3. Results

3.1. Geographical distribution

Geographical distribution of the disease is in part described for the observation period as a whole, in part time trends in different regions are related. Furthermore, the geographical distribution of the disease, according to some variables of possible aetiological relevance, is analyzed.

3.1.1. THE OBSERVATION PERIOD AS A WHOLE

Average incidence rate for the whole country was 4·8 (Table 12), however, the occurrence of the disease varied considerably from region to region (Fig. 1). Of 6,652 patients with year of onset within the observation period, 143 (2·2%) patients were living in the low frequency areas, where the average incidence rate was 0·19. The remaining 6,509 (97·8%) patients were living in the high frequency areas, where the average incidence rate was 10·0 (Table 13).

High frequency areas

Also within the high frequency areas the occurrence of the disease varied considerably. In the southern, middle and northern regions the average incidence rates amounted to 11·8, 9·8 and 7·6 respectively (Table 12).

Sogn & Fjordane (Fig. 1) with an average incidence rate of 28·1, was the county with the highest rate. Along the coast in both directions, average incidence rates declined, however, with a minor peak of 10·5 in Nordland. At health district level, the highest average incidence rate was found in Naustdal, Sogn & Fjordane, with a rate of 92·6. (Fig. 31).

Low frequency areas

The cases in the low frequency areas were particularly located in two counties. Of 143 patients registered during the observation period, 55 (38·4%) lived in the county of Oppland (Fig. 1); the neighbouring county of Sogn & Fjordane on the other side of the high mountain plateau and to some extent connected by transmountain communications. Another 51 (35·7%) of the patients lived in the south-eastern parts of the county of Hedmark, a county lacking any

Table 12. New cases of leprosy in Norway with annual incidence rates per 100,000 by year of onset and residential district. (The National Leprosy Registry of Norway)

Year of onset	Total		High frequency areas						Low frequency areas	
			Southern region		Middle region		Northern region			
	No.	Incidence	No.	Incidence	No.	Incidence	No.	Incidence	No.	Incidence
–1850	1,088		685		226		153		24	
1851–1855	1,201	16·6	697	47·3	342	26·9	135	21·5	27	0·81
1856–1860	1,154	14·9	604	39·0	366	27·2	174	25·2	10	0·28
1861–1865	1,009	12·2	490	30·1	343	23·9	160	21·4	16	0·42
1866–1870	996	11·4	425	25·2	393	26·1	162	20·0	16	0·40
1871–1875	716	8·0	327	18·7	248	16·0	129	14·7	12	0·29
1876–1880	525	5·4	209	11·7	204	12·9	99	10·9	13	0·30
1881–1885	340	3·6	116	6·2	124	7·6	90	8·8	10	0·22
1886–1890	275	2·6	89	4·6	104	6·2	75	6·6	7	0·15
1891–1895	165	1·6	70	3·5	49	2·9	39	3·3	7	0·14
1896–1900	111	1·0	44	2·1	38	2·2	23	1·8	6	0·12
1901–1905	87	0·6	33	1·5	28	1·5	17	1·3	9	0·16
1906–1910	30	0·2	15	0·7	5	0·3	6	0·4	4	0·07
1911–1915	31	0·2	10	0·4	8	0·4	8	0·5	5	0·08
1916–1920	12	0·1	3	0·1	3	0·2	5	0·3	1	0·02
1921–1970	14		6		1		3		4	
Unknown	477		273		140		50		14	
1851–1920	6,652	4·8†	3,132	11·8†	2,255	9·8†	1,122	7·6†	143	0·19†
Total	8,231		4,096		2,622		1,328		185	

†Average incidence rates

Table 13. New cases of leprosy with annual incidence rates per 100,000 in Norway, high frequency areas, 1851–1920, by year of onset in towns, rural coastal and rural inland health districts. (The National Leprosy Registry of Norway)

Year of onset	High frequency areas									
	Total		Towns		Rural districts					
					Total		Coastal districts		Inland districts	
	No.	Incidence	No.	Incidence	No.	Incidence	No.	Incidence	No.	Incidence
1851–1860	2,318	33·4	59	9·3	2,259	35·8	1,440	46·2	819	25·6
1861–1870	1,973	25·2	70	7·0	1,903	27·8	1,309	37·8	594	17·6
1871–1880	1,216	14·2	62	4·9	1,154	15·8	776	20·7	378	10·7
1881–1890	598	6·5	27	1·8	571	7·5	418	10·4	153	4·2
1891–1900	263	2·7	19	1·1	244	3·0	183	4·2	61	1·6
1901–1910	104	1·0	4	0·18	100	1·2	74	1·6	26	0·67
1911–1920	37	0·3	3	0·11	34	0·38	31	0·62	3	0·07
Total	6,509	10·0†	244	2·19†	6,265	11·7†	4,231	15·0†	2,034	7·98†

†Average incidence rates

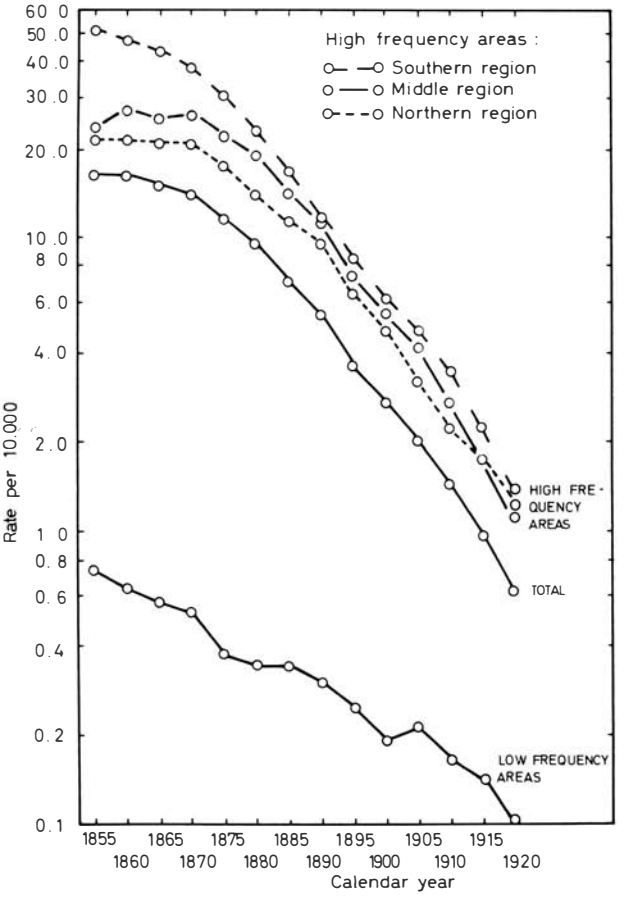

Figure 7. Prevalence rates of leprosy in Norway 1855–1920 by region. (The National Leprosy Registry of Norway.)

communications with the high frequency areas. The rest, 37 (25·9%) patients, were scattered, without any concentrations, in the other counties.

Towns and rural districts

Leprosy was most infrequent in towns. Of the patients taken ill in the high frequency areas during the observation period, 244 (3·7%) lived in towns and 6,265 (96·3%) in rural districts, and the average incidence rates were 2·2 and 11·7 respectively (Table 13).

Coast and inland

Leprosy was also more frequent in districts constituting the coast line than in districts distant from the sea. In the observation period 6,265 patients were taken ill in the rural districts of the high frequency areas; 4,231 (67·5%) patients

Table 14. Leprosy patients in Norway, 1836–1920, with prevalence rates per 10,000 by residential district when registered. (The National Leprosy Registry of Norway†)

			High frequency areas						Low frequency areas	
	Total		Southern region		Middle region		Northern region			
Year	No.	Prev.	No.	Prev.	No.	Prev.	No.	Prev.	No.	Prev.
1835			389	14·2	121	5·1	106	9·6	10	
1845			539	19·7	230	9·7	141	12·8	28	
1855	2,492	16·7	1,531	50·7	622	23·9	287	21·7	52	0·75
1860	2,626	16·5	1,510	47·5	756	27·2	312	21·8	48	0·65
1865	2,583	15·2	1,444	43·4	763	25·8	330	21·2	46	0·58
1870	2,489	14·1	1,292	38·0	801	26·3	352	21·1	44	0·54
1875	2,144	11·8	1,078	30·3	708	22·5	326	18·0	32	0·38
1880	1,785	9·5	854	23·1	617	19·1	283	14·0	31	0·36
1885	1,392	7·2	639	17·0	469	14·3	252	11·8	32	0·35
1890	1,091	5·5	459	11·9	385	11·6	218	9·6	29	0·31
1895	781	3·7	340	8·6	257	7·5	159	6·5	25	0·25
1900	614	2·7	264	6·2	201	5·7	128	4·9	21	0·20
1905	479	2·1	213	4·9	153	4·2	89	3·3	24	0·22
1910	347	1·5	159	3·5	105	2·8	64	2·3	19	0·17
1915	245	1·0	109	2·3	67	1·8	52	1·8	17	0·14
1920	167	0·6	70	1·4	47	1·1	38	1·2	12	0·09

†Numbers of cases for 1836 and 1845 are derived from special 'leper censuses'.

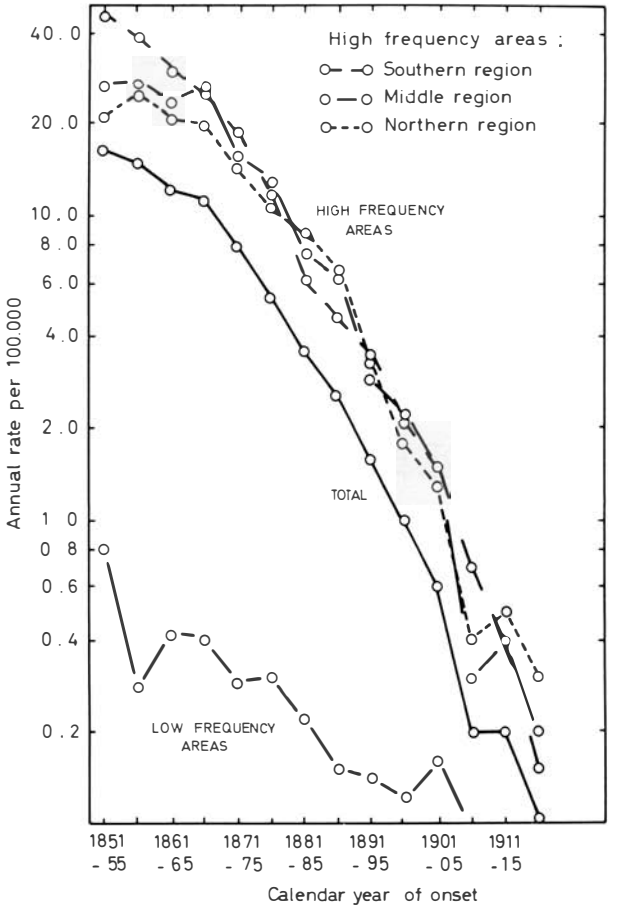

Figure 8. Incidence rates of leprosy in Norway 1851–1920 by region. Crude rates by year of onset. (The National Leprosy Registry of Norway.)

in the coastal districts and 2,034 (32·5%) in the remaining inland districts. The average incidence rates were 15·0 and 8·0 respectively (Table 13).

3.1.2. TIME TRENDS DURING THE OBSERVATION PERIOD

For the whole country, the highest morbidity rates were registered in the first part of the observation period with a subsequent rapid fall. The highest *prevalence* rate, 16·7 per 10,000, was registered in 1855 (Fig. 7, Table 14). In 1860 the rate was almost the same, 16·5. Then the rate declined, with an increasing relative fall throughout the observation period.

The highest *incidence* rate for the whole country, 16·6 per 100,000 per year, was registered in the period 1851–55 (Fig. 8, Table 12). Also relative fall in incidence rate increased with time. Accordingly, the observation period covered a continuous fall in incidence rates.

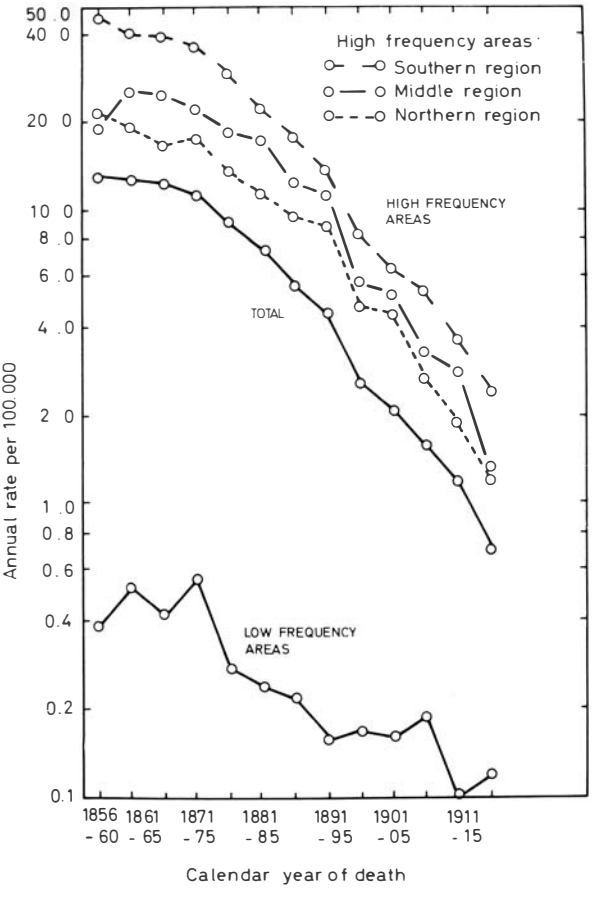

Figure 9. Mortality rates of leprosy in Norway, 1856–1920 by region. Crude rates. (The National Leprosy Registry of Norway)

However, trends in prevalence rates seemed to ascertain that the *maximum* of the epidemic occurred at the beginning of the period. Prevalence rates, also influenced by the duration of the disease and thus reflecting conditions prior to the time of registration, did not decline until after 1860.

Trends in *mortality* rates, still more retrospective than prevalence rates, confirmed the finding; mortality rates did not decline until after 1870 (Fig. 9, Table 15).

For 1,083 patients, taken ill between 1856 and 1860, mean duration of the disease, from year of onset to year of death, was calculated as 12·7 years. Accordingly, fall in incidence appeared to have commenced during the last half of the 1850s.

Although inaccurate and incomplete, the leprosy censuses of 1836 and 1845 also contributed to the documentation that the registry covers a period

Table 15. Deaths from leprosy in Norway 1856–1920, with annual mortality rates per 100,000, by year of death and residential district. (The National Leprosy Registry of Norway)

Year of death	Total		High frequency areas						Low frequency areas	
			Southern region		Middle region		Northern region			
	No.	Mort.	No.	Mort.	No.	Mort.	No.	Mort.	No.	Mort.
1856–1860	1,005	13·0	729	46·7	256	19·0	147	21·3	14	0·39
1861–1865	1,046	12·7	653	40·2	365	25·4	144	19·3	20	0·52
1866–1870	1,056	12·2	662	39·3	372	24·7	135	16·7	17	0·42
1871–1875	1,005	11·2	631	36·1	342	22·1	153	17·5	23	0·55
1876–1880	826	9·0	519	28·8	291	18·4	130	13·7	12	0·28
1881–1885	701	7·4	408	22·0	279	17·2	116	11·4	11	0·24
1886–1890	551	5·6	337	17·6	203	12·3	104	9·5	10	0·22
1891–1895	466	4·5	266	13·4	187	11·1	103	8·8	8	0·16
1896–1900	284	2·6	171	8·2	100	5·7	59	4·7	9	0·17
1901–1905	240	2·1	136	6·3	93	5·2	58	4·4	9	0·16
1906–1910	192	1·6	118	5·3	61	3·3	37	2·7	11	0·19
1911–1915	146	1·2	85	3·6	54	2·8	27	1·9	6	0·10
1916–1920	95	0·7	60	2·4	27	1·3	18	1·2	8	0·12

from the peak of the epidemic and not only the end of a wave with a far higher maximum at an earlier stage (Table 14).

High frequency areas

Highest prevalence and incidence rates were registered in the *southern region*. In 1855, the prevalence rate was 50·7 per 10,000, and in the quinquenniad 1851–55, the incidence rate was 47·3 per 100,000 per year. At the same time prevalence and incidence rates of 101·9 and 97·5 respectively were registered in the county of Sogn & Fjordance. In the health district of Naustdal, prevalence and incidence rates of 253·0 and 318·3 respectively were registered.

In the *southern region* a fall in the rates was registered from the beginning of the observation period, with respect to prevalence, incidence and mortality rates (Figs. 7, 8, 9). The relative fall in the rates increased with time.

Apparently, the fall in the rates commenced at a later stage in the other high frequency regions. In the *middle region* a maximum of the prevalence rates was registered between 1860 and 1870. A fall in incidence and mortality rates was registered after 1870. In the *northern region* prevalence rates declined from 1870, while incidence and mortality rates declined from 1860.

Incidence rates declined most rapidly in the southern region, less rapidly in the middle region, and even more slowly in the northern region. Expressed as incidence rate at a specified time in percent of incidence rate 1851–55, this tendency was obvious (Fig. 10).

