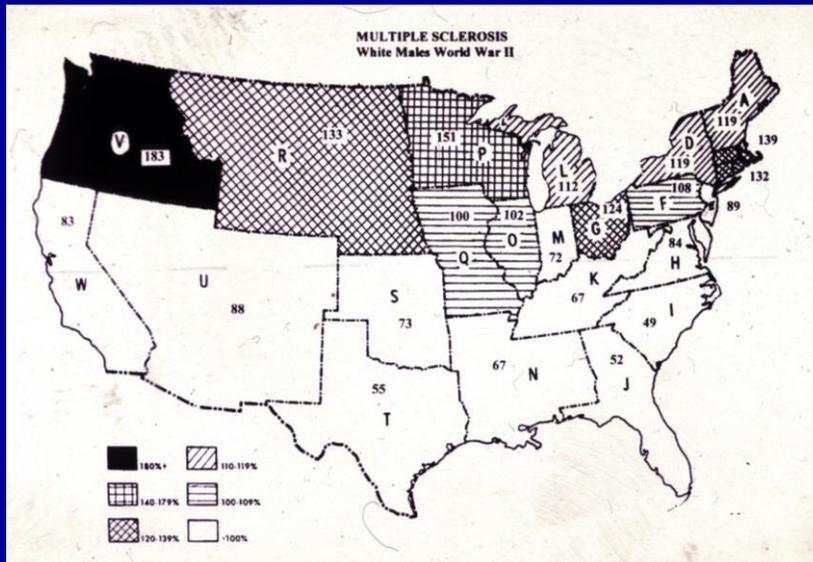
Actual (●) and approximate (Δ) locations of family homes in Norway

Homes of Swedish immigrants to Wisconsin and Minnesota in mid-19th century

Actual (●) and approximate (Δ) locations of family homes in Sweden (none in northern Sweden)



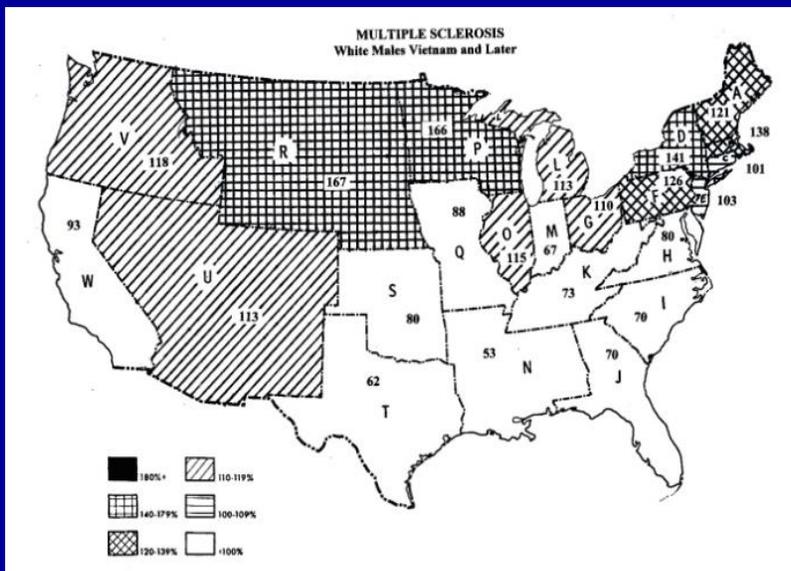
25



Percentages of adjusted MS/control ratios for white males of World War II by residence at EAD in 23 areas of the US

Data of Kurtzke et al. Neurology 1979; 29: 1228-35.

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Percentages of adjusted MS/control ratios for white males of Vietnam era and later service by residence at EAD in 23 areas of the US

Data of Wallin et al. Ann Neurol 2004; 55: 65-72.

27

Multiple sclerosis case/control ratios for all white veterans of World War II or the Korean Conflict by tier of residence at birth and at entry into active duty (EAD), coterminous US only.

Birth Tier	EAD Tier			Birth Total
	North	Middle (case/control ratios)	South	
North	1.48	1.27	.74	1.44
Middle	1.40	1.03	.73	1.04
South	.70	.65	.56	.57
EAD Total	1.46	1.03	.58	1.06
		(case/control numbers)		
North	2033/1377	133/105	39/53	2205/1535
Middle	160/114	1899/1836	80/110	2139/2060
South	21/30	50/77	565/1007	636/1114
EAD Total	2214/1521	2082/2018	684/1170	4980/4709

MS/control ratios for white veterans of WWII or Korean Conflict by tiers of residence (North, Middle, South) at birth and at EAD

Kurtzke et al. Neurology 1985;35:672-8

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Adjusted MS prevalence rates per 100,000 immigrants to South Africa, 1960, all ages, according to age at immigration (AAI) in northern European immigrants (all and those from UK (revised))*

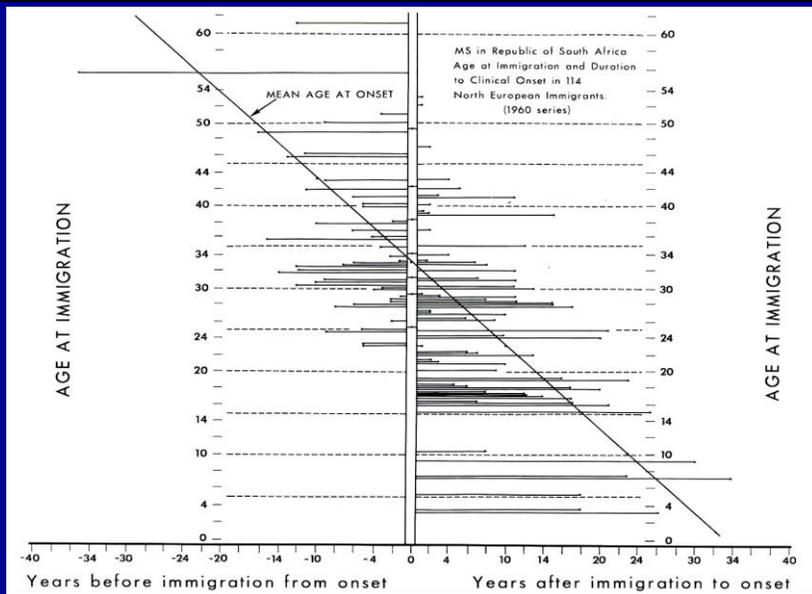
AAI	UK MS	UK Rate	all MS	all Rate
0-14	4	12.8	7	12.9
15-19	7	66.1	15	81.1
20-24	7	31.8	13	31.3
25-29	14	59.4	26	58.4
(20-29)	(21)	(45.7)	(39)	(44.9)
30-39	21	58.2	34	52.4
40-49	}12{	57.7	}23{	62.4
50+		70.5		80.8
Total	65	47.5	118	49.4

*adapted from SAfr Med J 1970; 44:663-669.

MS prevalence rates for North European immigrants to South Africa by age at immigration

Data of Kurtzke et al. S Afr Med J 1970; 44: 663-9

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MS in north European immigrants to South Africa: years to onset by age at immigration

Kurtzke JF. Epidemiology of multiple sclerosis. In Vinken PJ, Bruyn GW, Klawans HL (eds). Handbook of Clinical Neurology. Vol 47, Demyelinating Diseases. Elsevier, Amsterdam, 1985: 259-287.

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Table 6: Comparison of absolute risk of MS per 100,000 population with 95% confidence intervals by age at immigration: age 0-14 vs older ages. UKI immigrants (Group II) with MS onset after migration who entered Australia in or after 1947 and were age 0-79 in 1981, Four States combined.