Further information on time trends in the three regions was at hand in the leprosy censuses of 1836 and 1845 (Table 14). Provided the validity of a census was the same in different districts, the greatest increase in prevalence rates was found in the middle region. Here, prevalence rate increased from 5·1 in 1836 to 23·9 in 1856; i.e. by 90·2% between 1836 and 1845, and by 146·4% between 1845 and 1856. Also in the southern region, a considerable increase was found from 14·2 via 19·7 to 50·7; i.e. increases of 38·7% and 157·4%. In the northern region prevalence rate increased from 9·6 via 12·8 to 21·7 and the relative increases were as low as 33·3% and 69·5%.

Accordingly, the morbidity rates in the southern region declined rapidly from a high level which may have persisted, more or less, during several decades. The maximum in the middle region was lower, and apparently restricted to a shorter period around the middle of the century. The highest rates registered in the northern region were even lower, and the maximum rates were apparently not restricted to a well-defined, short period. In this region the rates fell relatively slowly.

Low frequency areas

Prevalence and incidence rates declined from the beginning of the observation period (Figs. 7, 8) with approximately constant relative fall in rates throughout

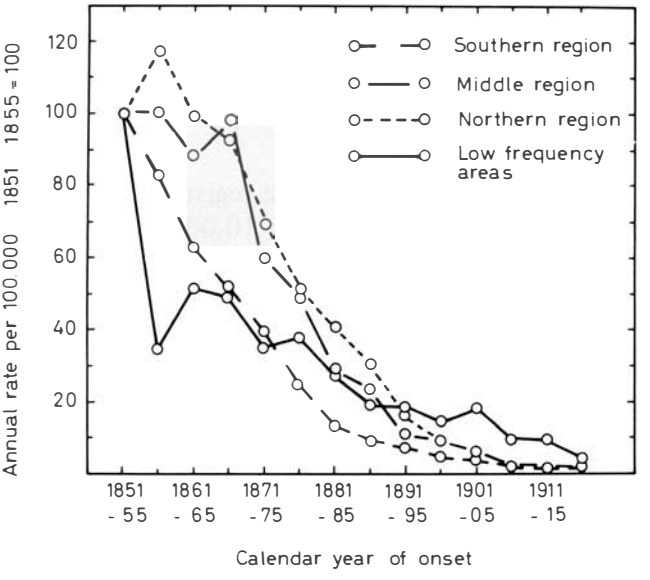

Figure 10. Incidence rates of leprosy in Norway 1851–1920 by region. Crude rates by year of onset, incidence rate 1851–55 = 100. (The National Leprosy Registry of Norway.)

the observation period. For mortality rate, a maximum was registered as late as 1871–75 (Fig. 9). The rates declined more slowly than in the high frequency areas (Fig. 10).

Time trends in mortality rates seemed to ascertain that also in the low frequency areas, the maximum of the epidemic occurred after the beginning of the observation period.

Towns and rural districts

Time trends in incidence rates for towns and rural districts within the high frequency areas were similar (Fig. 11); incidence rates in towns were approximately one quarter of incidence rates in rural districts throughout the observation period.

Coast and inland

Also time trends in incidence rates for coastal and inland rural districts were similar (Fig. 11); incidence rates in inland districts were approximately one half of incidence rates in coastal districts throughout the observation period.

3.1.3. DISTRIBUTION ACCORDING TO SOME CLIMATIC VARIABLES

Increasing evidence is currently published that a reservoir of mycobacteria, associated with leprosy in man, may be found outside the human body (Shield

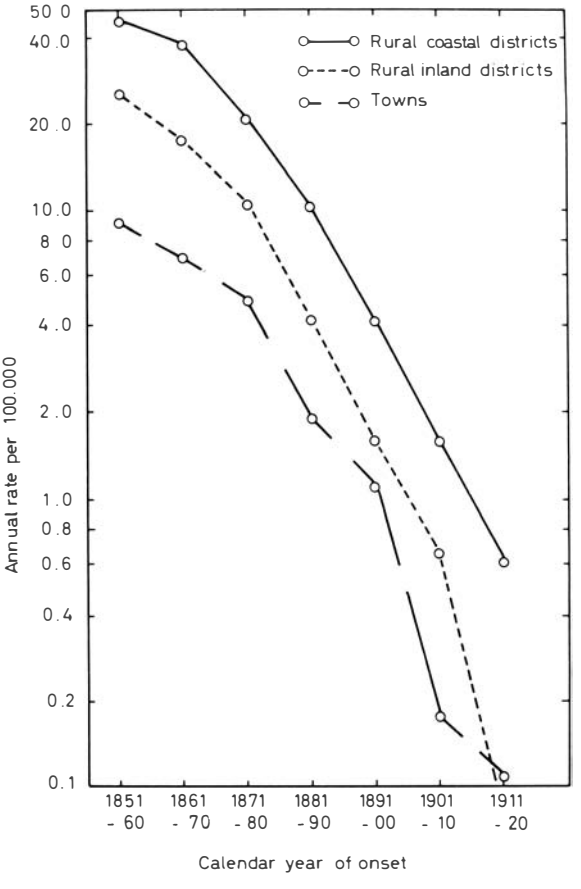

Figure 11. Incidence rates of leprosy in Norway, high frequency areas 1851–1920, in towns, rural coastal and rural inland districts. Crude rates by year of onset. (The National Leprosy Registry of Norway.)

and Stanford, 1977; Walsh *et al.*, 1975; Desikan and Sreevatsa, 1978; Kazda *et al.*, 1979). If it is true that *M. leprae* or other mycobacteria which may influence susceptibility of man to leprosy, may survive and multiply outside the human body, the distribution of such mycobacteria may be related to the occurrence of leprosy in man. Apparently, the distribution is dependent on local conditions of multiplication of which humidity and temperature are essential (Kazda, 1979). In an attempt to clarify the question, the occurrence of leprosy was compared with meteorological observations on humidity and temperature in Norway.

Humidity

Accurate relevant meteorological observations have been made in Norway since 1874 (Mohn, 1921). Mean relative *humidity* in July from 1874 through

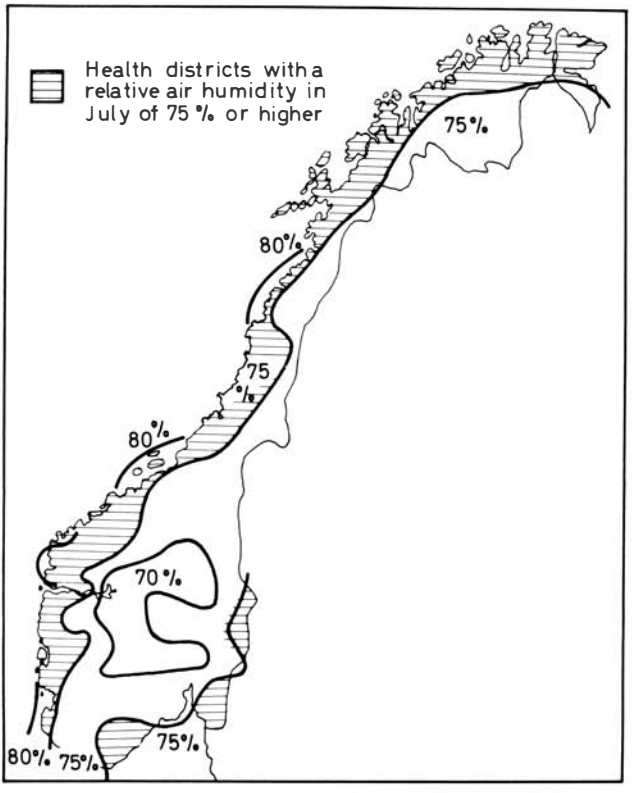

Figure 12. Average relative air humidity in July, 1874–1913, in Norway. (Mohn, 1921.)

1913 at 85 stations ranged from 65% to 85% (Fig. 12). In the health districts where relative humidity was 75% or higher, average incidence rate was 12·4, while in the other health districts, average incidence rate was 0·7 (Table 16).

Temperature

Mean air temperature in July ranged from 8·5°C to 17°C (Fig. 13). In health districts where the temperature was 15°C or higher, average incidence rate was 0·8, while in the other districts average incidence rate was 11·7. (Table 17).

3.1.4. COMMENTS

A considerable range of morbidity rates was demonstrated in Norway from region to region. This seems also to represent a common pattern of the epidemiology of leprosy in other countries (Hilpert, 1972). Accordingly, WHO has introduced the term 'rate in highest endemic area' (Bechelli and Martinez Dominguez, 1972) as a measure to describe the epidemiological situation in a country.

The highest endemic area in Norway at county level was Sogn & Fjordane

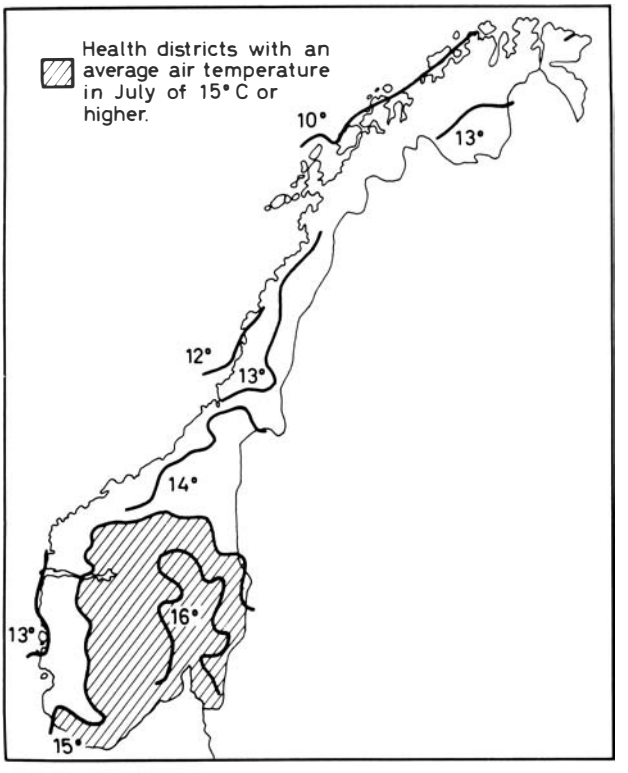

Figure 13. Average air temperature (°C) in July, 1874–1913, in Norway. (Mohn, 1921.)

Table 16. New cases of leprosy 1851–1920 and population in 1865, with average incidence rates, in health districts where relative humidity in July was above or below 75%. (The National Leprosy Registry of Norway)

Relative humidity	Patients 1851–1920	Population 1865	Average incidence rate
⩽ 74%	512	993,517	12·4
⩾ 75%	6,140	708,239	0·7
Total	6,652	1,701,756	5·6†

†Based on mean population 1851–1920 instead of population 1865, average incidence rate was 4·8 and not 5·6.

with prevalence and annual incidence rates of 101·9 per 10,000 and 97·5 per 100,000 population respectively. Due to a series of practical problems, comparable statistics from countries where leprosy is prevalent today, are difficult to obtain (Meade, 1971; Lechat, 1973). However, the situation at present may, to some extent, be clarified by WHO-statistics from 1972. Highest *prevalence* rates were found in Zaire with 1,163 per 10,000. In other African countries, prevalence rates ranged from 20 to 350. Besides some small areas on islands in the Pacific Ocean, prevalence rates did not exceed 100 in the countries covered by

Table 17. New cases of leprosy 1851–1920 and population in 1865, with average incidence rates, in health districts where mean temperature in July was above or below 15°C. (The National Leprosy Registry of Norway)

Temperature	Patients 1851–1920	Population 1865	Average incidence rate
⩽14°C	6,128	750,554	11·7
⩾15°C	524	951,202	0·8
Total	6,652	1,701,756	5·6†

†Based on mean population 1851–1920 instead of population 1865, average incidence rate was 4·8 and not 5·6.

this report. Information from India was lacking, however; in areas selected for special surveys, prevalence rates seem to range between 100 and 1,000 per 10,000 (Meade, 1971; Vellut, 1969; Rao *et al.*, 1972a).

Comparable information on *incidence* rates is even more difficult to obtain. In general, the calculation of reliable incidence rates for a chronic disease, with remissions and relapses like leprosy, has to be based on a patient register. If the exact year of onset is impossible to ascertain, number of new cases in the beginning of an observation period tends to be too high. In special surveys, annual incidence rates range from 1,490 per 100,000 in Zaire (Browne, 1965) to 2·6 in Costa Rica (Monge and Castro, 1968). In New Guinea a level of approximately 600 has been registered (Russell, 1968) and in India the rates have ranged between 86 (Rao *et al.*, 1972b) and 700 (Suresh *et al.*, 1969) per 100,000.

Accordingly, the morbidity rates registered in Norway at the beginning of the observation period, were of the same magnitude as morbidity rates registered in countries where leprosy represents a public health problem today.

3.2. Distribution according to sex, age and type

3.2.1. DISTRIBUTION BY SEX

According to place

In the *high frequency areas*, 3,790 (58·2%) males and 2,719 (41·8%) females were taken ill during the observation period, i.e. 139·4 males per 100 females. In the *low frequency areas*, 83 (58·0%) males and 60 (42·0%) females were taken ill during the observation period, i.e. 138·3 males per 100 females (Table 18) (*vide* also Table 38).

According to year of onset

Of 1,088 patients with year of onset before 1851, 546 (50·2%) were males and 542 (49·8%) were females; i.e. 100·7 males per 100 females (Table 18). Of

Table 18. Leprosy cases in Norway by sex with mean age at onset according to residential district and year of onset. (The National Leprosy Registry of Norway)

Year of onset	Total (No.)	Sex		Of these: Known age at onset	
		Male (No.)	Female (No.)	(No.)	(mean†)
High frequency areas:					
–1850	1,064	534	530	1,063	32·9
1851–1920	6,509	3,790	2,719	6,471	38·1
1921–1970	10	7	3	10	–
Unknown	463	229	234	0	–
Total	8,046	4,560	3,486	7,544	37·4
Low frequency areas:					
–1850	24	12	12	23	38·3
1851–1920	143	83	60	141	44·2
1921–1970	4	4	0	4	–
Unknown	14	9	5	0	–
Total	185	108	77	168	43·3
Total:					
–1850	1,088	546	542	1,086	33·0
1851–1920	6,652	3,873	2,779	6,612	38·3
1921–1970	14	11	3	14	–
Unknown	477	238	239	0	–
Total	8,231	4,668	3,563	7,712	37·5

†Mean based on crude number of patients.

6,666 patients with year of onset after 1850, 3,884 (58·3%) were males and 2,782 (41·7%) were females; i.e. 139·6 males per 100 females.

In the high frequency areas, average annual age-adjusted incidence rates during the observation period were 13·5 for males and 9·5 for females, with a sex ratio of 142·6. During the observation period age-adjusted sex-specific incidence rates declined continuously; from 37·5 to 0·4 for males, and from 27·5 to 0·2 for females, in the decades 1851–60 and 1911–20 respectively (Table 19, Fig. 14).

Sex ratio increased during the observation period from 136·4 in the decade 1851–60 to 160·3 in the decade 1911–20. A temporary fall was observed 1891–1900 when sex ratio was as low as 118·5 (Table 19, Fig. 15).

According to age

Highest average incidence rate for males, 19·9, was observed in the age group 30–49 years and for females, 13·5, in the age group 15–29 years (Table 20, Fig. 16).

Highest sex ratio was observed in the age group 30–40 years with 187·2. In

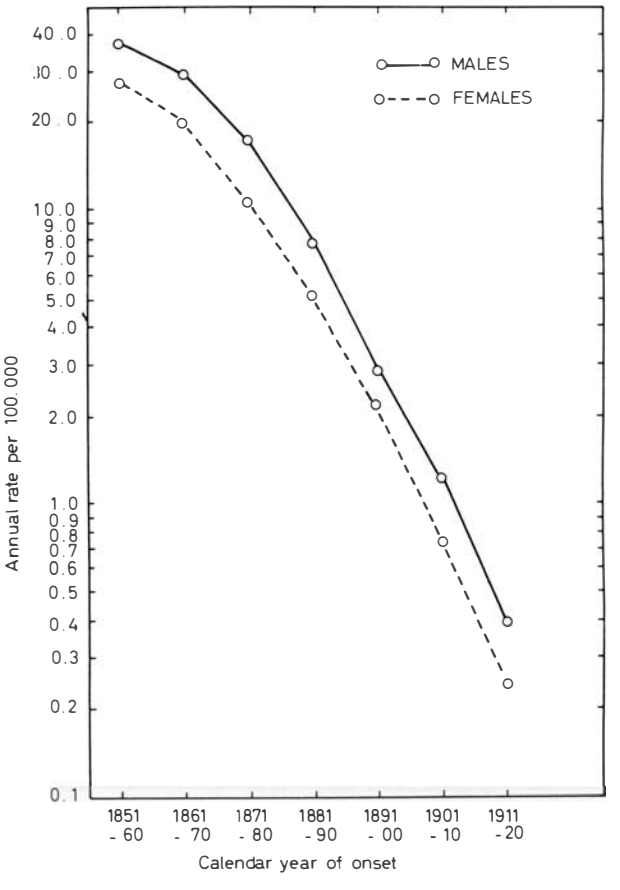

Figure 14. Incidence rates of leprosy in Norway, high frequency areas, 1851–1920. Sex-specific age-adjusted rates by year of onset. (The National Leprosy Registry of Norway.)

the age groups 0–14 and 15–29 years, sex ratio was approximately 132, while in the age group 50 + sex ratio was 168·2 (Table 20, Fig. 17).