<u>AAI</u>	<u>At risk population</u>	<u>MS</u>	<u>Risk</u>	<u>95% CI</u>	<u>Significance</u>
Total	696735	258	37.03	32.64-41.84	
0-14	250631	56	22.34	16.88-29.02	<u>Reference</u>
15-19	52335	30	57.32	38.68-81.84	+
15-24	131907	73	55.34	43.38-69.60	+
15-29	218185	129	59.12	49.36-70.25	+
15-34	292784	168	57.38	49.03-66.74	+
15-39	350778	189	53.88	46.47-62.13	+
15-44	388338	200	51.50	44.61-59.16	+
15-49	408856	201	49.16	42.60-56.45	+
15-54	420522	202	48.04	41.64-55.14	+
15+	446104	202	45.28	39.25-51.98	+

Absolute risk of MS by age at immigration for UKI immigrants with onset after migration into four states of Australia combined: age 0-14 vs older age groups

McLeod et al. J Neurol 2011; 258: 1140-1149.

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Rates per 100,000 population for multiple sclerosis by age in 1986 vs 1982 population of France: A. North African migrants with Φ presumed acquisition of MS in North Africa (a), and Φ presumed acquisition in France; B. All French MS.

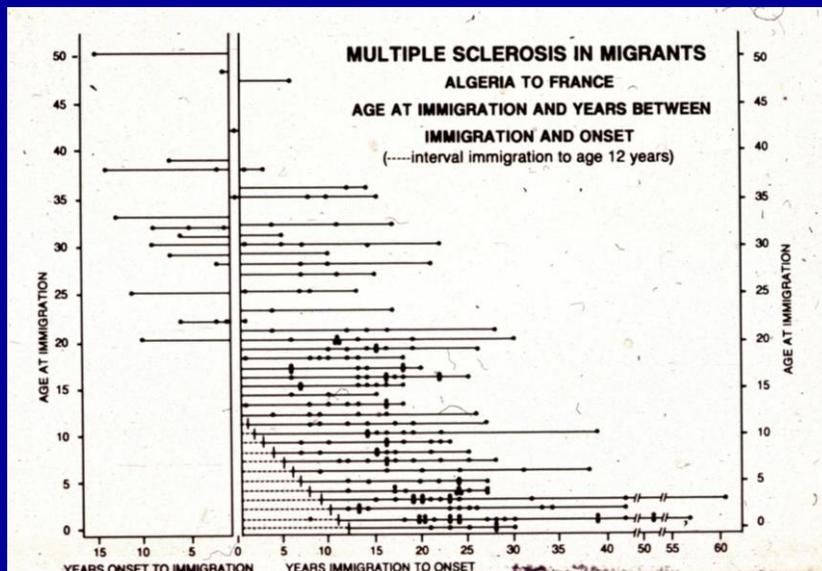
Age	A. Migrant MS (b)					B. All MS		
	Population (c)	N Φ	(calculated rates)			Population (k)	N	rate
			rate Φ	N Φ	rate Φ			
0-14	124612	0	---	0	---	11232.80	20	0.18
15-24	132097	0	---	1	0.76	8593.52	138	1.61
25-34	236732	2	0.84	53	22.39	8568.20	1104	12.88
35-54	401748	9	2.24	132	32.86	12798.82	4177	32.64
55+	78140	16	20.48	39	49.91	13079.68	2068	15.81
Total	973329	27	2.77	225	23.12	54273.20	7507	13.83
Age adj. (d)			4.33		20.06			12.854
Age adj. (e)								13.067
			(estimated rates per 100,000 population)					
Est. rate			16.57		76.76			50.00
95% CI (f)			(10.92-24.10)		(67.06-87.47)			

- (a) clinical onset before, at, or one year after immigration
- (b) excludes cases and population of undefined age
- (c) source: Table 3, Nationalité RP 1982, INSEE Paris (10)
- (d) age adjusted to US 1960 population
- (e) age adjusted (US 1960) from five-year age specific rates.
- (f) 95% confidence interval (Poisson)

MS prevalence rates by age for North African immigrants to France and for all residents of Metropolitan France, 1986

Kurtzke et al. Acta Neurol Scand 1998; 98: 302-309.

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MS in immigrants from North Africa to France
Age at immigration and years from immigration to clinical onset

Kurtzke et al. Acta Neurol Scand 1998; 98: 302-309.

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An Epidemiologic Overview of Multiple Sclerosis

- MS is a place-related but spreading acquired disease with (to 2011) an increasing predilection for white women
- Earliest nationwide distributions in northern Europe show in each country a single focus of high frequency suggesting in some way person-to-person acquisition, since only people are affected
- Migration alters MS risk:

For high to low moves, risk is retained for those about age 15 years old or older, but much decreased for those then younger

For low to high moves, susceptibility is limited to about age 11 to 45 at first exposure, and risk higher than for new land.

The simplest explanation is that MS is the result of a geographically delimited persistent infectious agent with a long latency and an age-limited host susceptibility.

If this is true, then "MS" must be a much more widespread disease than clinical cases indicate, or there must be a non-human reservoir (for which there is no evidence).

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- An epidemic is the occurrence of a disease at a frequency well above normal expectation, and which is derived from a common or propagated source.
 - Type 1 epidemics occur in susceptible populations exposed for the first time to a virulent infectious agent.
 - Type 2 epidemics occur in populations in which the organism is already established.

Epidemics – definition and types

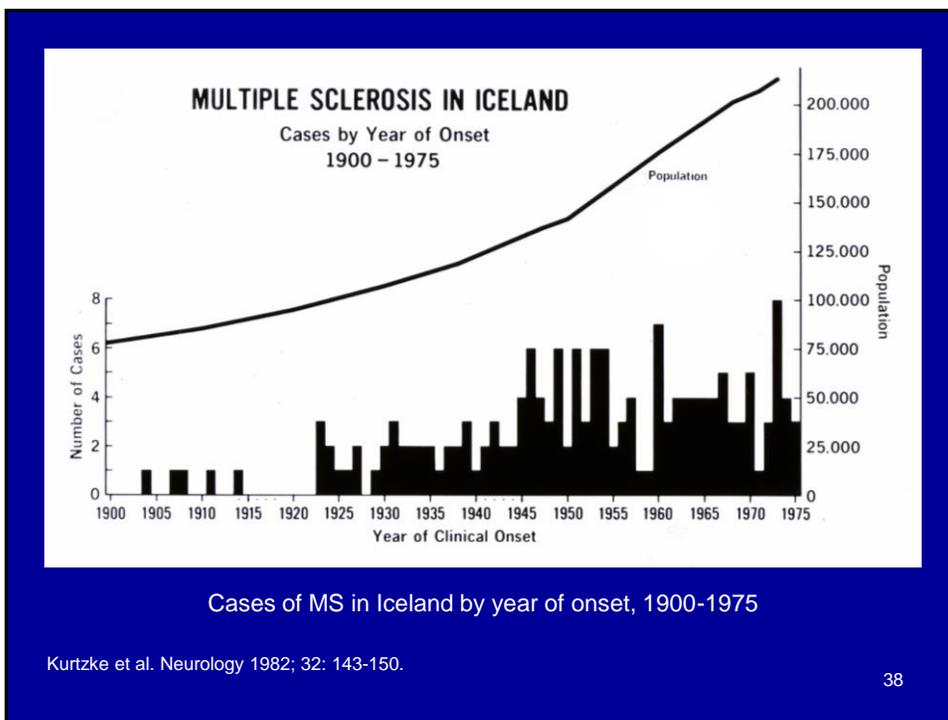
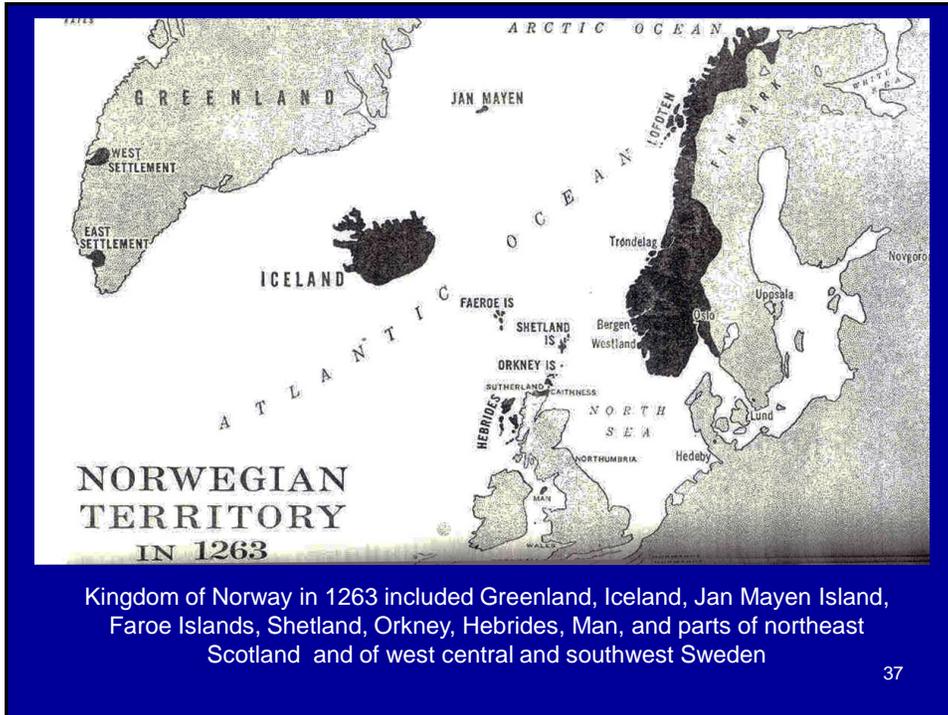
35