According to age by year of onset

When sex ratio according to age was calculated in subsequent decades, it appeared that the maximum found in the age group 30–49 years, was present only between 1851 and 1880 (Table 20, Fig. 18). After 1880 a maximum in the age group 50+ became more and more evident. Accordingly, the increasing sex ratio towards the end of the observation period, appeared to be due to an increasing sex ratio in elderly patients.

Table 19. New cases of leprosy in Norway, high frequency areas 1851–1920 by year of onset, with sex ratio based on incidence rates in consecutive decades, and average incidence rates in the observation period per 100,000. (The National Leprosy Registry of Norway)

Year of onset	Male (No.) (Incidence)	Female (No.) (Incidence)	Sex ratio
1851–1860	1,323	993	
	37·5	27·5	136·4
1861–1870	1,150	816	
	29·1	20·3	143·4
1871–1880	727	479	
	17·4	10·8	160·6
1881–1890	342	242	
	7·8	5·1	152·3
1891–1900	135	124	
	2·9	2·4	118·5
1901–1910	61	42	
	1·2	0·8	160·2
1911–1920	22	15	
	0·4	0·2	160·3
Total	3,760	2,711	
	13·5†	9·5†	142·6

†Average incidence rates.

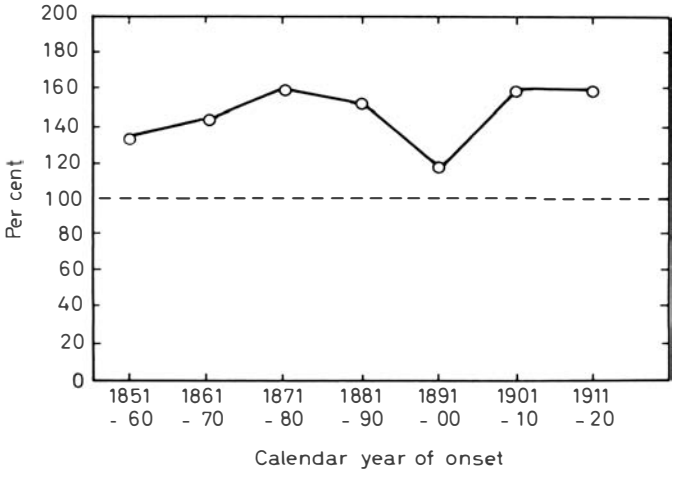

Figure 15. Sex ratio of leprosy in Norway, high frequency areas; 1851–1920 by year of onset. Ratio based on sex-specific age-adjusted incidence rates. (The National Leprosy Registry of Norway.)

Table 20. New cases of leprosy in Norway, high frequency areas, 1851–1920 by year of onset, with sex ratio based on annual incidence rates in consecutive decades and average incidence rates in the observation period, per 100,000 according to age and sex. (The National Leprosy Registry of Norway)

Year of onset	0–14 years (No.) (Incidence)	Ratio	15–29 years (No.) (Incidence)	Ratio	30–49 years (No.) (Incidence)	Ratio	50 + years (No.) (Incidence)	Ratio
Male								
1851–1860	175	126·3	512	132·6	447	165·2	189	137·1
	14·4		58·6		58·0		35·1	
1861–1880	222	142·6	644	121·7	682	200·0	329	185·9
	7·7		33·1		37·8		25·1	
1881–1900	58	120·7	162	147·4	144	142·1	113	174·1
	1·7		7·9		8·0		6·5	
1901–1920	5	95·3	17	143·0	24	133·8	37	274·4
	0·1		0·7		1·2		1·9	
Total	460	132·3	1,335	131·7	1,297	187·1	668	168·2
	4·0		17·8		19·9		11·9	
Female								
1851–1860	133		411		280		169	
	11·4		44·2		35·1		25·6	
1861–1880	150		569		367		209	
	5·4		27·2		18·9		13·5	
1880–1900	46		127		118		75	
	1·4		5·4		5·6		3·7	
1901–1920	5		14		22		16	
	0·1		0·5		0·9		0·7	
Total	334		1,121		787		469	
	3·0		13·5		10·6		7·1	

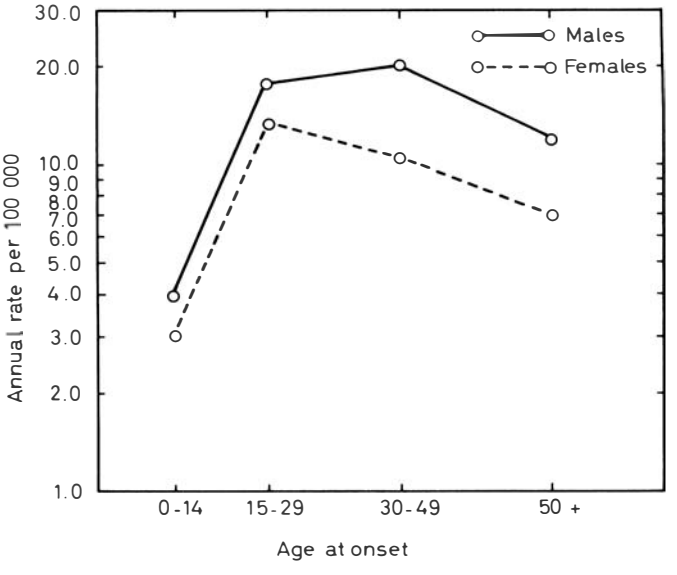

Figure 16. Incidence rates of leprosy in Norway, high frequency areas, 1851–1920. Average age- and sex-specific rates. (The National Leprosy Registry of Norway.)

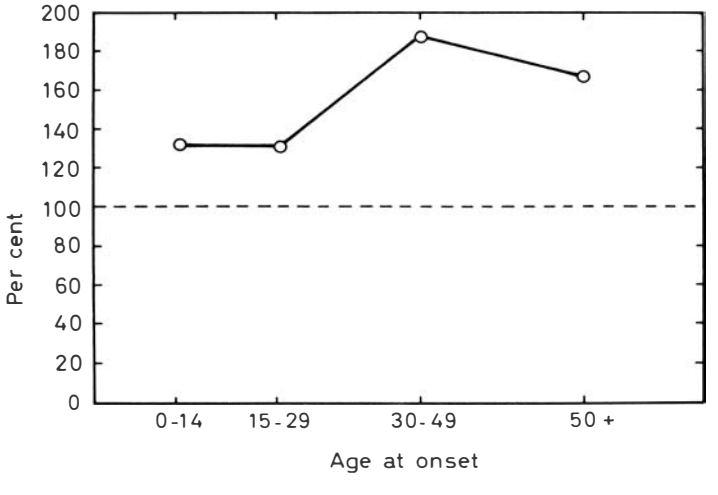

Figure 17. Sex ratio of leprosy in Norway, high frequency areas, 1851–1920, by age. Ratio based on average age- and sex-specific incidence rates. (The National Leprosy Registry of Norway.)

3.2.2. DISTRIBUTION BY AGE

According to place

In the *high frequency areas* mean age at onset of 6,471 patients taken ill during the observation period was 38·1 years. In the *low frequency areas* during the

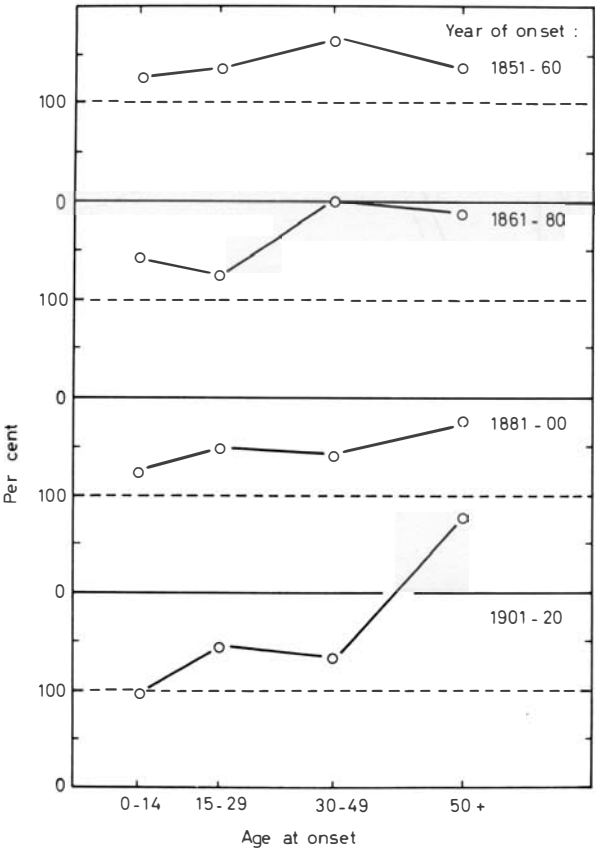

Figure 18. Sex ratio of leprosy in Norway, high frequency areas, 1851–1920, by age and year of onset. Ratio based on age- and sex-specific incidence rates. (The National Leprosy Registry of Norway.)

same period, mean age at onset of 141 patients was 44·2 (Table 18) (*vide* also Table 38).

According to year of onset

Mean age at onset of 1,086 patients with known age at onset and with year of onset before 1851 was 33·0 years (Table 18). Mean age at onset of 6,626 patients with known age at onset and with year of onset after 1850 was 38·3.

During the observation period mean age at onset by year of onset, based on age- and sex-specific incidence rates and the standard population of 1885 (*vide* 2.5.3.), increased almost continuously; for males from 33·0 to 45·9 years, and for females from 32·9 to 43·9 years in the periods 1851–60 and 1911–20 respectively (Table 21, Fig. 19). In all decades, mean age at onset of males was higher than mean age at onset of females.

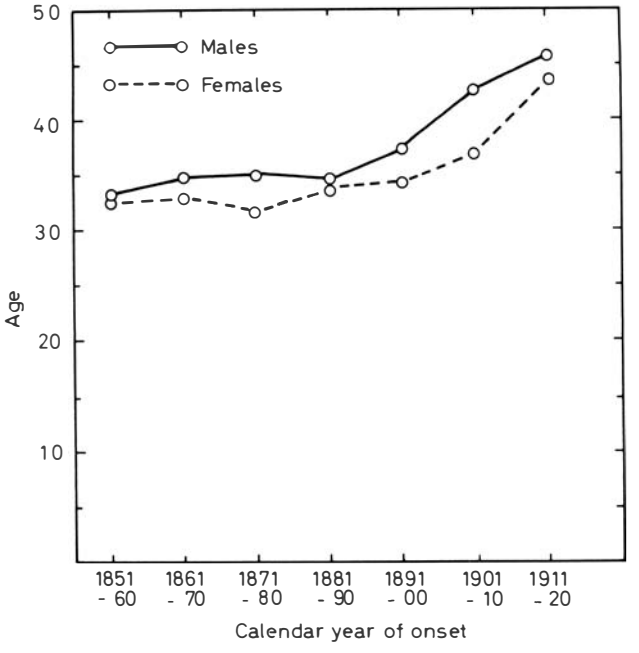

Figure 19. Mean age at onset of leprosy in Norway, high frequency areas, 1851–1920, by sex and year of onset. (The National Leprosy Register of Norway.)

Also age- and sex-specific incidence rates, calculated in consecutive decades, demonstrated that the disease, to an ever increasing extent, attacked *older* individuals (Table 20, Fig. 20). Thus, in the decade 1851–60, number of patients in the age group 50 + years, calculated as age- and sex-adjusted patient number (*vide* 2.5.3.), amounted to 18·2% of all patients taken ill during the decade (Table 21, Fig. 21). This percentage increased to 46·5 in the decade 1911–20.

According to year of birth

When age at onset was studied in consecutive birth cohorts, an inverse trend appeared. Mean age at onset, based on age- and sex-specific incidence rates and the standard cohort born 1851–60 (*vide* 2.5.3.), decreased almost continuously during the observation period; for males from 23·1 to 15·1 years and for females from 22·9 to 10·7 years, for patients born in the decades 1841–50 and 1891–1900 respectively (Table 23, Fig. 22). In most cohorts mean age at onset of males was higher than mean age at onset of females.

Also age- and sex-specific incidence rates demonstrated that when studied in consecutive cohorts, the disease gradually attacked *younger* individuals (Table 22, Fig. 23). In the cohort of patients born 1841–50, patients with age at onset between 0 and 14 years, calculated as age- and sex-adjusted patient number (*vide* 2.5.3.), amounted to 26·4% of the total cohort, while in the

Table 21. New cases of leprosy in Norway high frequency areas 1851–1920, by year of onset; actual registered number (n_1) and number calculated on the basis of a standard population and age- and sex-specific incidence rates (n_2), with mean age at onset. (The National Leprosy Registry of Norway)

Year of onset	Total						
	Total (n_1) (n_2) (%)	0–14 yrs (n_1) (n_2) (%)	15–29 yrs (n_1) (n_2) (%)	30–49 yrs (n_1) (n_2) (%)	50 + yrs (n_1) (n_2) (%)	Male (mean age at onset)	Female (mean age at onset)
1851–1860	2,316	308	923	727	358		
	2,942·4	416·8	1,108·2	882·1	535·3	33·0	32·9
	100·0	14·2	37·6	30·0	18·2		
1861–1870	1,966	234	742	669	321		
	2,229·5	274·7	830·1	675·8	448·9	34·6	33·1
	100·0	12·3	37·2	30·3	20·2		
1871–1880	1,206	138	471	380	217		
	1,273·4	115·5	486·0	390·2	245·7	35·0	32·0
	100·0	11·9	38·2	30·6	19·3		
1881–1890	584	72	205	183	124		
	584·0	72·0	205·0	183·0	124·0	34·7	34·3
	100·0	12·3	35·1	31·3	21·3		
1891–1900	259	32	84	79	64		
	240·3	29·3	77·9	75·4	57·7	36·6	34·6
	100·0	12·2	32·4	31·4	24·0		
1901–1910	103	8	25	34	36		
	88·8	6·8	21·5	30·1	30·5	42·9	37·0
	100·0	7·6	24·1	33·9	34·4		
1911–1920	37	2	6	12	17		
	29·1	1·7	4·5	9·4	13·5	45·9	43·9
	100·0	5·8	15·3	32·4	46·5		
Total	6,471	794	2,456	2,084	1,137		
	7,387·5	952·8	2,733·2	2,246·0	1,455·6	34·3	33·0
	100·0	12·9	37·0	30·4	19·7		

cohort born 1891–1900 the same group represented 79·7% of the cohort (Table 23, Fig. 24).

3.2.3. DISTRIBUTION BY TYPE

According to sex and place

In the *high frequency areas* during the observation period, type index was 64·8 (Table 24); 65·4 in males and 64·1 in females. Variations between regions and counties were insignificant; in the northern region, type index was 66·9, in the middle region 66·0, and in the two northern counties of the southern region, the counties of Sogn & Fjordane and Hordaland, type index was 64·2. However, in the most southern county of the high frequency areas, the county of Rogaland, type index was 56·9.

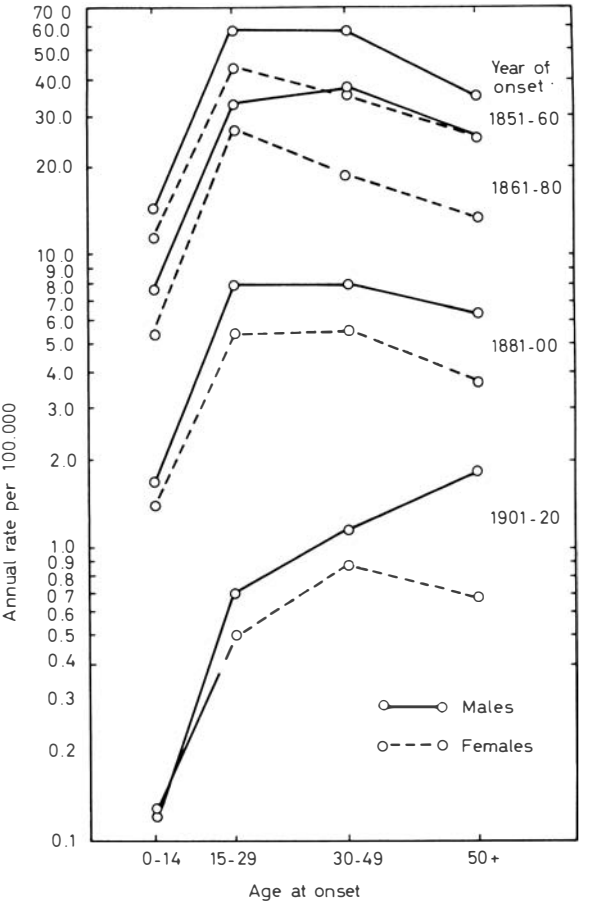

Figure 20. Incidence rates of leprosy in Norway, high frequency areas, 1851–1920. Age- and sex-specific rates by year of onset. (The National Leprosy Registry of Norway.)

In the *low frequency areas* during the same period, type index was 45·5 (Table 24); 49·3 in males and 40·0 in females. Highest type index in these areas, 47·5, was found in the county with the highest total incidence, Hedmark. Type index in the other counties of the low frequency areas was 44·7 (*vide* also Table 38).

According to sex and year of onset

Type index of 543 males and 537 females with known type of leprosy and with year of onset before 1851, was 55·3 and 47·0 respectively (Table 24). Type index of 3,861 males and 2,766 females with known type of leprosy and with year of onset after 1850, was 65·1 and 63·6 respectively (Table 24). For the same 6,627 patients with type 1, 2 and 3 respectively, number of males per 100 females was 138·8, 160·0 and 130·4.

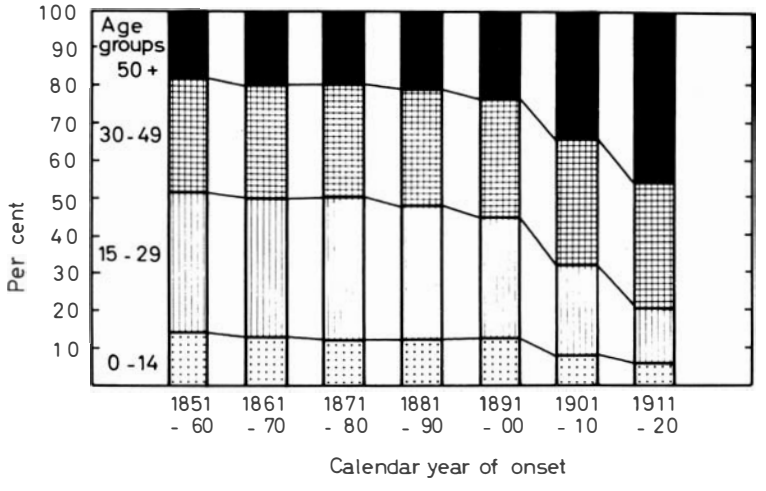

Figure 21. Relative frequencies in Norway, high frequency areas, 1851–1920, of leprosy cases in different age groups by year of onset. Relative frequencies based on age- and sex-specific incidence rates and a standard population. (The National Leprosy Registry of Norway.)

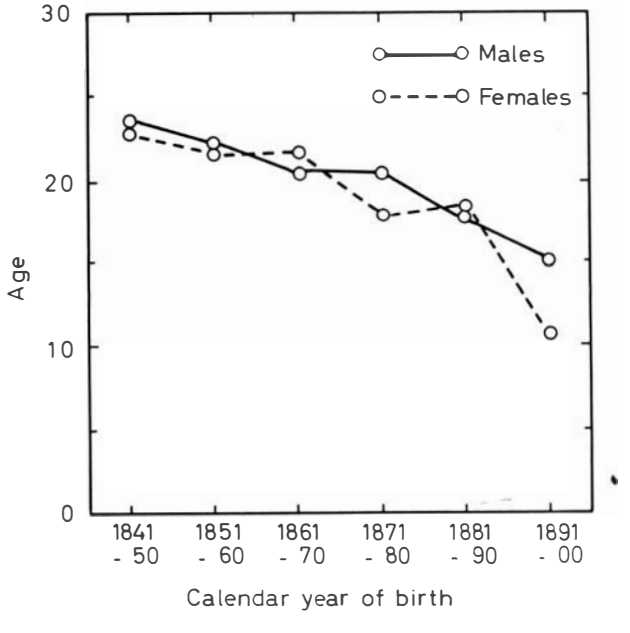

Figure 22. Mean age at onset of leprosy in Norway, high frequency areas, 1851–1920, by sex and year of birth. (The National Leprosy Registry of Norway.)

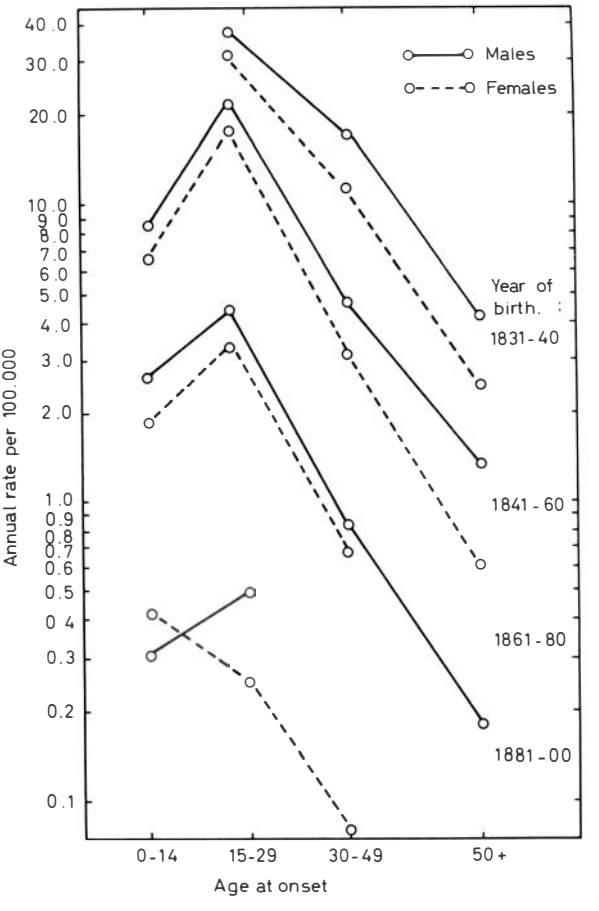

Figure 23. Incidence rates of leprosy in Norway, high frequency areas, 1851–1920. Age- and sex-specific rates by year of birth. (The National Leprosy Registry of Norway.)

During the observation period from 1851 to 1890 type index in both sexes ranged between 62·0 and 66·5 (Table 25, Fig. 25); however, males at a somewhat higher level than females. After 1890 type index of males increased, while the index of females decreased after a peak in the decade 1891–1900. Similar trends occurred in all parts of the country.

According to sex and year of birth

Studied in consecutive birth cohorts, sex-specific type index of patients born between 1841 and 1900 ranged from 64·8 to 70·7, except the decade 1871–80 (Table 26, Fig. 26). Type index of male patients born in this decade was 76·3.

Table 22. New cases of leprosy in Norway, high frequency areas, 1851–1920 by year of birth, with sex ratio based on annual incidence rates per 100,000, according to age and sex. (The National Leprosy Registry of Norway)

Year of birth	0–14 years (No.) (Incidence)	Ratio	15–29 years (No.) (Incidence)	Ratio	30–49 years (No.) (Incidence)	Ratio	50 + years (No.) (Incidence)	Ratio
Male								
1831–1840	–	–	474	117·9	265	152·0	39	171·8
			37·4		17·2		4·3	
1841–1860	317	131·5	597	123·0	175	149·2	31	223·0
	8·7		21·9		4·7		1·4	
1861–1880	120	140·9	134	132·2	32	120·3	5	–
	2·6		4·4		0·8		0·18	
1881–1900	17	73·8	18	166·7	0	–	0	–
	0·3		0·5					
Female								
1831–1840	–		414		181		26	
			31·7		11·3		2·5	
1841–1860	233		512		125		16	
	6·6		17·8		3·2		0·6	
1861–1880	82		115		28		0	
	1·9		3·4		0·7		–	
1881–1900	22		10		4		0	
	0·4		0·3		0·1		–	

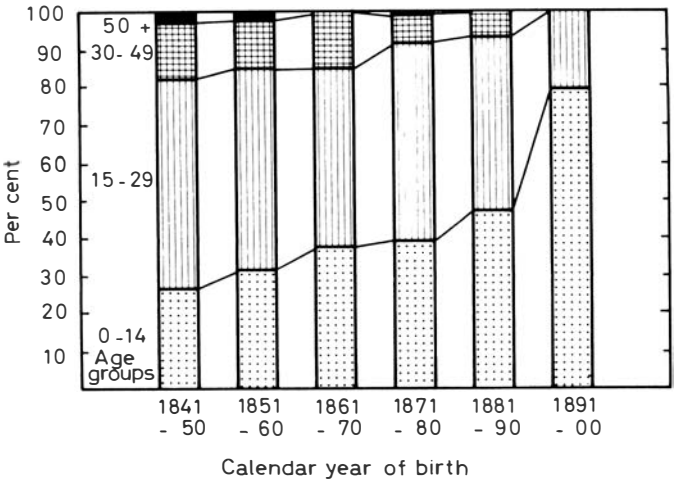

Figure 24. Relative frequencies in Norway, high frequency areas, 1851–1920, of leprosy cases in different age groups, by year of birth. Relative frequencies based on age- and sex-specific incidence rates and a standard population. (The National Leprosy Registry of Norway.)

Table 23. New cases of leprosy in Norway, high frequency areas 1851–1920 by year of birth, actual registered number (n_1) and number calculated on the basis of a standard population and age- and sex-specific incidence rates (n_2), with mean age at onset. (The National Leprosy Registry of Norway)

	Total						
Year of birth	Total (n_1) (n_2) (%)	0–14 yrs (n_1) (n_2) (%)	15–29 yrs (n_1) (n_2) (%)	30–49 yrs (n_1) (n_2) (%)	50 + yrs (n_1) (n_2) (%)	Male (mean age at onset)	Female (mean age at onset)
1841–1850	1,210	302	681	198	29		
	1,313·3	346·7	732·4	202·5	31·7	23·1	22·9
	100·0	26·4	55·8	15·4	2·4		
1851–1860	796	248	428	102	18		
	796·0	248·0	428·0	102·0	18·0	22·1	21·7
	100·0	31·2	53·7	12·8	2·3		
1861–1870	350	134	164	49	3		
	318·8	118·4	151·2	46·9	2·3	20·5	21·6
	100·0	37·2	47·4	14·7	0·7		
1871–1880	166	68	85	11	2		
	144·5	56·3	76·6	10·0	1·6	20·5	18·0
	100·0	39·0	53·0	6·9	1·1		
1881–1890	60	30	26	4	0		
	47·5	22·6	21·7	3·2		17·6	18·5
	100·0	47·6	45·7	6·8			
1891–1900	11	9	2	0	0		
	7·7	6·1	1·6			15·1	10·7
	100·0	79·7	20·3				

Table 24. Leprosy cases in Norway with type index, by sex, residential district and year of onset. (The National Leprosy Registry of Norway)

	Total		Sex				Residential district			
			Male		Female		High frequency areas		Low frequency areas	
Year of onset	No.	Type index	No.	Type index	No.	Type index	No.	Type index	No.	Type index
–1850	1,080	51·1	543	55·3	537	47·0	1,057	51·7	23	22·2
1851–1920	6,613	64·4	3,850	65·1	2,763	63·6	6,473	64·8	140	45·5
1921–1970	14		11		3		10		4	
Unknown	320	53·5	157	63·6	163	44·3	308	53·3	12	60·0
Subtotal	8,027	62·7	4,561	63·9	3,466	60·1	7,848	62·6	179	44·1
Type unknown	204		107		97		198		6	
Total	8,231		4,668		3,563		8,046		185	

Table 25. New cases of leprosy in Norway 1851–1920 with type index, by age, sex and year of onset. (The National Leprosy Registry of Norway)

Year of onset	Total		0–14 years		15–29 years		30–49 years		50 + years	
	No.	Type index	No.	Type index	No.	Type index	No.	Type index	No.	Type index
Male										
1851–1860	1,324	63·4	174	62·0	511	67·1	447	64·2	192	53·2
1861–1880	1,907	65·4	225	69·7	648	68·0	696	67·4	338	53·2
1881–1900	495	66·5	58	66·0	170	71·2	149	70·2	118	55·1
1901–1920	92	72·2	6	83·3	23	68·2	24	87·5	39	63·2
Total	3,818	64·5	463	66·7	1,352	68·1	1,316	67·1	687	54·2
Female										
1851–1860	997	63·9	135	64·5	412	67·7	281	63·0	169	55·7
1861–1880	1,314	62·7	152	69·7	571	68·0	377	67·4	214	53·2
1881–1900	377	67·9	46	78·6	129	71·2	122	70·2	80	55·1
1901–1920	67	51·6	6	66·6	18	68·8	24	47·8	19	36·8
Total	2,755	65·1	339	68·8	1,130	68·2	804	61·2	482	52·9
Total										
1851–1860	2,321	63·6	309	63·1	923	67·3	728	63·8	361	54·4
1861–1880	3,221	64·3	377	69·6	1,219	68·0	1,073	64·8	552	50·8
1881–1900	872	67·1	104	71·7	299	70·8	271	67·0	198	59·4
1901–1920	159	63·6	12	75·0	41	68·4	48	68·1	58	54·4
Total	6,573	63·6	802	67·6	2,482	68·1	2,120	64·8	1,169	53·7

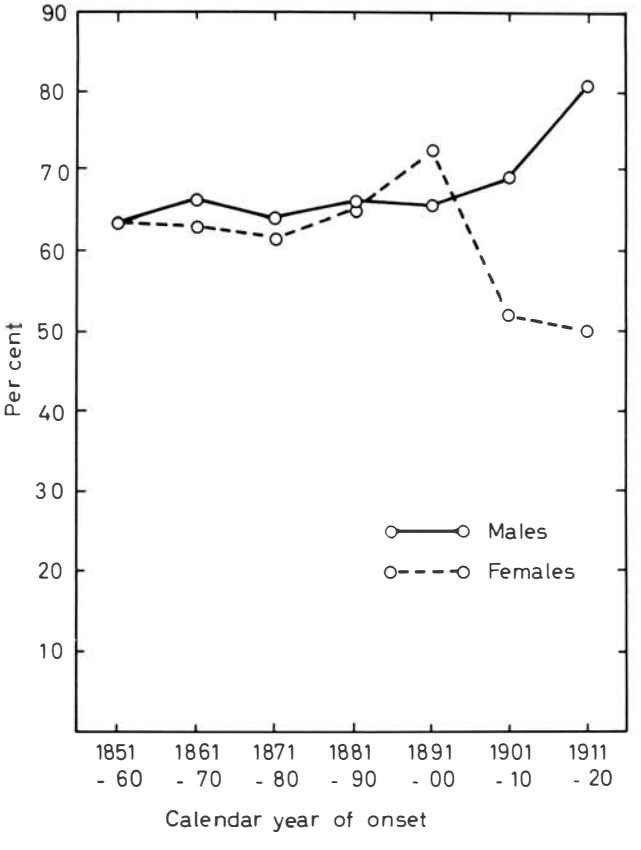

Figure 25. Type index of leprosy in Norway, 1851–1920, by sex and year of onset. (The National Leprosy Registry of Norway.)

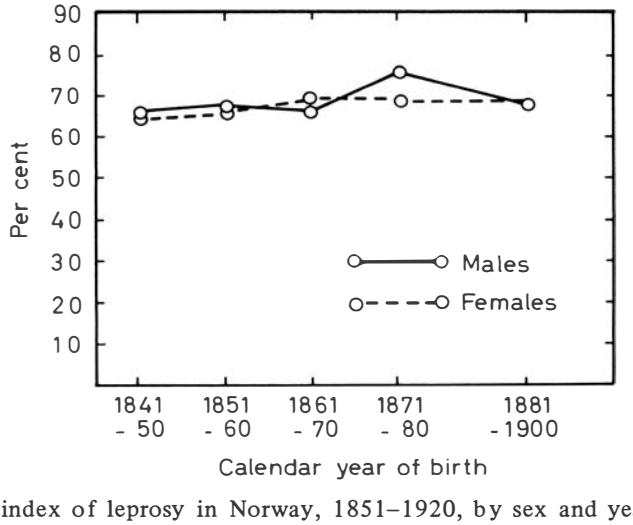

Figure 26. Type index of leprosy in Norway, 1851–1920, by sex and year of birth. (The National Leprosy Registry of Norway.)

Table 26. New cases of leprosy in Norway 1851–1920 with type index, by age, sex and year of birth. (The National Leprosy Registry of Norway)

Year of birth	Total		0–14 years		15–29 years		30–49 years		50 + years	
	No.	Type index	No.	Type index	No.	Type index	No.	Type index	No.	Type index
Male										
1831–1840			–		475	68·1	273	65·8	39	35·3
1841–1860	1,147	67·1	316	65·8	616	66·3	181	71·7	34	70·6
1861–1880	300	71·2	122	67·9	139	70·9	34	81·8	5	80·0
1881–1900	44	68·3	18	70·6	24	65·2	2	–	0	–
Female										
1831–1840			–		418	67·6	183	63·9	29	64·3
1841–1860	901	66·0	238	67·0	514	67·5	131	62·0	18	44·4
1861–1880	228	71·0	82	75·3	118	71·2	28	57·7	0	–
1881–1900	43	67·6	26	68·2	13	72·7	4	–	0	–

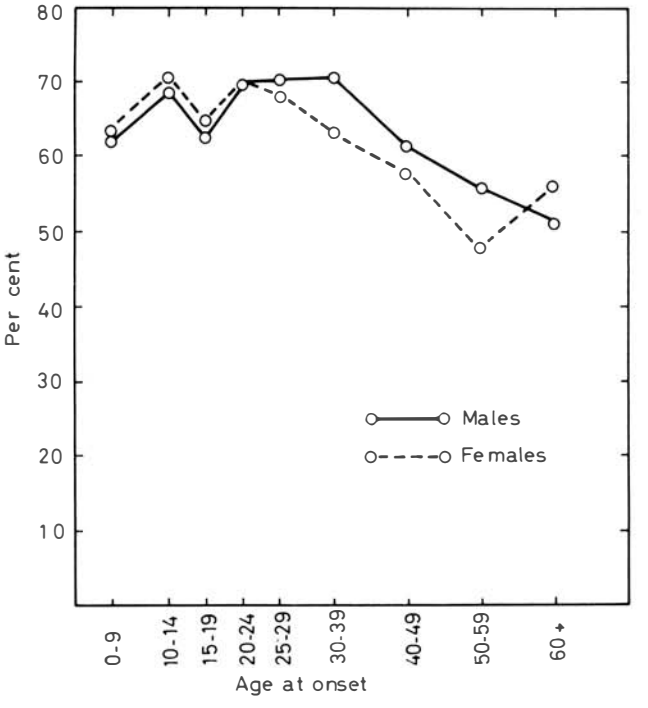

Figure 27. Type index of leprosy in Norway, 1851–1920, by sex and age at onset. (The National Leprosy Registry of Norway.)