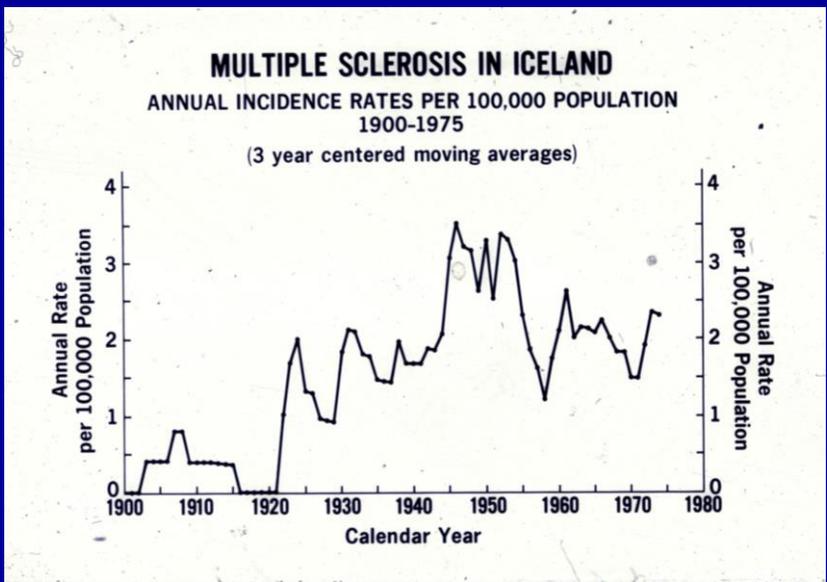
There is in human nature generally more of the fool than of the wise.... Wonderful like is the case of boldness.... And... you shall see a bold fellow many times do Mahomet's miracle. Mahomet made the people believe that he would call a hill to him, and from the top of it offer up his prayers for the observers of his law. The people assembled; Mahomet called the hill to come to him again and again; and when the hill stood still, he was never a whit abashed, but said, *If the hill will not come to Mahomet, Mahomet will go to the hill....*

Francis Bacon. Essay 12. Of Boldness. In: *Essays** and *New Atlantis*, Gordon S. Haight, ed. Published for the Classics Club by Walter J Black, New York, 1942, pp 47-49. *Third edition, 1625

Migration in MS and the hill of Mahomet

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Annual incidence rates for MS in Iceland

Kurtzke et al. Neurology 1982; 32: 143-150.

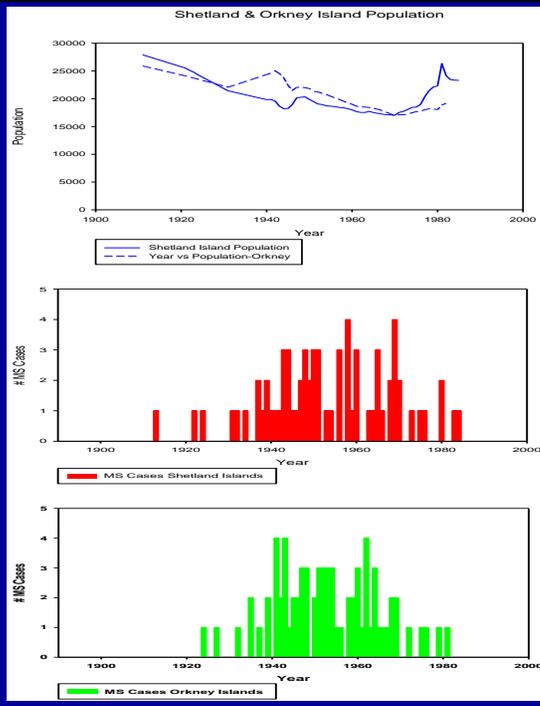
39

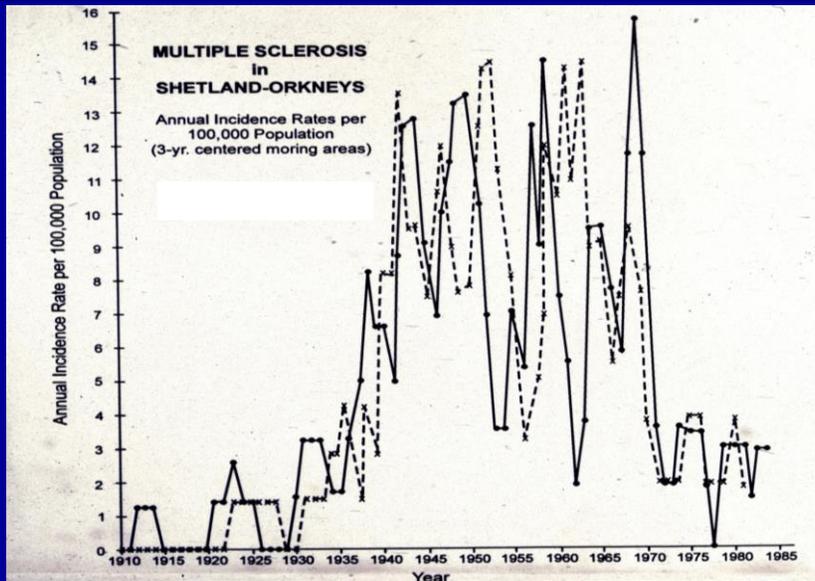
Multiple Sclerosis in Shetland & Orkney 1910-1985

Annual populations
Shetland (solid line)
Orkney (dashes)

Number of new cases of MS
by year of onset:
Shetland (top, red bars)
Orkney (bottom, green bars)

Data of Poskanzer et al.
J Epidemiol Commun Hlth
1980;34:229-39, and Cook et al.
Neurology 1985;35:345-51, Acta
Neurol Scand 1988;77:148-51





Annual incidence rates per 100,000 for MS in Shetland (solid line) and Orkney (dotted line); 3-year centered moving averages

Data of Poskanzer et al. J Epidemiol Commun Hlth 1980;34:229-39 and Cook et al. Neurology 1985;35:545-51, Acta Neurol Scand 1988;77:148-51

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THE FAROESE SAGA

Translation of
Ole Jacobsen
Copenhagen
1981

The Faroese Saga
With sketches by
Sven Havsteen-Mikkelsen
translation of Ole Jacobsen
with postscript by
Jørgen Haugan
Forum København
1981