According to sex and age

For patients with type 1, 2 and 3 mean age at onset (based on crude number of patients) was 31·9, 34·3 and 35·7 years, respectively. However, type index varied considerably in different age groups (Table 25, Fig. 27). In males, the highest type index was found in the age group 20–39 years; in females a maximum was found in the age group 20–24 years. In both sexes, type index declined towards a lower and also towards a higher age. However, in the higher age groups, type index was considerably lower in females than in males.

According to sex and age by year of onset

When sex-specific type index according to age was calculated in subsequent decades, it appeared that an evident maximum in adolescents was present only between 1851 and 1860 (Table 25, Fig. 28). In this decade, small differences between male and female type index were found.

During the next decades, type index in the age group 15–29 years appeared to remain at a constant level; in both sexes between 67·1 and 70·2 (Table 25, Fig. 29). However, particularly in the age groups over 30 years, increasing differences between male and female type index were observed towards the end of

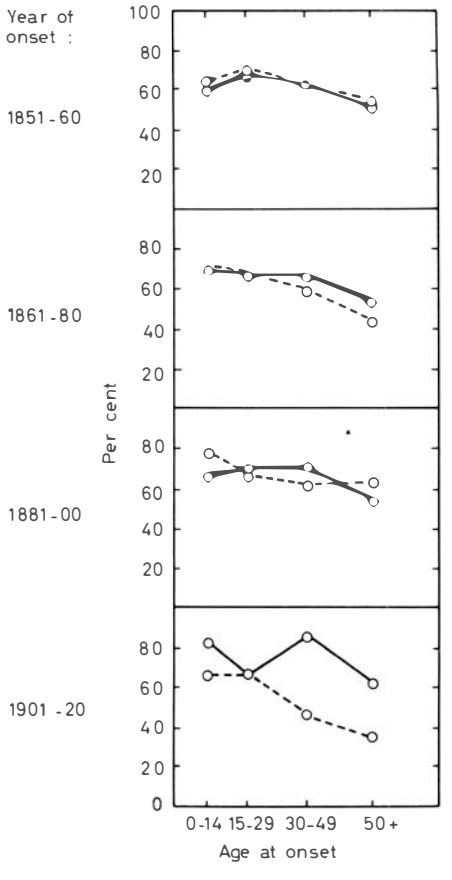

Figure 28. Type index of leprosy in Norway, 1851–1920, by age, sex and year of onset. (The National Leprosy Registry of Norway.)

the observation period, highest type index being observed in males (Fig. 28). Accordingly, type index in all age groups in males, except 15–29 years, increased during the observation period (Fig. 29), and particularly towards the end of the observation period. This trend was not found in females. On the contrary, towards the end of the observation period, female type index declined in all age groups except 15–29 years.

3.2.4. MOVEMENTS IN THE DIAGNOSTIC SPECTRUM

When nothing else is indicated, type, in the present study, refers to the chronologically last classification of a case (*vide* 2.5.3.). However, in 483 (5·9%) cases, the last diagnosis was not identical to the first (Table 27).

In 3,855 (91·6%) of 4,209 cases primarily diagnosed as *type 1*, no movements were registered, while in 354 (8·4%) (208 + 146) cases, movements towards type 2 and 3 were registered. However, the relative frequency of

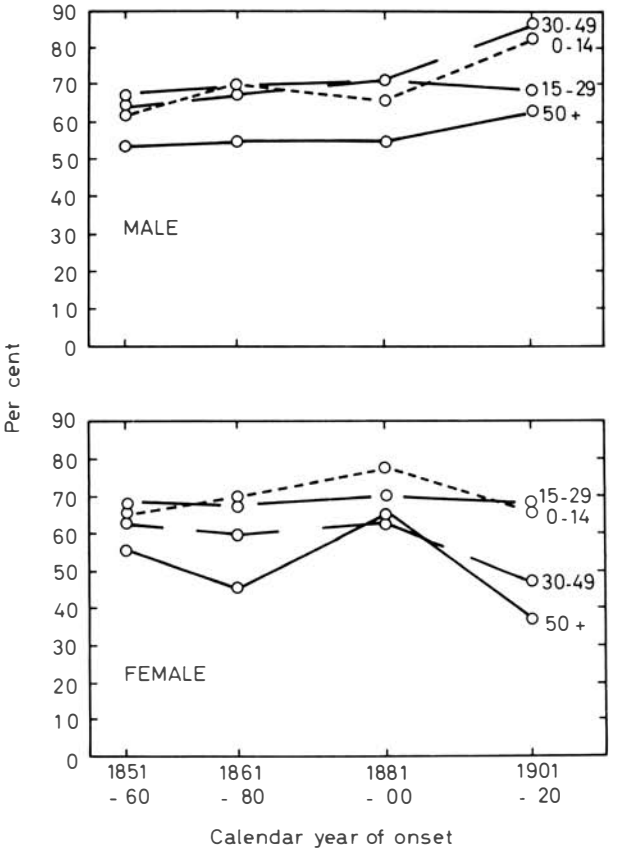

Figure 29. Type index of leprosy in Norway, 1851–1920, by age and year of onset in males and females. (The National Leprosy Registry of Norway.)

movements towards 2 and 3 did not correspond to the relative frequencies of *all* type 2 and type 3 cases registered (expected values); relatively more cases moved towards 2, the intermediate type. Of 354 cases, 208 moved towards type 2 and 146 towards type 3, against expected values of 126·4 and 227·6, respectively.

In 1,357 cases primarily diagnosed as *type 2*, 290 (21·4%) movements were registered, and in accordance with expected values; 180 cases moved towards type 1 and 110 towards type 3, while expected values were 183·3 and 106·7 respectively.

In 2,447 cases primarily diagnosed as *type 3*, 219 (8·9%) movements were registered, and with the same trend as found for the type 1 cases; 148 cases moved towards type 1 and 71 towards type 2, against expected values of 165·6 and 53·4 respectively.

Table 27. Leprosy cases according to first and last diagnosis with respect to the type of disease. (The National Leprosy Registry of Norway)

	First diagnosis									
	Type 1		Type 2		Type 3		Unknown		Total	
Last diagnosis	(No.) (%)	(%)	(No.) (%)	(%)	(No.) (%)	(%)	(No.) (%)	(%)	(No.) (%)	(%)
Type 1	3,855 92·1	91·6	180 4·3	13·3	148 3·5	6·0	4 0·1	1·8	4,187 100·0	50·8
Type 2	208 15·4	4·9	1,067 79·0	78·6	71 5·3	2·9	4 0·3	1·8	1,350 100·0	16·4
Type 3	146 5·9	3·5	110 4·4	8·1	2,228 89·5	91·1	6 0·2	2·8	2,490 100·0	30·3
Unknown	0	–	0	–	0	–	204 100·0	93·6	204 100·0	2·5
Total	4,209 51·2	100·0	1,357 16·5	100·0	2,447 29·7	100·0	218 2·6	100·0	8,231 100·0	100·0

3.2.5. COMMENTS

The patient group with year of onset before 1851, had a lower proportion of males to females, a lower mean age at onset, and a lower type index than the other patients. Compared with time trends observed after 1851, the low values might reflect a continuation of these trends backwards. However, data collected in the prevalence survey, which represented the initial phase in the registration work, are obviously not completely comparable with data collected by continuous registration. The findings, for a greater part, are most likely due to higher mortality rates in males, elderly patients and patients with type 1 of leprosy.

The conspicuous dip in the curve of sex ratio by time (Fig. 15) registered in the decade 1891–1900, was most likely due to a lower incidence rate in males than anticipated and not the opposite, a higher rate in females. This seems to emerge from the curves of sex-specific incidence rates (Fig. 14). The dip was so marked that it was hardly attributable to temporary variations in exposure or susceptibility in males.

However, the finding might be related to the *emigration* to the USA provided that there was an excess of males among the emigrants, that a maximum in emigration rates occurred in the previous decade (1881–90), and that the emigrants represented a high risk group with a high incidence rate, i.e. high 'potential incidence rate', if not removed from their local society.

Calculated on the basis of the official statistics (NOS, 1921) as number of males per 100 females, male excess among emigrants in the age group 5–30 years, the group probably most threatened by exposure to infection, increased from 118·7 in the decade 1856–65 to 184·7 in the decade 1895–1905. In the counties with the highest incidence rates, the emigration rates reached a maximum of 845 emigrants per 100,000 per year in the decade 1881–90.

On the basis of two assumptions, estimation of the number of 'potential patients', removed by emigration, was possible. First, that sex ratio, in the case of no emigration, should be on the level found in the previous and subsequent decades; viz. 150. Second, that the sex ratio, based on sex-specific 'potential incidence rates' *among emigrants*, should be on the same level as the sex ratio in the age group 15–49 years during the period 1861–80; viz. 162. Based on these assumptions, 'potential incidence rates' of males and females among emigrants were found to be 26·9 and 16·6 respectively. Most of the emigrants during the period 1856–85 had their homes in the southern region; number of emigrants from the southern and middle regions were respectively 2·56 and 1·43 times higher than number of emigrants from the northern region. In the southern region, emigration rates were highest in the county of Sogn & Fjordane. In this county, sex-specific incidence rates of the age groups 15–49 years in 1881–90, varied between 17 and 22. Accordingly, 'potential incidence rates' among emigrants was of the same level as comparable incidence rates of high risk groups.

Obviously, emigration prior to the decade 1881–90, though of minor extent, must have influenced incidence rates. However, possible adjustments made on this basis were considered questionable.

However, emigration most likely influenced incidence rates more directly too. There are indications (*vide* 2.3.3.) that some patients emigrated without being registered; accordingly some of the 'potential patients' appeared to be manifest cases. Apparently, most of these patients must have been affected by a benign type of leprosy (type 3). According to the official statistics, females emigrated mainly as wives together with their husbands and families, while solitary emigrants were particularly found among males. Presumably, emigrants with leprosy particularly would be female patients, looked after by their male heads of the family. This is consistent with the peak of the female type-index-curve in the decade 1891–1900, close to the culmination of the emigration wave in the southern region (Fig. 25).

3.3. Prediction of incidence rates based on information on sex, age and type[1]

Time trends in the distribution of leprosy according to sex, age and type of the disease, demonstrated to exist in the present material, formed the basis for analyses of possible associations between these characteristics of patients and incidence rates. The intention was in part to attempt to clarify general aspects of the epidemiology of the disease, in part to outline principles relevant to the construction of indices, useful in leprosy control. Such indices are still needed today because in most areas where leprosy is prevalent, accurate incidence rates may be impossible to obtain due to lack of vital statistics and incomplete registration of cases.

3.3.1. LEVEL OF INCIDENCE RATES

The associations between each of the independent variables, mean age at onset, sex ratio and type index (*vide* 2.5.3. and 2.5.5.) and *incidence rate* were studied by simple regression analyses. The correlation coefficients were $-0{\cdot}73$, $-0{\cdot}38$ and $0{\cdot}04$ respectively (Table 28).

By the inclusion in a stepwise regression analysis of type index, in addition to mean age at onset, a multiple correlation coefficient of 0·74 was obtained (Table 28). By the inclusion of sex ratio, the multiple correlation coefficient did not increase. This regression function reduced significantly the total variance of the dependent variable ($p < 0{\cdot}001$).

The regression line was:

$$\hat{Y} = 8{\cdot}85 - 0{\cdot}23X_1 + 0{\cdot}05X_2 + 1{\cdot}92X_3$$

(X_1: mean age at onset, X_2: sex ratio, X_3: type index)

[1] Preliminary results reported by Bjerkedal and Irgens (1973) and Irgens *et al.* (1978).

Table 28. Simple and multiple regression in 7 counties of incidence rate in a period on mean age at onset, sex ratio and type index of patients taken ill during the same period. (The National Leprosy Registry of Norway)

Independent variables	Regression line	Level of significance	Correlation coefficient
X_1 (Mean age at onset)	$Y = 9{\cdot}86 - 0{\cdot}22X_1$	$p < 0{\cdot}01$	$-0{\cdot}73$
X_2 (Sex ratio)	$\hat{Y} = 2{\cdot}68 - 0{\cdot}5X_2$	$p = 0{\cdot}02$	$-0{\cdot}38$
X_3 (Type index)		$p > 0{\cdot}05$	0·04
X_1, X_3	$\hat{Y} = 8{\cdot}53 - 0{\cdot}22X_1 + 2{\cdot}16X_3$	$p < 0{\cdot}01$	0·74
X_1, X_2, X_3	$\hat{Y} = 8{\cdot}85 - 0{\cdot}23X_1 + 0{\cdot}05X_2 + 1{\cdot}92X_3$	$p < 0{\cdot}01$	0·74

Table 29. Simple and multiple regression in 7 counties of difference between incidence rates in two subsequent periods, on mean age at onset, sex ratio and type index of patients taken ill during the first of the two periods. (The National Leprosy Registry of Norway)

Independent variables	Regression line	Level of significance	Correlation coefficient
X_1 (Mean age at onset)	$\hat{Y} = 3{\cdot}84 - 0{\cdot}09X_1$	$p < 0{\cdot}01$	$-0{\cdot}68$
X_2 (Sex ratio)		$p > 0{\cdot}05$	$-0{\cdot}24$
X_3 (Type index)		$p > 0{\cdot}05$	0·01
X_1, X_3	$\hat{Y} = 3{\cdot}07 - 0{\cdot}09X_1 + 1{\cdot}4X_3$	$p < 0{\cdot}01$	0·70
X_1, X_2, X_3	$\hat{Y} = 3{\cdot}33 - 0{\cdot}1X_1 + 0{\cdot}01X_2 + 0{\cdot}01X_3$	$p < 0{\cdot}01$	0·70

Table 30. Evaluation of the prediction of level and time trend of incidence rates calculated on the basis of observations of mean age at onset, sex ratio and type index. (The National Leprosy Registry of Norway)

	Observations		
	Total	Of these correctly classified	
Predictions	No.	No.	%
Prediction of level	36	27	75·0†
Prediction of time trend	30	23	76·6†

†Significantly different from a random classification (sign test: $p < 0{\cdot}005$)

3.3.2 TIME TREND IN INCIDENCE RATES

The associations between each of the independent variables and *time trend in incidence rate* (*vide* 2.5.5.) were studied by simple regression analysis, and the correlation coefficients of mean age at onset, sex ratio and type index were $-0{\cdot}68$, $-0{\cdot}24$ and 0·01 respectively (Table 29).

By the inclusion in a stepwise regression analysis of type index in addition to mean age at onset, a multiple correlation coefficient of 0·70 was obtained (Table 29). By the inclusion of sex ratio, the multiple correlation coefficient did not increase. Also this regression function reduced significantly the total variance of the dependent variable ($p < 0{\cdot}001$).

The regression line was:

$$\hat{Y} = 3{\cdot}33 - 0{\cdot}1X_1 + 0{\cdot}01X_2 + 0{\cdot}01X_3$$

3.3.3. EVALUATION

The results of the evaluation of prediction of incidence *level* varied according to the cut-off point set to divide the observed incidence rates into high or low. At a cut-off point of $Y = 4{\cdot}5$, which represented the median of the observations, 75% of the observations were correctly classified on the basis of their predictions (Table 30).

Also in the prediction of *time trends* the results of the evaluation varied according to the cut-off point. At a cut-off point of $Y = 4{\cdot}0$, also the median of the observations, 76·7% of the observations were correctly classified on the basis of their predictions.

According to a sign test, the results of the classifications differed significantly from a random distribution of the observations into two groups ($p < 0{\cdot}005$).

3.3.4. COMMENTS

The general epidemiological situation in Norway during the observation period was that of a rapid decline in incidence rates. Accordingly, this part of the study was focusing on how the characteristics of patients registered changed during such an observation period. The attempts to make valid predictions of level and trend in incidence rates were also restricted to this situation. However, not all observations were derived from a situation of rapid decline. Accordingly, to avoid a mixture of observations, in part from a situation of steady state, in part from a situation of rapid decline, only observations pertaining to the first decade in a county after which decrease in the incidence rate was observed and all subsequent decades, were used (*vide* 2.5.5.).