FÆRINGE SAGA

med tegninger af
Sven Havsteen-Mikkelsen



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Føroya Løgting on parade at Ólavsøka (St Olav's Day) led by Formaður and the (Danish) Ríkisumboðsmaðurin í Føroyum, 29 Júlí 1980

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THE FAROE ISLANDS relief map

Published by Faroe Sea Food
L/f Føroya Fiskasola with
permission of Geodetisk Institut,
1977



44



Tórshavn, Strey moy, from the air, 1975

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Landsjúkrahúset (The National Hospital), Tórshavn, 1983

46



Klaksvík Hospital, Klaksvík, Borðoy, 1988

47



Tvøroyri Hospital, Tvøroyri, Suðuroy, 1983

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John Kurtzke, Anne Heltberg, (the late) Kay Hyllested
at Kirkjubøur, Streymoy, 1991

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CASE ASCERTAINMENT FOR FAROES MULTIPLE SCLEROSIS PATIENTS

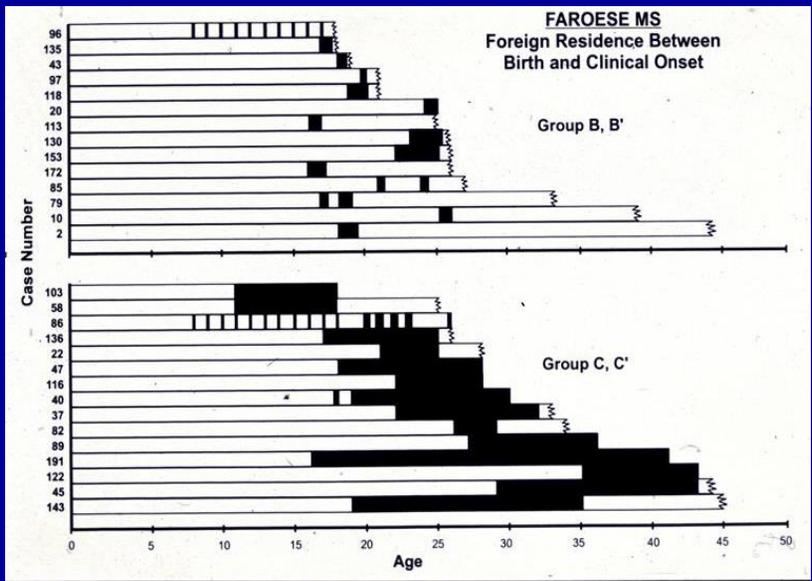
Faroese death certificates.....	1900-1977
Faroese hospital (3) records.....	1900- *
Rigshospitalet (RH) records.....	1900-1983
Sundhedsstyrelsen National Patient Registry..	1921- *
Disability Compensation Board records.....	1921-1977
Neuromed Department (RH) records.....	1929- *
All physicians, hospitals DK.....	1944-1949
Danish MS Registry files.....	1947- *
Faroes survey (KH).....	1957
Faroes-Shetland survey (KH).....	1960-1962
Neurologic symptoms Faroe hospitals.....	1960-1976
Haslev Hospital records.....	1965-
Faroes patients, relatives, friends.....	1974-
Danish neurologists.....	1975-
Faroese physicians.....	1975-
Faroese Multiple Sclerosis Club.....	1977- *
National Registry Causes of Death.....	1978-

* Principal ongoing resources

Resources used to ascertain possible cases of MS on the Faroes, 1900-1998

Modified from Table 1, Kurtzke & Hyllested. Neuroepidemiology 1988;7:190-227.

50



Years from birth to onset in Groups B and C of Faroese MS patients. Black portions show age and duration of foreign residences

Kurtzke & Heltberg. J Clin Epidemiol 2001; 54: 1-22.

51

Multiple Sclerosis in the Faroe Islands 1900-1998

Population 1900-1998 (top)

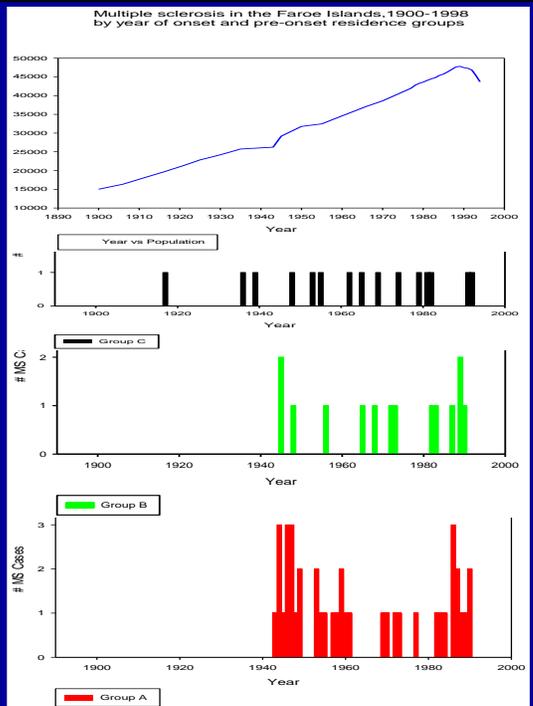
MS cases by year of onset and residence history:

- Group C (3+ yrs overseas)
- Group B (<2, 2 yrs overseas)
- Group A (<6 mos overseas)

- Gp C upper set
- Gp B middle set
- Gp A bottom set

A+B = native resident series

Data of Kurtzke & Heltberg
J Clin Epidemiol 2001; 54: 1-22.



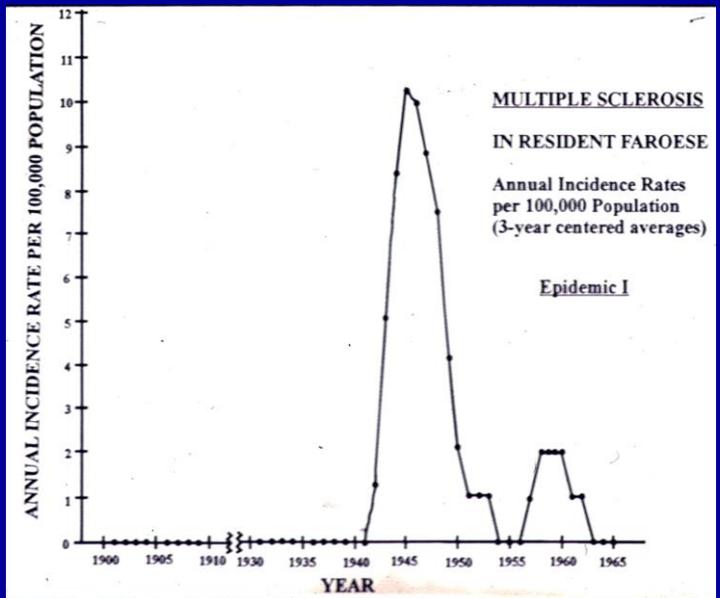
Multiple sclerosis in native resident Faroese. A. Epidemic I: exposure 1941-1944 (1998)

Case number	group: A (not live overseas before onset), B, C (live overseas short periods before onset)	Sex	year of birth	first year of exposure to FMMSA	age at first exposure to FMMSA	year of clinical onset	age at clinical onset	year of death
2	B	F	1901	1941	40	1945	44	1966
3	A	F	1910	1941	31	1952	42	1963
6	A	M	1915	1941	26	1947	32	1965
8	A	M	1930	1941	11	1959	29	1981
9	A	M	1913	1941	28	1943	30	1971
10	B	F	1906	1941	35	1945	39	1990
13	A	M	1929	1941	12	1944	15	1995
15	A	F	1926	1941	15	1945	19	A*
16	A	F	1928	1941	13	1947	19	A
18	A	M	1921	1941	20	1958	37	1993
19	A	M	1920	1941	21	1944	24	1989**
20	B	M	1923	1941	18	1948	25	A
21	A	F	1917	1941	24	1949	32	1984
38	A	M	1895	1941	45	1944	48	1945
41	A	F	1920	1941	21	1946	26	1957
42	A	M	1929	1941	12	1949	20	1970
44	A	M	1922	1941	19	1946	24	1970
73	A	F	1920	1941	21	1947	27	A
84	A	M	1921	1941	20	1961	40	1990
88	A	F	1932	1943	11	1948	16	A
100	A	M	1907	1941	33	1946	38	1973

*Alive June 1998 **Autopsy proved

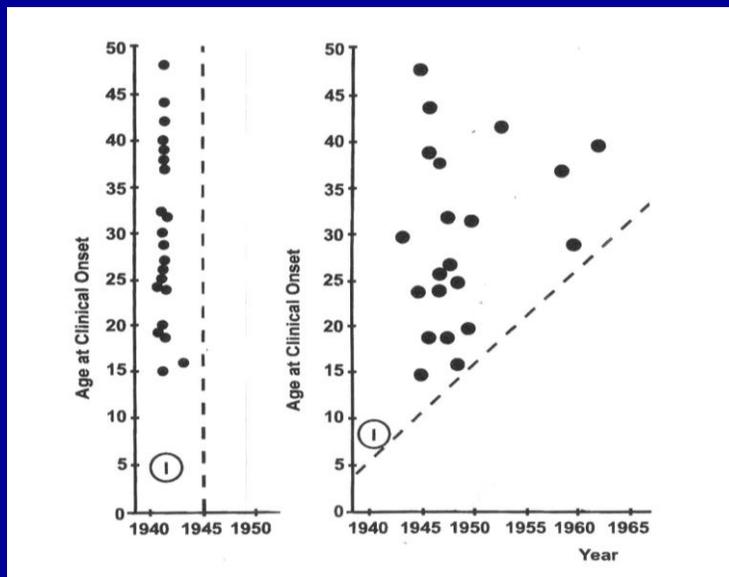
Faroese MS: Epidemic I cases (exposure 1941-1944)

Kurtzke & Heltberg. J Clin Epidemiol 2001; 54: 1-22.



Annual incidence rates for MS in Faroese of Epidemic I (n = 21)

Kurtzke & Heltberg. J Clin Epidemiol 2001; 54: 1-22.



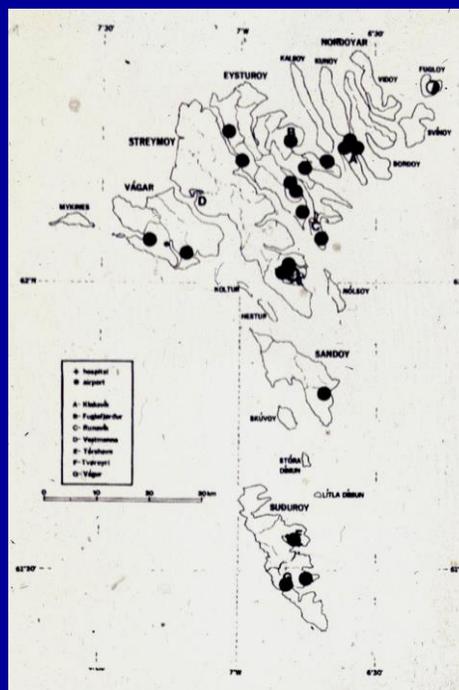
MS in Faroe islands. Cases of Epidemic I by age at onset vs: [a] year of exposure (left) and [b] year of onset (right)

Data of Kurtzke & Heltberg. J Clin Epidemiol 2001; 54: 1-22.

55

Residence of patients of Epidemic I at time of exposure in 1941 (-43); each patient is shown as a solid circle

Kurtzke & Heltberg. J Clin Epidemiol 2001; 54:1-22.



Book of Faroese
recollections of
World War II



THE WAR YEARS
1940-45
[on the Faroe Islands]
by
Niels Juel Arge



NIELS JUEL ARGE

STRÍÐSÁRINI

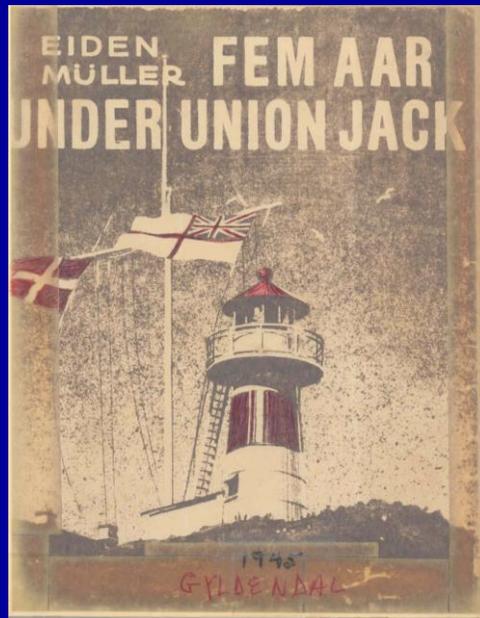
1940-45

58

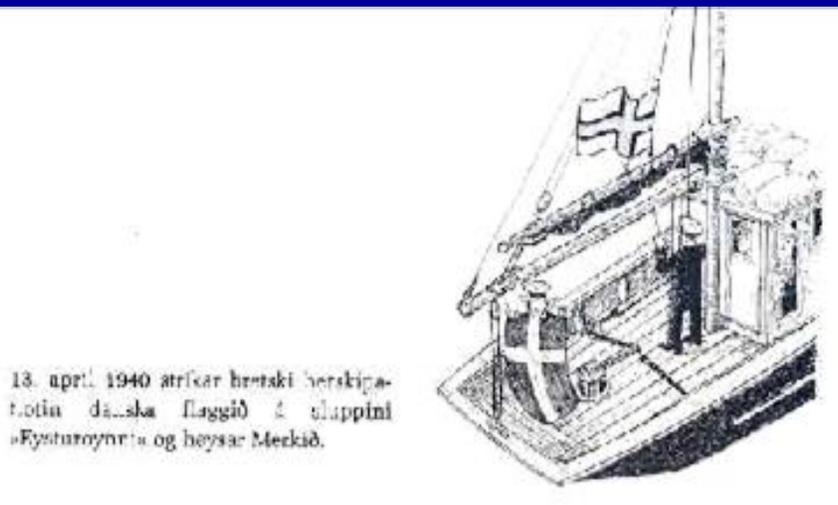
Five Years
Under the Union Jack

Eiden Müller
1945

Dannebrog and
the Royal Navy White Ensign
flying at Skansen, Tórshavn,
Faroe Islands



59



18. apríl 1940 stríkar bretska herskipa-
trotin danska flaggið á slappini
«Eysturoyar» og heysar Merkið.

British naval officer strikes the Danish flag and hoists the Faroese
flag aboard the Faroese ship "Eysturoyar" 18 April 1940

from THE WAR YEARS

60



Original Faroese flag in church in Fámjin, Suðuroy

61

British
occupation
forces in the
Faroes in World
War II by unit
and dates
stationed:
Arms (line or
combatant
branches)

Kurtzke & Hyllested.
Acta Neurol Scand
1987; 76: 317-339.