Since the data were registered during a long observation period, sex- and age-adjusted measures were used. Obviously, this is not possible when incidence rates are unknown. However, in a practical situation of leprosy control today, the need for adjustment will be smaller since data usually will relate to a short period of observation.

The distributions of the dependent variables were skewed, and since log transformation of these variables gave approximate normal curves, log transformed dependent variables were used in the analyses (*vide* 2.5.5.). The observations of the independent variables were evenly distributed along the x-axis, and results of analyses based on log transformation of one or more of the variables did not differ from results obtained using untransformed variables.

Evaluation of the predictions had to be based on data used in the calculation of the predictions. Preferably, evaluation should be based on a set of

data pertaining to a situation to which one wants to generalize. However, application without adjustments in other areas, of the equations obtained in the present analyses, does not seem feasible. Areas in which leprosy is prevalent today, may differ considerably with respect to epidemiological conditions, such as sociological features, which may influence the equations.

Negative associations appeared to exist between mean age at onset and sex ratio on one hand and the dependent variables on the other. This was consistent with other findings in the present study and with findings by other authors (*vide* 4.2.3.). However, the low values of the correlation coefficient found in the analyses of the dependent variables on type index (regression coefficients not significant different from zero), were attributable to the selection of unit of observation; viz. counties in the high frequency areas. The range in type index was low (*vide* 3.2.3.), and the trend of a positive association between type index and incidence rates, found in other parts of this study (*vide* 3.6.1., 3.6.3.) did not appear at county level.

It should be stated that mean age at onset, sex ratio and type index represent rather rough epidemiological measures relinquishing valuable information, e.g., *distribution* of patients according to age at onset is much more informative than *mean* age at onset. Accordingly, even more useful predictions may be obtained on the basis of distributions of patients according to age, sex and type rather than the simple measures.

The results presented were based on knowledge of *all* patients taken ill. If, in field work, predictions are to be based only on a *fraction* of an unknown total patient group, as will be the case, this fraction should not differ significantly from the total patient group with respect to the independent variables. However, ascertainment of cases, or degree of completeness of reporting, usually is related to all these three independent variables, and, accordingly, adjustments will be needed.

3.4. Isolation of patients and trends in subsequent incidence rates[1]

Isolation of patients in special leprosy hospitals was in force in Norway from the middle of the last century; initially not to limit infection, but to attain sexual isolation and thereby limit further propagation of a disease presumed to be hereditary (Irgens, 1973). After the discovery of the leprosy bacillus in 1873, isolation was enforced even more consistently, however, now because leprosy was considered an infectious disease. Thus, degree of isolation in the 7 central leprosy counties (*vide* 2.5.5.) increased from 22·2% in the decade 1856–65, to 55·1% in the decade 1906–15 (Fig. 30). As time went on, the Norwegian control programme, with its acts on segregation, became a prototype in an international perspective.

[1] Preliminary results reported by Irgens (1973a).

Table 31. Simple linear regression in 7 counties 1856–1920 of incidence rate in a period on previous prevalence rate. (The National Leprosy Registry of Norway)

Independent variable	Regression line	Level of significance	Correlation coefficient
Prevalence rates, total	$\hat{Y} = -0{\cdot}15 + 0{\cdot}19X$	$< 0{\cdot}01$	0·81
Prevalence rates, district	$\hat{Y} = -0{\cdot}54 + 0{\cdot}33X$	$< 0{\cdot}01$	0·90

However, the effectiveness of this segregation policy has been questioned ever since it was introduced, not only in Norway, but in most parts of the world. Today, when the infectiousness of most patients seems to be significantly reduced by regular chemotherapy (Meade, 1978; Skinsnes, 1975 among others) segregation represents no adequate control policy, mostly for humanitarian reasons. However, it may also be argued that isolation of an infectious person is without any effect, because isolation is first attained after the person has infected his environment. In an attempt to clarify these questions, which are closely related to important aspects of the epidemiology of leprosy, the possible effects of isolation of patients were studied.

3.4.1. PREVALENCE RATES AND SUBSEQUENT INCIDENCE RATES

If isolation, in an area, of infectious patients is to have an impact on subsequent incidence rates, incidence rates are to be considered the effect of previous prevalence rates. Accordingly, an association should exist between prevalence rates and subsequent incidence rates. In a simple regression analysis between these variables the regression line was:

$$\hat{Y} = -0{\cdot}15 + 0{\cdot}19X \ (p < 0{\cdot}01)$$

with a correlation coefficient of 0·81 (Table 31).

Obviously, such an association will exist for a series of diseases, and, under given epidemiological conditions, even irrespective of the aetiology of the disease. However, an even higher coefficient was obtained using, as the independent variable, prevalence rates based on patient years spent in homes only, rather than total patient years. This finding was consistent with transmission of the disease from person to person and, accordingly, formed a rationale for isolation as a control measure. The regression line was:

$$\hat{Y} = -0{\cdot}54 + 0{\cdot}33X \ (p < 0{\cdot}01)$$

with a correlation coefficient of 0·90 (Table 31).

3.4.2. ISOLATION AND SUBSEQUENT RELATIVE FALL IN INCIDENCE RATES

In a simple regression analysis, based on all 7 counties, between degree of isolation registered in the 5 decades between 1856 and 1905, and subsequent relative fall in incidence rates, the regression line was

Table 32. Simple linear regression in 7 counties 1856–1920 of relative fall in incidence rate in a period on previous degree of isolation. (The National Leprosy Registry of Norway)

Independent variable. Groups of observations by time and prevalence	Regression line	Level of significance	Correlation coefficient
Time: 1856–1910 Prevalence: all levels	$\hat{Y} = 7{\cdot}30 + 1{\cdot}28X$	$< 0{\cdot}01$	0·80
Time: 1856–1875 Prevalence: all levels	$\hat{Y} = 1{\cdot}02 + 1{\cdot}45X$	$< 0{\cdot}01$	0·77
Time: 1881–1910 Prevalence: all levels		$> 0{\cdot}05$	0·16
Time: 1856–1875 Prevalence: $> 15{\cdot}0$	$\hat{Y} = -3{\cdot}93 + 1{\cdot}63X$	$< 0{\cdot}01$	0·81
Time: 1881–1910 Prevalence: $\leqq 15{\cdot}0$		$> 0{\cdot}05$	0·32
Time: 1856–1875 Prevalence: $> 29{\cdot}0$	$\hat{Y} = 3{\cdot}41 + 1{\cdot}32X$	0·04	0·79
Time: 1856–1875 Prevalence: $\leqq 29{\cdot}0$	$\hat{Y} = -4{\cdot}76 + 1{\cdot}76X$	0·05	0·75

$$\hat{Y} = 7{\cdot}30 + 1{\cdot}28X \; (p < 0{\cdot}01)$$

with a correlation coefficient of 0·80 (Table 32).

Apparently, isolation led to an evident fall in incidence rates. However, in the evaluation of this association it should be taken into account that both the degree of isolation and the relative fall in incidence rates increased with time (Fig. 30). Accordingly, the association found to exist between these variables might be non-causal or secondary.

In an attempt to eliminate this effect of time on the association, the material was split into two groups; the first covering all counties during 2 decades of isolation, 1856–75, and the second covering all counties during 3 decades of isolation, 1881–1910.

In the first group of observations, covering the 2 decades 1856–75, a strong positive association was found to persist between degree of isolation and subsequent relative fall in incidence rates; the regression line was:

$$\hat{Y} = 1{\cdot}02 + 1{\cdot}45X \; (p < 0{\cdot}01)$$

with a correlation coefficient of 0·77 (Table 32).

However, in the last group of observations, covering the 3 decades 1881–1910, no association between the variables was demonstrated; the correlation coefficient was 0·16 ($p = 0{\cdot}49$).

The decrease in the correlation coefficient with time might be associated with a decreasing prevalence experienced through the observation period from 1851 to 1920. To find out whether the association between degree of isolation

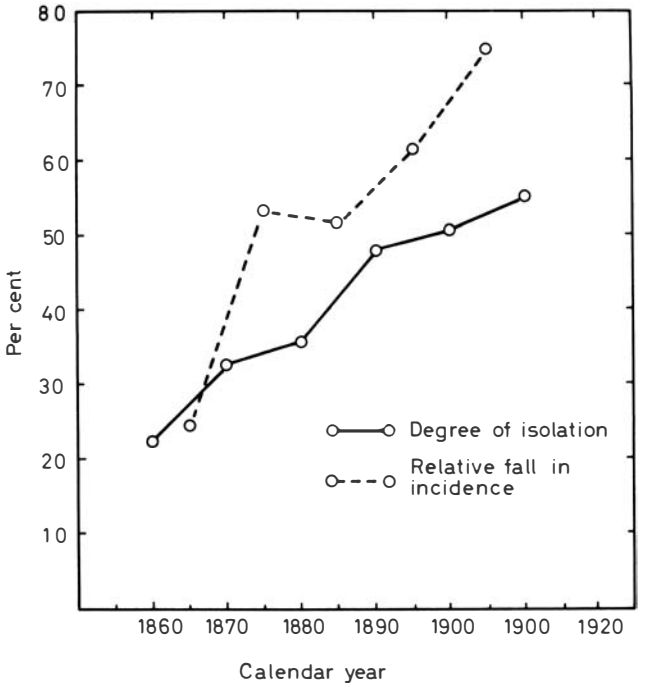

Figure 30. Degree of isolation of leprosy patients and relative fall in incidence of leprosy during the observation period. (The National Leprosy Registry of Norway.)

and relative fall in incidence rates was dependent on level of prevalence, and, at the same time, to eliminate the effect of time, the two groups of the material were split according to whether prevalence in period 1 was above or below 15 per 10,000.

It appeared that in the first group of observations with low prevalence rates and in the last group with high prevalence rates, numbers of observations were too small for calculation of statistics. Still, in the remaining first group with *high prevalence rates*, the regression line was:

$$\hat{Y} = -3{\cdot}93 + 1{\cdot}63X \ (p < 0{\cdot}01)$$

with a correlation coefficient of 0·81 (Table 32).

Furthermore, the regression coefficient indicated a stronger association between the variables in the high prevalence initial group than in the total initial group.

On the other hand, in the remaining last group, with *low prevalence rates*, the correlation coefficient was 0·32 ($p = 0{\cdot}22$).

However, the association between the variables did not appear to increase when the prevalence rates increased above 15 per 10,000. The first group of observations was divided according to whether prevalence rates were above or

below the median of the group, 29 per 10,000. For the high prevalence observations the line was:

$$\hat{Y} = 3{\cdot}41 + 1{\cdot}32X \text{ (p} = 0{\cdot}04)$$

with a correlation coefficient of 0·79 (Table 32).

For the low prevalence observations the regression line was:

$$\hat{Y} = -4{\cdot}76 + 1{\cdot}76X \text{ (p} = 0{\cdot}05)$$

with a correlation coefficient of 0·75 (Table 32).

3.4.3. COMMENTS

After observations were divided into two groups according to time, a strong association persisted in the first group between degree of isolation and relative fall in incidence. It should be noted that this group of observations covered only 2 decades of isolation compared with 3 decades in the last group. Yet, no association was found in the last group in which a factor associated with time, due to a longer span, might have been more efficient.

Furthermore, it appeared that the association between degree of isolation and relative fall in incidence was stronger when the level of prevalence was relatively high.

The organization of observations in consecutive double periods, each of 10 years' duration (*vide* 2.5.5.), represented a choice, justified in part by considerations with respect to length of incubation periods. Obviously, however, other combinations of periods for registration of possible causes and effects were possible. In fact, a series of such combinations were tried, changing systematically lengths and relative positions of the periods. It appeared that the combination of periods applied in the present study, justified by considering incubation periods, provided correlation and regression coefficients which indicated the strongest association between the variables. Besides, a far weaker association between degree of isolation and relative fall in incidence was found when fall in incidence was registered in a period *prior to* the period of registering degree of isolation. This finding also, seemed to indicate that the association found to exist between the variables was not secondary, viz. dependent on another factor associated with time.

Degree of isolation, calculated on the basis of type 1 (most infectious) patients only, might have been even stronger associated with relative fall in incidence rates. However, since there were indications that also type 3 patients were infectious (*vide* 4.2.4.) such an analysis was not attempted.

Nevertheless, it might be argued that the lack of association, observed in the low prevalence observations, towards the end of the observation period, was the result of a bias based on trends in the isolation policy; when degree of isolation was low, mostly type 1 patients were hospitalized, while when degree of isolation was high, a higher percentage of the isolated patients was not type

Table 33. Families consisting of leprosy patients with type index, by number of patients per family. (The National Leprosy Registry of Norway)

Patients per family	Families (No.)	Patients (No.)	Type index
1	5,710	5,710	60·4
2	618	1,236	66·3
3	203	609	71·0
4	79	316	67·8
5 +	28	156	75·8
Total	6,638	8,027	62·7

1 patients. Accordingly, degree of isolation towards the end of the period, in terms of percentage of isolated *infectious* patients, would have been lower than indicated in the results presented. Thus, relative fall in incidence rates would have been expected to be lower towards the end of the observation period. However, the opposite trend was found (Fig. 30).

3.5. Leprosy in families

In Norway, as in most countries where leprosy is prevalent today, the disease was known to affect certain families more than others (Danielssen and Boeck, 1847; Sand, 1910; Lie, 1911). This fact has led several authors to the conclusion that genetic factors play a part in the aetiology of leprosy (Spickett, 1962a and 1962b; Chakravartti and Vogel, 1973; Mohammed Ali, 1965). Obviously, for relatives, often living closely together, separation of genetic factors from environmental factors represents a serious methodological problem. However, due to sociological patterns, groups of people presumably with a common genetic background may differ with respect to environmental factors. In an attempt to isolate environmental factors from a joint genetic background, and vice versa, the information of the Leprosy Registry on kinship between patients was used to study factors responsible for the development of the disease into different types.

3.5.1. ALL PATIENTS MUTUALLY RELATED

Of 8,027 patients with known type of leprosy, as many as 2,317 (28·9%) were registered as mutually related in some way (Table 33). In addition, unspecified information on non-identified 'leprous relatives' was registered for a considerable number of patients.

Type index increased with increasing number of patients in the family, from 60·4 in 5,710 patients without any affected relatives to 75·8 in 156 patients representing families with 5 or more patients (Table 33).

Table 34. Sibship groups consisting of leprosy patients with type index, by age at onset and number of patients per group. (The National Leprosy Registry of Norway)

Patients per sibship group	Total			Age at onset					
				All patients in the sibship < 30 years			One or more patients in the sibship ≧ 30 years		
	Groups	Patients	Type index	Groups	Patients	Type index	Groups	Patients	Type index
2	399	798	67·6	227	454	64·9	172	344	71·2
3	89	267	70·6	51	153	78·2	38	114	60·2
4 +	28	121	77·6	17	77	80·3	11	44	72·2
Mean		2·30			2·32			2·27	
Total	516	1,186	69·4	295	684	69·9	221	502	68·7

The distribution of cases by type within each of these families differed significantly from the expected distribution calculated on the basis of relative frequencies of the three types in each group, demonstrating that special subgroups of families were more frequent than expected (*vide* 2.5.5.). The patients in these families tended to be more concordant with respect to type of the disease than expected. Mean distance between patients in a family was 0·76, while expected distance was 0·87; i.e. families with concordant cases were more frequent and families with disconcordant cases less frequent than expected. For instance, in the group with 2 patients per family, 213 families with two type 1 cases were observed against 183·8 expected families, and 68 families with two type 3 cases were observed against 47·6 expected families. On the other hand, only 149 families with one type 1 case and one type 3 case were observed against 187·0 expected families.

3.5.2. SIBSHIPS

Of the 2,317 patients mutually related, 1,186 (51·2%) belonged to a sibship of two or more patients (Table 34).

The trend of an increasing type index with an increasing number of patients per family was evident also in sibship groups. Type index increased from 67·6 in 798 patients representing families consisting of 2 affected siblings to 77·6 in 121 patients representing families consisting of 4 or more affected siblings (Table 34).

This trend was particularly expressed in the 295 sibships in which all patients were taken ill before the age of 30 (Table 34). No such trend was found in the other 221 sibships. Apparently, the association demonstrated between type index and number of patients per family was dependent on age at onset. Type index for the totals in both groups was almost the same, 69·9 and 68·7, and so was mean number of patients per sibship: 2·32 and 2·27 respectively (Table 34).

Table 35. Patient groups consisting of parents and their children, with type index. (The National Leprosy Registry of Norway)

	Total					Of these: One or both parents with type 1				
	Parents		Children		Children	Parents		Children		Children
Parent affected	No.	Type index	No.	Type index	per marriage	No.	Type index	No.	Type index	per marriage
Fathers affected	199	66·4	270	65·9	1·36	99	100·0	137	76·3	1·38
Mothers affected	161	67·4	264	77·2	1·64	87	100·0	151	78·6	1·74
Both parents affected	40	52·9	26	73·9	1·30	30	64·3	21	66·7	1·40
Total	400	65·4	560	71·5	1·47	216	95·3	309	76·8	1·54

Also in this category, the distribution of cases by type within each of the families differed significantly from the expected distribution, and the patients were also more concordant with respect to type than expected. However, within families in which age at onset was 30 years or more, the distribution did not differ significantly from the expected distribution.

3.5.3. PARENTS AND CHILDREN

A total of 400 affected parents in 380 marriages had 560 affected children; 1·47 children per marriage (Table 35). Type index in these children was 71·5. In 216 marriages in which one or both parents were affected with type 1, type index of the 309 children was 76·8 and children per marriage was 1·54.

A total of 199 affected fathers had 270 affected children, on average 1·36 children per parent; while 161 affected mothers had 264 affected children, on average 1·64 children per parent (Table 35). Type index in children of fathers (65·9) was lower than type index in children of mothers (77·2) despite the fact that the type index of the fathers (66·4) was not far from the type index of the mothers (67·4).

Considering parents affected with type 1, type index in children of fathers (76·3) was almost equal to type index in children of mothers (78·6). However, the difference mentioned with respect to number of children per parent was even greater for parents affected with type 1; on average a father had 1·38 affected children while a mother had 1·74 children.

A total of 26 children had parents both of whom were affected with leprosy. Type index in these children was 73·9.

Type index in children of affected mothers increased with an increasing

Table 36. Spouses who both were affected by leprosy, with type index, mean age at onset and number of males per 100 females. (The National Leprosy Registry of Norway)

Class of spouses	Spouses	Type index	Mean age at onset	Males per 100 females
First cases	34	46·2	43·9	88·8
Second cases	34	63·3	50·8	112·5
Second cases†	24	60·0	45·2	60·0
Contemporary cases	26	80·8	48·8	100·0
Total	118	62·7	46·9	–

†First case not registered

number of children per mother from 73·2 for 1 child to 81·7 for 3 or more children. Such a trend was not found in children of affected fathers.

The distribution of children by type of disease and by type of their parent's disease differed significantly from the expected distribution both for children of affected fathers ($p = 0{\cdot}004$) and for children of affected mothers ($p = 0{\cdot}02$). It was evident that concordance between parents and children with respect to type of the disease was more frequent than expected; e.g. fathers with type 1 had 97 children with type 1 against 85·0 expected and 30 children with type 3 against 42·5 expected.

Consistent with the finding of a more significant dependence between fathers and children than between mothers and children, significant dependence was found within sibships of patients with sick fathers. Within sibships of patients with a sick mother, however, the distribution of cases by type in each of the families did not differ significantly from what was expected; i.e. the observed frequencies of the different subgroups did not differ significantly from the expected frequencies.

3.5.4. MARRIAGES

Total number of marriages in which only one spouse was affected, is unknown. However, 380 marriages were registered in which one spouse and one or more children were affected. In 20 of these marriages the other spouse also became affected. Accordingly, secondary attack rate among spouses in marriages in which the other spouse and one or more children were affected was 5·3%.

Information was registered on a total of 71 marriages in which both spouses were affected. Of the total of 142 spouses, 24 were not registered as patients; apparently because they died before compulsory notification was effected (Table 36). Type index of the remaining 118 spouses registered was 62·7 (Table 36).

According to onset of disease in the marriages, the spouses were considered as belonging to one of four different classes (Table 36). Onset was regarded contemporary (i.e. difference between years of onset in two spouses less than 3 years) for 26 spouses, whose type index was 80·8. In the marriages without

contemporary onset, type index of the first cases was 46·2, while type index of the second cases was 63·3. Type index of the spouses whose affected spouse was not registered, mostly second cases, was 60·0.

Number of males per 100 females was 88·8 among the first cases and 112·5 among the second cases. Mean age at onset was 43·9 years in the first cases, 50·8 years in the second cases and 48·8 years in the spouses with contemporary onset of the disease.

In the whole category of spouses as well as in the different classes, the distribution of cases by type did not differ from what was expected.

3.5.5. COMMENTS

Most likely, information on an unknown number of mutual relationships between patients registered in the Leprosy Registry is lacking. Furthermore, information on relationships between patients registered and patients who died before registration was initiated, is most incomplete. Still, the information used in the present study, focusing on trends in intrafamilial distributions of the type of disease rather than intrafamilial rates, is considered satisfactory.

The trends demonstrated are probably not influenced by a biased registration. The possibility exists, for instance, that many sibships, consisting of only two patients were overlooked; however, this should have occurred most often in cases never admitted to hospital, i.e. particularly in type 3 cases. In the hospital register as well as in the hospital patient records, detailed information on affected relatives is at hand. Accordingly, such a bias would mask rather than produce a trend that indicated an increase in type index by number of patients per family.

A bias in registration, influencing concordance with respect to type index in one or the other way, seems unlikely.

In the calculation of secondary attack rate among spouses it was not possible to state whether the second case taken ill was infected by the first case. This problem is always encountered in the calculation of secondary attack rates. However, if it is true that duration of exposure plays a part in the aetiology of leprosy, it may be difficult to identify a single source of infection, and the practical importance of the problem might be low.

3.6. Leprosy in a high frequency district

A considerable variation in the geographical distribution of the disease, demonstrated in the whole *country* as well as in the *high frequency areas*, was also found to exist between the health districts in the *county* with the highest average incidence rate, Sogn & Fjordane. However, even in the *health district* with the highest average incidence rate in the country, Naustdal, the frequency of the disease varied considerably from village to village and from farm to farm.

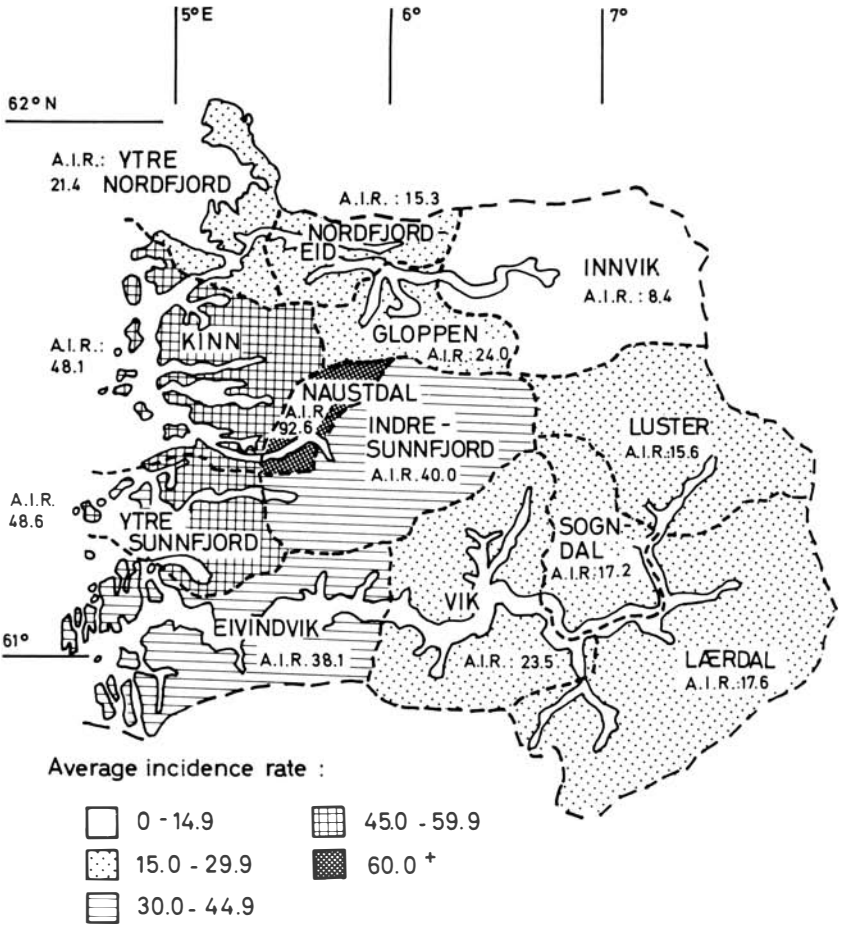

Figure 31. Average incidence rates (A.I.R.) of leprosy in Norway, 1851–1920, in the health districts of Sogn & Fjordane. (The National Leprosy Registry of Norway.)

In an attempt to characterize conditions in localities where the disease was particularly frequent compared with localities without leprosy, the occurrence of the disease in Naustdal was studied in detail.

Viewed by contemporary physicians, living conditions in the western regions of South Norway, and particularly in Naustdal, were bad in the middle of the last century (Bidenkap, 1858; 1860; Hjort, 1871). The intention of this part of the study was to study possible associations between leprosy and environmental factors like overcrowding, malnutrition and poverty. Furthermore, the geographical distribution of cases was envisaged in an attempt to test a hypothesis suggesting sphagnum bog vegetation as a possible reservoir of non cultivable mycobacteria (Kazda *et al.*, 1979, Kazda 1979) which may be associated with disease in man.

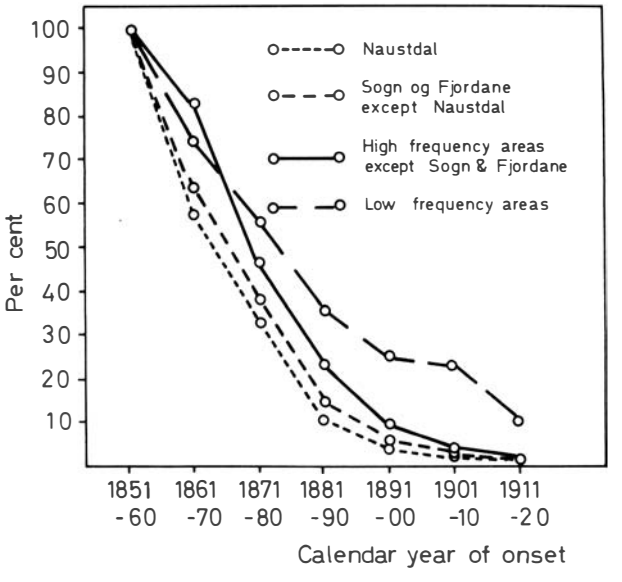

Figure 32. Incidence rates of leprosy in Norway, 1851–1920, by residential district. Crude rates by year of onset, 1851–60 = 100. (The National Leprosy Registry of Norway.)

3.6.1. DISTRICT LEVEL

From an evident maximum of 92·6 in Naustdal, *average incidence rates* in the health districts of Sogn & Fjordane decreased in all directions, the highest rates being confined to the coastal health districts near Naustdal (Fig. 31).

Annual *incidence rates* declined more rapidly in Naustdal through the observation period than in many other districts. Of the 171 patients with year of onset after 1850, the last patient was taken ill in 1903. Relative fall in incidence was slower in the rest of the high frequency areas. The slowest decrease of the disease was found in the low frequency areas (Table 37, Fig. 32).

Average age-specific incidence rates in the different areas demonstrated that the younger age groups of patients were relatively more frequent in areas with high incidence rates (Table 38, Fig. 33). Relative frequency of patients taken ill at an age of 50 years or more was particularly high in the low frequency areas. Thus, *mean age at onset* for patients taken ill during the observation period was particularly low, 31·0, in Naustdal and increased through the areas mentioned above to 39·3 in the low frequency areas (Table 38).

Table 37. New cases of leprosy by residential district in Norway, 1851–1920, according to year of onset with annual incidence rates in consecutive decades and average incidence rates in the observation period, per 100,000. (The National Leprosy Registry of Norway)

Year of onset	Total country		Naustdal		Sogn & Fjordane except Naustdal		High frequency areas except Sogn & Fjord.		Low frequency areas	
	Patients No.	Incidence	Patients No.	Incidence	Patients No.	Incidence	Patients No.	Incidence	Patients No.	Incidence
1851–1860	2,355	15·8	84	318·3	667	84·6	1,567	25·6	37	0·47
1861–1870	2,005	11·8	48	181·9	447	53·1	1,478	21·2	32	0·35
1871–1880	1,241	6·8	27	102·3	265	31·7	924	12·0	25	0·26
1881–1890	615	3·2	9	34·1	100	11·9	489	5·9	17	0·17
1891–1900	276	1·3	2	7·5	41	4·8	220	2·5	13	0·12
1901–1910	117	0·51	1	3·8	19	2·2	84	0·85	13	0·11
1911–1920	43	0·17	0	–	4	0·46	33	0·30	6	0·05
1851–1920	6,652	4·8†	171	92·6	1,543	26·1†	4,795	8·1†	143	0·19

†Average incidence rates

Table 38. Average age-specific incidence rates with mean age at onset, sex ratio and type index of leprosy by residential district in Norway, 1851–1920. (The National Leprosy Registry of Norway)

Residential district	Age-specific incidence rates				Mean age at onset	Sex ratio	Type index
	0–14 yrs	15–29 yrs	30–49 yrs	50 + yrs			
Naustdal	39·3	156·6	119·2	63·2	31·0	108·7	73·6
Sogn & Fjordane except Naustdal	11·1	45·2	36·4	19·2	31·5	126·4	63·8
High frequency areas except Sogn & Fjordane	2·65	12·2	12·6	8·04	34·5	160·3	64·9
Low frequency areas	0·05	0·22	0·29	0·31	39·3	145·1	45·5

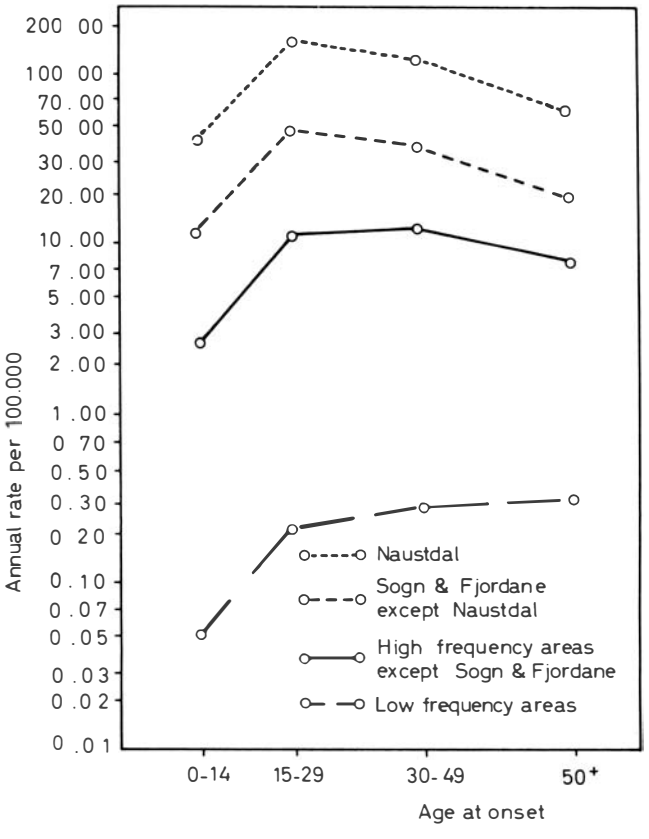

Figure 33. Incidence rates of leprosy in Norway, 1851–1920, by residential district. Age-specific average incidence rates. (The National Leprosy Registry of Norway.)

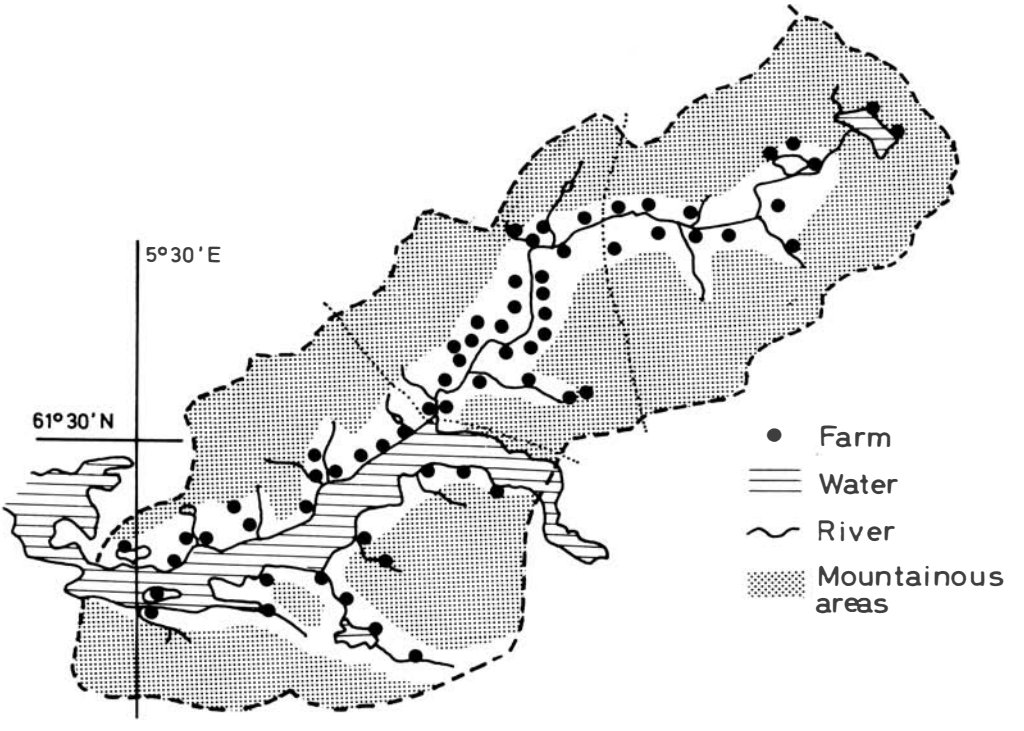

Figure 34. Health district of Naustdal.