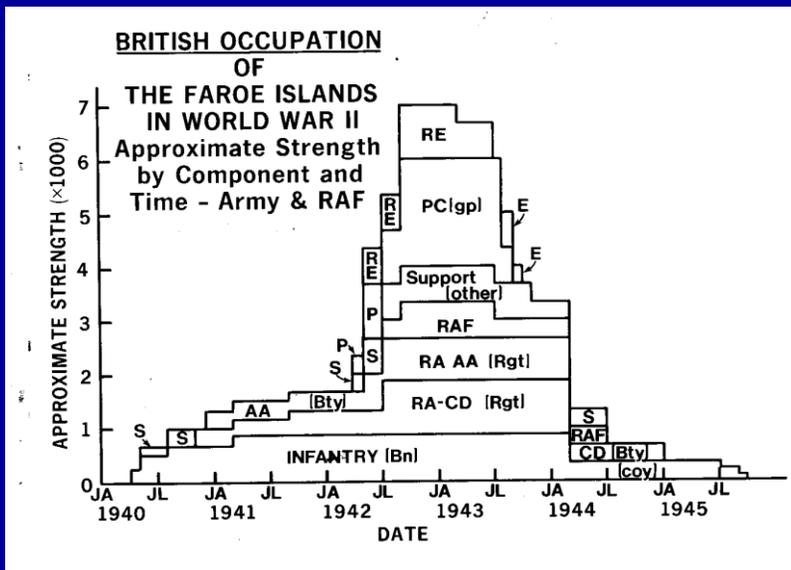
Faroes occupation WW II. 1. Line forces		
Source	Unit	Dates
Adm 116/5334, 199/671	NOIC	4.40-9.45
WO 176/73,74	HQ, FIF (Tórshavn)	4.42-4.45
WO 176/75	HQ, FIF "X" (Vágar)	12.42-9.43
AIR 28/873	RAF Sta Vágar	(4.41-5.42)
		6.42-8.44
Adm 202/432, 199/672	Force Sandall RM	4.40-5.40
WO 176/337	Lovat Scouts	5.40-6.42
WO 176/84	12 Bn Cameronians SR	6.42-7.43
WO 176/85	15 Bn So. Staffordshire Reg	8.43-2.44
---	Seaforths Rifle Coy	3.44-9.45
WO 176/76	537 Coast Reg	12.40-2.44
WO 176/76	205 Coast Bty	11.40-6.42
WO 176/76	238 Coast Bty	6.42-2.44
WO 176/76	421 Coast Bty	11.40-7.42
WO 176/76	240 Coast Bty	7.42-2.44
WO 176/76	187 Coast Bty	4.41-6.42
WO 176/76	426 Coast Bty	6.42-2.44
WO 176/76	265 Coast Bty	7.42-2.44
WO 176/76	249 Coast Bty	8.42-2.44
WO 176/82	285 LAA Bty(-)	12.40-3.41
WO 176/80,81,83	178 HAA Reg	1.43-2.44
WO 176/82	(285 LAA) -56 LAA Bty	4.41-1.43
WO 176/80	11/144 (Ulster) LAA Bty	1.43-2.44
WO 176/83	205 LAA Bty/A291 Bty	(6.42-12.43?)
----	(563 LAA Tp)	(6.43-12.43)
WO 176/81	290 HAA Bty	5.42-2.44
WO 176/79	Comp Coast Bty	3.44
WO 176/78	465 Coast Bty	4.44-12.44

Source	Faroes occupation WW II:2. Support forces Unit	Dates
WO 176/86	CRE No 5 Works (Aerodrome) "X"	3.42-11.43
WO 176/92	RASC Supply Det "X"	3.42-7.43
WO 176/93	REME Workshop/LAD, RAOC "X"	4.42-5.44
WO 176/94	RAOC Det (No 3, 25 Mob Laundry) "X"	5.42-3.44
WO 176/87	No 2 sec 135 M.E. Coy RE	5.42-2.43
WO 176/88	681 Gen Constr Coy RE "X"	4.42-9.43
WO 176/337	663 Artisan Coy RE	8.40-11.40
WO 176/89	125 & 856 Quarrying Coys RE "X"	6.42-7.43
WO 176/90	802 Road Constr Coy RE "X"	7.42-10.43
WO 176/91	716 Artisan Works Coy RE "X"	9.42-8.43
WO 176/95	309 Gp Pioneer Corps "X"	5.42-10.43
WO 176/99	228 Coy Pioneer Corps "X"	4.42-8.43
WO 176/96	35 Coy Pioneer Corps "X"	5.42-10.43
WO 176.100	234 Coy Pioneer Corps "X"	5.42-7.43
WO 176/101	237 Coy Pioneer Corps "X"	5.42-9.43
WO 176/97	56 Coy Pioneer Corps "X"	5.42-9.43
WO 196/98	192 Coy Pioneer Corps "X"	9.42-7.43
WO 176/102	303 Coy Pioneer Corps "X"	9.42-6.43
(WO 176/337)	#9 Field Hospital Tórshavn	6.40-4.45(?)
WO 177/957	#4 Field Hospital Vágur	4.42-3.44

British occupation forces in the Faroes in World War II by unit and dates stationed: Services (support). Note – RE and PC are Arms

Kurtzke & Hyllested. Acta Neurol Scand 1987; 76: 317-39.

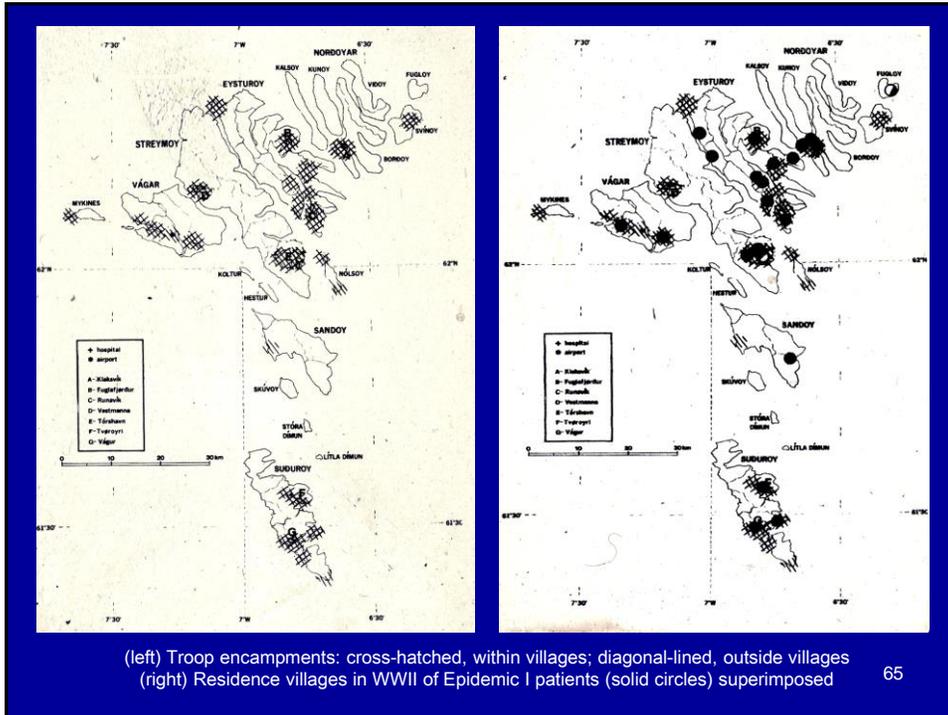
63



British occupation of the Faroes, April 1940-September 1945
all units with war diaries

Kurtzke & Hyllested. Acta Neurol Scand 1987; 76: 317-339.

64

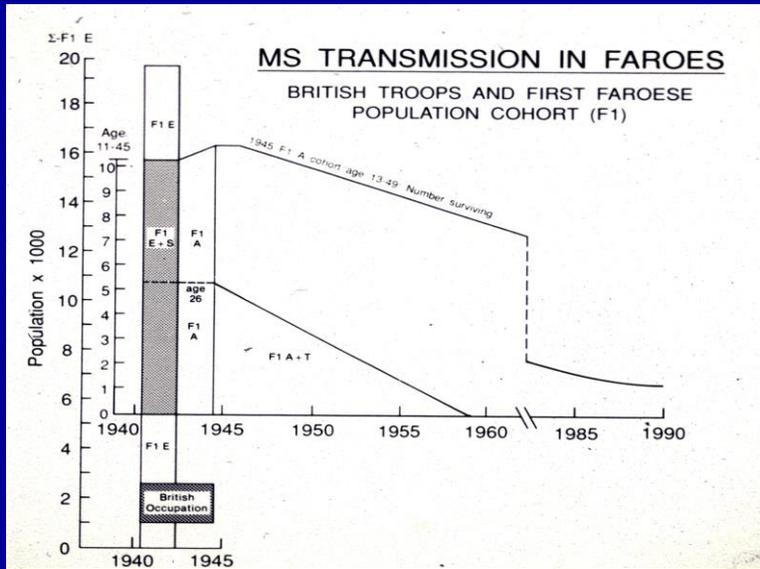


65

Introduction of MS into the Faroes

- The Faroes were occupied by British troops for five years from April 1940. From 1941 they numbered at least 1500, reached 7000 in 1942 -1943, then began to decrease to none in September 1945
- Locations of troop encampments were highly correlated with the residences of the MS patients
- We concluded the British troops brought MS to the Faroese of the Faroe Islands as a persistent (latent) infection
- This infection was presumably carried by a large proportion of troops (because of its wide distribution) in an asymptomatic fashion (because they were healthy troops).
- We call this infection the Primary Multiple Sclerosis Affection (PMSA)

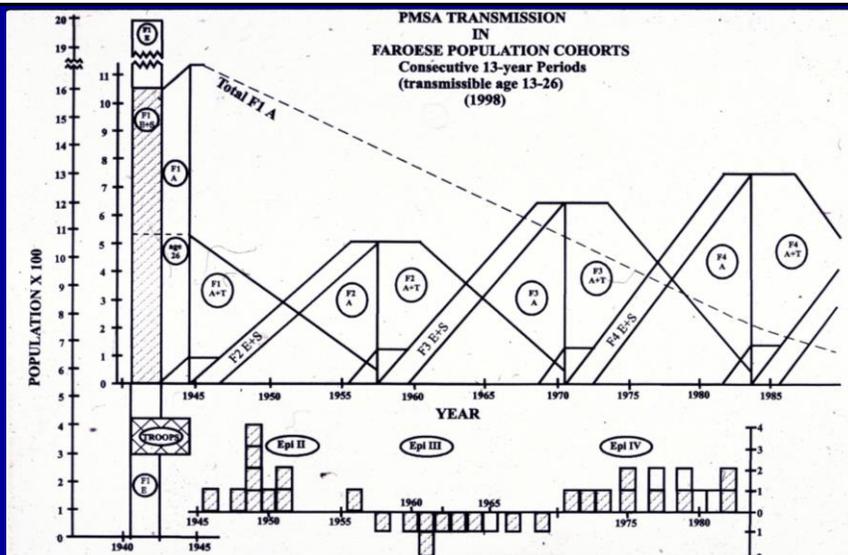
66



Transmission of PMSA from British troops to first exposed Faroese population cohort (the F1 E cohort) and the course of F1.

Modified from Kurtzke. Clin Microbiol Rev 1993; 6: 382-427.

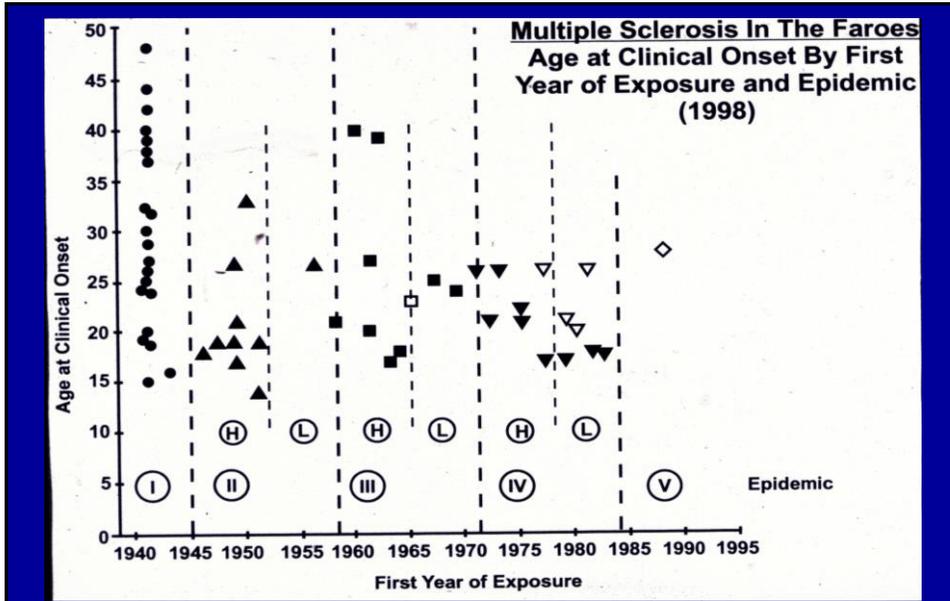
67



PMSA transmission across four consecutive Faroese population cohorts, with times of exposure for later members of Epidemics II, III, IV (bottom)

Kurtzke & Heltberg. J Clin Epidemiol 2001; 54: 1-22.

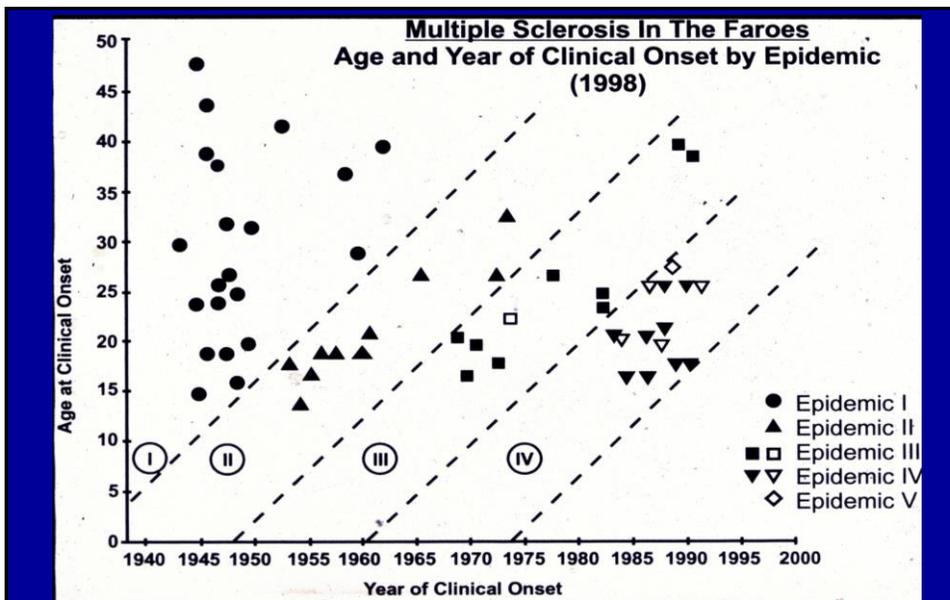
68



Faroese MS by age at onset and year of exposure for each Epidemic I-IV

Kurtzke & Heltberg. J Clin Epidemiol 2001; 54: 1-22.

69



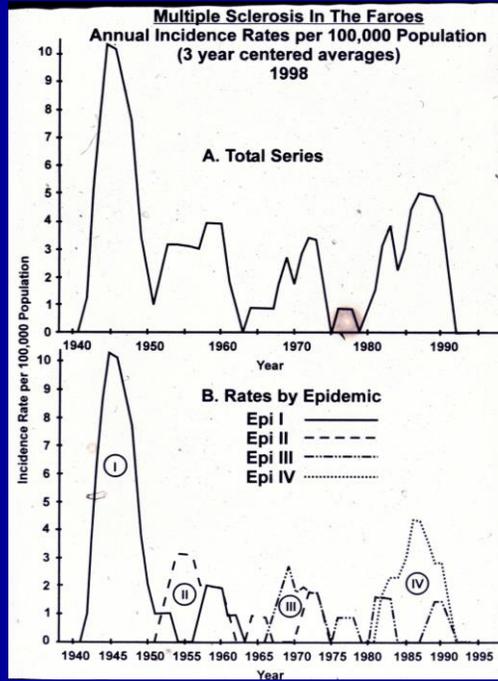
Faroese MS by age at onset and year of onset for each epidemic I-IV

Kurtzke & Heltberg. J Clin Epidemiol 2001; 54: 1-22.

70

MS in the Faroes
Annual incidence rates for
A, total series, and
B, each epidemic I-IV

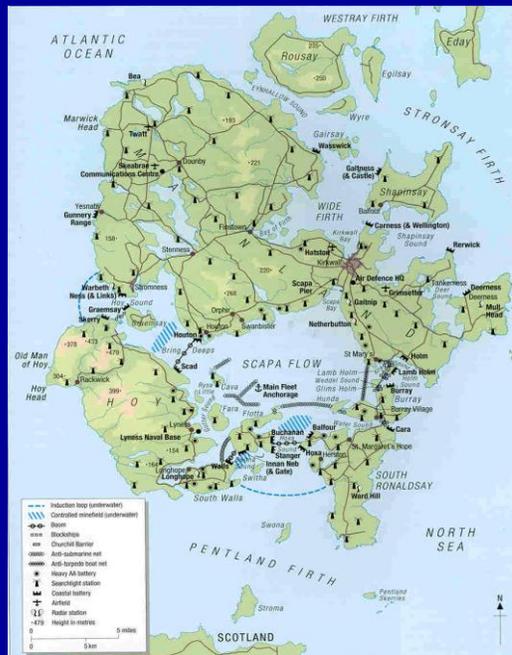
Kurtzke & Heltberg,
J Clin Epidemiol 2001; 54: 1-22.



ORKNEY
Scapa Flow and its
defences in World War II

Angus Konstam.
SCAPA FLOW.
The defences of Britain's great
fleet anchorage 1914-45.

Osprey Publishing,
Oxford, Eng, 2009, p.23



The Nature of MS from the Faroese Experience (1999)

1. There is a specific, widespread but unidentified infection called the primary multiple sclerosis affection (PMSA).
2. PMSA is a persistent infection transmitted person to person.
3. A small proportion of persons with PMSA will years later develop clinical neurologic multiple sclerosis (CNMS).
4. Prolonged exposure (2 years or more) is needed to acquire PMSA. Acquisition follows first adequate exposure.
5. Susceptibility to PMSA is limited to about age 11 to 45 at start of exposure.
6. CNMS is not transmissible.
7. Therefore PMSA transmissibility is limited to a period under usual age of CNMS onset. On the Faroes this period is about age 13 to 26.
8. At present the existence of PMSA can only be inferred from the presence of CNMS.

One view of the nature of MS,
from the Faroese Saga and other epidemiologic findings

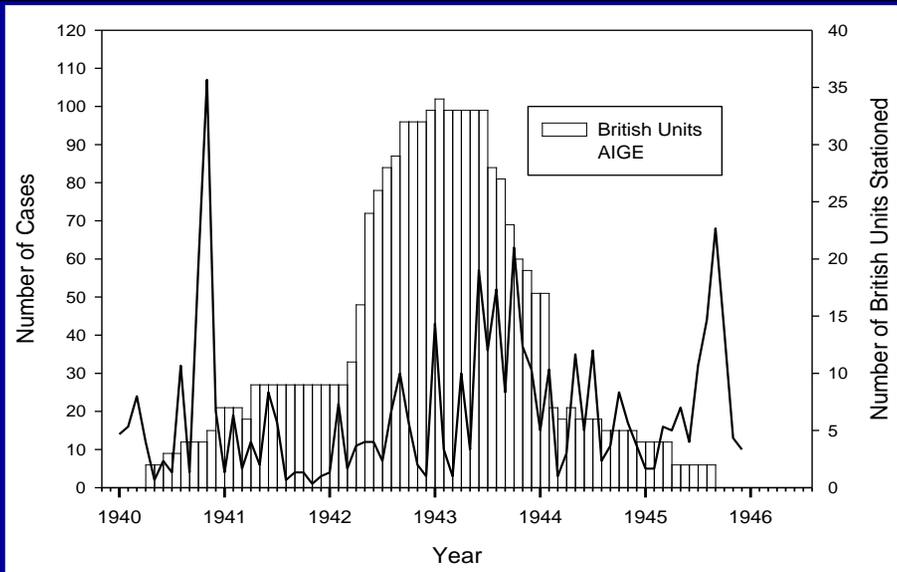
73

Cases of selected notifiable diseases in the Faroe Islands in World War II as quarterly %, with quarterly mean N for British units, January 1940-June 1945

Year & Quarter	AIGE	Paradysentery	Syphilis	Gonorrhoea	Mumps	Scarlatina	Rubella	British Units
1940-1	96	154		55	0	4	0	0
2	37	43	79	120	6	0	0	2.33
3	71	177		131	26	0	0	3.67
4	329	201	39	131	10	22	0	5.33
1941-1	50	130		153	187	31	78	6.67
2	76	109	177	361	468	57	491	9
3	41	25		438	330	105	452	9
4	14	32	354	142	404	681	304	9
1942-1	55	0		11	355	738	265	9.67
2	62	47	79	77	120	162	234	22
3	101	7		88	26	61	16	29.67
4	46	0	137	99	87	119	8	32.33
1943-1	100	7		131	0	48	62	33.33
2	173	102	20	55	155	44	47	33
3	201	363		88	10	9	0	26
4	233	273	59	22	16	13	8	18.67
1944-1	87	95		22	0	26	8	10
2	105	50	39	44	0	0	47	6.33
3	96	132		0	0	13	0	5.33
4	94	22	20	0	0	9	31	4.67
1945-1	46	100		11	0	57	109	4
2	85	130	98	22	0	0	39	2
Total	100	100	100	100	100	100	100	
mean	55.227	59.773	2.545	9.136	30.955	22.773	12.818	
chi-sq	640.8	1423.3	48	230.8	935.3	1142.7	715.5	
df	21	21	10	21	21	21	21	
N	1237	1315	56	201	681	501	282	
p <0.00001								

Wallin et al. Acta Neurol Scand 1995; 91: 321-325.

74



Faroe Islands: Cases of acute infectious gastroenteritis (AIGE) and number of British military units remaining, by month, January 1940 – December 1945

Wallin et al. Acta Neurol Scand 2010; 122: 102-109.

75

Number of cases of acute infectious gastroenteritis (AIGE) by single years of age, 1930s vs. World War II (1940-1944)

Year	Age					TOTAL
	<1 year	1-4 yrs*	5-14 yrs*	15-64 yrs*	65+ yrs*	
1930-39	15.5	4.7	1.2	0.39	0.06	66.4 mean
1940	20	16.5	8.6	2.44	0.43	300
1941	6	7	1.8	0.96	0.14	102
1942	12	11	3	1.2	0.21	149
1943	24	19.5	8	3.88	1.5	397
1944	19	13.5	4.3	1.74	0.86	215

*number of cases at each year of age in the cited age-group

Data of Wallin et al.
Acta Neurol Scand
2010; 122: 102-109.

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How could PMSA be the cause of MS?

One formulation

- PMSA is a persistent, specific gastrointestinal infection, presumably viral
- Susceptibility to PMSA is mostly limited to age 11 to 45 or so, but transmissibility ends after some 25 to 30 years of age
- In natives of high MS risk areas, PMSA acquisition requires some 4 years of exposure from age 11 and is likely to be asymptomatic
- Immigrants from lower into high areas require some 3 years of exposure from age 11 for acquisition, also likely asymptomatic
- In virgin populations, PMSA infection begins as an acute illness acquired by persons of all ages (cf measles), but persistent PMSA requires some 2 years of exposure, also from age 11 to 45 or so
- Early after acquisition the PMSA agent becomes established in regional lymph nodes in only a small proportion of the affected, and thus begins from them a lifelong invasion of the CNS via blood stream and CSF (cf acute poliomyelitis)
- This is at present a testable hypothesis

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Lítla Dímun with Suðuroy in background, 1975

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