Sex ratio, based on average sex-specific incidence rates, was close to 100 in Naustdal. Sex ratio appeared to increase with decreasing incidence rates, to 126·4 in Sogn & Fjordane except Naustdal and to 160·3 in the high frequency areas except Sogn & Fjordane. In the low frequency areas sex ratio was 145·1 (Table 38).

For *type index*, calculated on the basis of all patients taken ill during the observation period, the highest value was found in Naustdal, with 73·6. Type index decreased through the same areas and the lowest value, 45·5, was found in the low frequency areas (Table 38).

For the measures mean age at onset, sex ratio and type index no evident *time trend* was demonstrated in Naustdal.

3.6.2. COUNTRYSIDE LEVEL

On the basis of communications and topography, Naustdal was divided into 4 parts: the southern and northern banks of the fjord, and the lower and upper parts of the valley (Fig. 34). Total number of patients registered in these areas per 1,000 inhabitants present in 1865 were 49·6, 87·0, 72·5 and 76·4 respectively, indicating a difference between the two banks of the fjord with a higher rate on the northern bank.

Table 39. Number of farms and patients living at the farms with mean age at onset,† sex ratio† and type index of leprosy in Naustdal, Norway, 1851–1920, by total farm rate. (The National Leprosy Registry of Norway)

Total farm rate	Farms	Patients	Mean age at onset	Males per 100 females	Type index
0	29	0	–	–	–
0·1–59·9	15	29	31·2	70·6	60·8
60·0–119·9	25	86	32·1	95·5	70·4
⩾ 120·0	15	77	26·7	108·1	79·4

†The measures are based on crude number of patients

3.6.3. FARM LEVEL

Even at farm level the occurrence of the disease varied considerably. At 29 out of a total of 84 farms in Naustdal, no case was registered, while 192 cases were registered at the remaining 55 farms. *Total farm rate* (*vide* 2.5.3.) of these farms ranged between 10·7 and 428·6. In 3 cases information necessary for allocating the patient to a farm was lacking.

The farms were grouped according to total farm rate (Table 39). At farms where total farm rate exceeded 120·0, *mean age at onset* was particularly low, 26·7 years, compared with the farms where total farm rate was lower. For number of *males per 100 females* no significant trend was demonstrated. *Type index* at the high rate farms was particularly high, 79·4, and a gradual decrease was found at farms with lower total farm rates. This was consistent with the finding of a median total farm rate of 81·9 at farms where type index was below 70, while at the remaining farms, median total farm rate amounted to 110·1.

Distance from the sea

The difference in incidence rates already demonstrated, between inland and coastal districts (*vide* 3.1.1.), called to a similar analysis on farm level. All farms except one were grouped according to whether distance from the farm to the sea was below or above 0·5 km. (Due to the large area of the farm, one farm could not be grouped according to this criterion.) First of all fishing, but also shipping were considered far more common trades at farms closer to the sea than 0·5 km.

Of 63 farms, with a distance from the sea of more than 0·5 km, 40 (63·5%) were leprosy positive farms. Median total farm rate was 62·7 (Table 40). Of 20 farms, with a distance from the sea of 0·5 km or less, 14 (70·0%) were leprosy positive farms, and median total farm rate was 51·3. No association was demonstrated between distance from the farm to the sea and leprosy status of the farm, $p = 0{\cdot}59$.

Table 40. Farms in Naustdal, Norway, by leprosy status with median total farm rate, according to whether distance to the sea was below or above 0·5 km. (The National Leprosy Registry of Norway)

Distance from the sea (km)	Total (No.) (%)	Leprosy status		Total farm rate (median)
		L. positive (No.) (%)	L. negative (No.) (%)	
0–0·50	20	14	6	51·3
	100·0	70·0	30·0	
⩾ 0·51	63	40	23	62·7
	100·0	63·5	36·5	
Total	83	54	29	55·0
	100·0	65·1	34·9	

p = 0·59

Table 41. Farms in Naustdal, Norway, by leprosy status with median total farm rate, according to whether production of oats per person was below or above the median. (The National Leprosy Registry of Norway)

Production of oats per person	Total (No.) (%)	Leprosy status		Total farm rate (median)
		L. positive (No.) (%)	L. negative (No.) (%)	
Below median	42	31	11	53·0
	100·0	73·8	26·2	
Above median	42	24	18	58·0
	100·0	57·1	42·9	
Total	84	55	29	55·0
	100·0	65·5	34·5	

p = 0·08

Table 42. Farms in Naustdal, Norway, by leprosy status with median total farm rate, according to whether production of potatoes per person was below or above the median. (The National Leprosy Registry of Norway)

Production of potatoes per person	Total (No.) (%)	Leprosy status		Total farm rate (median)
		L. positive (No.) (%)	L. negative (No.) (%)	
Below median	42	30	12	58·0
	100·0	71·4	28·6	
Above median	42	25	17	50·0
	100·0	59·5	40·5	
Total	84	55	29	55·0
	100·0	65·5	34·5	

p = 0·18

Table 43. Farms in Naustdal, Norway, by leprosy status with median total farm rate, according to whether production of milk per person was below or above the median. (The National Leprosy Registry of Norway)

Production of milk per person	Total (No.) (%)	Leprosy status		Total farm rate (median)
		L. positive (No.) (%)	L. negative (No.) (%)	
Below median	43	33	10	80·0
	100·0	76·7	23·3	
Above median	41	22	19	28·0
	100·0	53·7	46·3	
Total	84	55	29	55·0
	100·0	65·5	34·5	

$p = 0{\cdot}02$

Malnutrition

In the last half of the 19th century barter economy was predominant in Naustdal as in rural Norway in general. Furthermore, the nutritional status of the population in Naustdal at the time was poor (Bidenkap, 1858; 1860). Under such conditions an association may be assumed to exist between production of a farm, i.e. oats, potatoes and milk, on one hand, and nutrition of its inhabitants on the other. Accordingly, data on production of each farm, derived from the general population censuses (*vide* 2.4.3), were used to ascertain whether leprosy was related to malnutrition.

Production of *oats* ranged from 0 to 11·4 production units (*vide* 2.5.5.) per person and the median was 5·3. Grouped according to the median, no association was demonstrated between production of oats per person and leprosy status of the farm, $p = 0{\cdot}08$ (Table 41). At farms where production of oats per person was low, median total farm rate was 53·0, while at farms where production was high, median total farm rate was 58·0.

Production of *potatoes* ranged from 0·9 to 10·0 production units per person, and the median was 3·0. Grouped according to the median, no association was demonstrated between production of potatoes per person and leprosy status of the farm, $p = 0{\cdot}18$ (Table 42). At farms where production of potatoes was low, median total farm rate was 58·0, while at the other farms, median total farm rate was 50·0.

Production of *milk*, based on number of cows (*vide* 2.5.5.), ranged from 3·8 to 18·1 production units per person, and the median was 8·3. Grouped according to the median, a significant association was demonstrated between production of milk per person and leprosy status of the farm, $p = 0{\cdot}02$ (Table 43). The frequency of leprosy positive farms was far higher among farms with a low production than among farms with a high production of milk, and median total farm rates were 80 and 28 respectively.

Table 44. Farms in Naustdal, Norway, by leprosy status, with median total farm rate, according to whether total production per person was below or above the median. (The National Leprosy Registry of Norway)

Total production per person	Total (No.) (%)	Leprosy status		Total farm rate (median)
		L. positive (No.) (%)	L. negative (No.) (%)	
Below median	42	32	10	67·0
	100·0	76·2	23·8	
Above median	42	23	19	37·0
	100·0	54·8	45·2	
Total	84	55	29	55·0
	100·0	65·5	34·5	

$p = 0{\cdot}03$

Table 45. Farms in Naustdal, Norway, by total production per farm according to number of persons per farm

Number of persons per farm	Total (No.) (%)	Total production per person	
		Above median (No.) (%)	Below median (No.) (%)
1–20	42	23	19
	100·0	54·8	45·2
⩾ 21	42	19	23
	100·0	45·2	54·8
Total	84	42	42
	100·0	50·0	50·0

$p = 0{\cdot}51$

Total production of the farm ranged from 7·3 to 35·8 production units per person, and the median was 16·3. Grouped according to the median, a significant association was demonstrated between total production of a farm and its leprosy status, $p = 0{\cdot}03$ (Table 44). Leprosy positive farms were far more frequent among farms with a low production than among the other farms, and median total farm rates were 67 and 37 respectively.

However, number of persons per farm ranged from 5 to 187, and the median was 20. Obviously, the risk of having a leprosy patient on a farm, converting its leprosy status from negative to positive, was related to number of persons living at the farm. To find out whether the association between production and leprosy might be non-causal or secondary, and due to a possible negative correlation between production per person and number of persons per farm, the farms were tabled according to total production per person and number of persons per farm (Table 45). No association was demonstrated between the variables, $p = 0{\cdot}51$.

Table 46. Farms in Naustdal, Norway, by leprosy status with median total farm rate, according to whether farm index for production of oats and milk was below or above the median. (The National Leprosy Registry of Norway)

Farm index, production of oats and milk†	Total (No.) (%)	Leprosy status		Total farm rate (median)
		L. positive (No.) (%)	L. negative (No.) (%)	
Below median	42	20	22	1·0
	100·0	47·6	52·4	
Above median	42	35	7	74·0
	100·0	83·3	16·7	
Total	84	55	29	55·0
	100·0	65·5	34·5	

p = 0·0006

†A high index for a farm implies a high proportion of farm sections with a *low* production per person. (*Vide* 2.5.5.)

Table 47. Farms in Naustdal, Norway, by leprosy status with median total farm rate, according to whether tax value per farm section was below or above the median. (The National Leprosy Registry of Norway)

Tax value per farm section	Total (No.) (%)	Leprosy status		Total farm rate (median)
		L. positive (No.) (%)	L. negative (No.) (%)	
Below median	41	31	10	72·0
	100·0	75·6	24·4	
Above median	41	24	17	50·0
	100·0	58·5	41·5	
Total	82†	55	27	55·0
	100·0	67·1	32·9	

p = 0·08

†For 2 farms tax value was unknown

Subsequently, the farms were grouped according to median *farm index for total production*, which was 0·13. A more significant association was demonstrated to exist between this independent variable and leprosy status of the farms, p = 0·003. Leprosy positive farms were far more frequent among the farms with a high farm index for total production than among the other farms, and median total farm rates were 74 and 0 respectively.

An even more significant association with the same trend was found to exist between *farm index for production of oats and milk* and leprosy status of the farms, p = 0·0006 (Table 46).

Table 48. Farms in Naustdal, Norway, by leprosy status with median total farm rate, according to whether number of persons per house was below or above the median. (The National Leprosy Registry of Norway)

Persons per house	Total (No.) (%)	Leprosy status		Total farm rate (median)
		L. positive (No.) (%)	L. negative (No.) (%)	
Below median	42	27	15	53·0
	100·0	64·3	35·7	
Above median	42	28	14	55·0
	100·0	66·7	33·3	
Total	84	55	29	55·0
	100·0	65·5	34·5	

$p = 0{\cdot}50$

Poverty

Obviously, poverty, in an area with barter economy, is related to low production. However, further information on poverty was available. The tax value system was based on *potential assets* of the farm; i.e. *potential* optimal production in barn and fields (*vide* 2.4.3., 2.5.5.).

Tax value per farm section ranged from 84·9 to 619·0 oere, and the median was 252·0. Grouped according to the median, no significant association was demonstrated between tax value per farm section and leprosy status of the farm, $p = 0{\cdot}08$ (Table 47). At farms where tax value was low, median total farm rate was 72·0, while at the other farms, median total farm rate was 50·0.

Overcrowding

From studies on prevailing customs in this part of Norway, and particularly in Naustdal, it appears that the farm-houses differed little with respect to construction, number of rooms and size (Kloster, 1940). Accordingly, the variable 'number of persons per house' (*vide* 2.5.5.) might be used in comparisons between farms, being indicative of overcrowding.

Number of persons per house ranged from 3·5 to 10·5, and the median was 6·8. Grouped according to the median, no association was demonstrated between number of persons per house and leprosy status of the farm, $p = 0{\cdot}50$ (Table 48). At farms where number of persons per house was high, median total farm rate was 55·0 against 53·0 at the other farms.

Grouped according to median *farm index for housing*, (*vide* 2.5.5.), 0·25, still no association was demonstrated, $p = 0{\cdot}33$, and median total farm rate was almost the same in the two groups, 56·0 and 50·0 (Table 49).

Table 49. Farms in Naustdal, Norway, by leprosy status with median total farm rate, according to whether farm index for housing was below or above the median. (The National Leprosy Registry of Norway)

Farm index, housing†	Total (No.) (%)	Leprosy status: L. positive (No.) (%)	Leprosy status: L. negative (No.) (%)	Total farm rate (median)
Below median	45	28	17	50·0
	100·0	62·2	37·8	
Above median	39	27	12	56·0
	100·0	69·2	30·8	
Total	84	55	29	55·0
	100·0	65·5	34·5	

p = 0·33

†A high index for a farm implies a high proportion of farm sections with a *high* number of persons per house. (*Vide* 2.5.5.).

Table 50. Farms in Naustdal, Norway, by leprosy status with median total farm rate, according to whether sphagnum index was below or above the median. (The National Leprosy Registry of Norway)

Sphagnum index	Total (No.) (%)	Leprosy status: L. positive (No.) (%)	Leprosy status: L. negative (No.) (%)	Total farm rate (median)
Below median	39	18	21	0
	100·0	46·2	53·8	
Above median	40	32	8	71·6
	100·0	80·0	20·0	
Total	79	50	29	55·0
	100·0	63·3	36·7	

p = 0·002

Sphagnum vegetation

Sphagnum index ranged from −1·88 to +1·66, and the median was +0·15. For 5 farms data necessary for the calculation of a sphagnum index were lacking.

When the farms were grouped according to median sphagnum index, a significant association was demonstrated between sphagnum index and leprosy status of the farm, p = 0·002 (Table 50). The frequency of leprosy positive farms was far higher among the farms with a high sphagnum index than among the other farms, and median total farm rates were 72 and 0 respectively.

Table 51. Extent of correct classification and ratio of risks in different groups of farms in Naustdal, Norway. Groups defined by discriminant functions for sphagnum variables, farm variables and all variables pooled together and an optimal cut-off point. (The National Leprosy Registry of Norway)

	Leprosy status of farm		
Discriminant function	L +	L −	Total
Sphagnum variables			
Above cut-off point	44	11	55
Below cut-off point	6	16	22
Total	50	27	77
Correctly classified: 77·9%			
Ratio of risks: 2·9			
Farm variables			
Above cut-off point	39	9	48
Below cut-off point	11	18	29
Total	50	27	77
Correctly classified: 74·0%			
Ratio of risks: 2·1			
Sphagnum variables + *Farm variables*			
Above cut-off point	46	11	57
Below cut-off point	4	16	20
Total	50	27	77
Correctly classified: 80·5%			
Ratio of risks: 4·0			

A comparison of environmental variables

For a total of 77 farms data on all farm- and sphagnum-variables were used as a basis for discriminant analyses. Data from 7 farms were not used in the analyses, in part due to incomplete information, in part because the farm was considered too big (*vide* 3.6.4.).

The relative importance of the 7 variables used in the construction of the *sphagnum index* was assessed by a stepwise analysis. According to the analysis, *water supply* (*var. 7*) was the variable which alone had the best discriminating power, $p = 0{\cdot}002$. The variable which, in addition to the first, gave the best discriminating power was *sphagnum vegetation* (*var. 1*). The significance of change was $p = 0{\cdot}007$ and the significance of the total function was $p = 0{\cdot}001$. Addition of the next variable did not produce a significant change, and the analysis was ended.

The total function, based on all 7 sphagnum variables, was assessed by its ability to classify correctly the farms as leprosy positive or negative (Table 51).

At the optimal cut-off point, 60 (77·9%) of the 77 farms were correctly classified. The risk that farms, with a value of the function exceeding the cut-off point, were leprosy farms (*vide* 2.5.5.), was 2·9 times higher than the risk of being a leprosy farm for those below the cut-off point.

In a stepwise analysis based on the 3 *farm variables*, farm index for production of oats and milk, tax value, and farm index for housing, *farm index for production of oats and milk* was the variable which alone had the best discriminating power, $p = 0{\cdot}02$. Addition of further variables did not produce a significant change.

By the total function based on all 3 farm variables and an optimal cut-off point, 57 (74·0%) of the 77 farms were correctly classified. The ratio of risks was 2·1.

According to a stepwise analysis, based on *all 10 variables*, *water supply* was the variable which alone had the best discriminating power, $p = 0{\cdot}002$. By adding the next variable, *farm index for production of oats and milk*, the significance of change was $p = 0{\cdot}005$ and the significance of the total function was $p < 0{\cdot}001$. The next variable to be added was *orientation of the vegetation* which also produced a significant change, $p = 0{\cdot}01$. Addition of the next variable did not produce a significant change, and the analysis was ended.

By a total function based on all 10 variables and an optimal cut-off point, 62 (80·5%) of the 77 farms were correctly classified. The ratio of risks was 4·0.

3.6.4. COMMENTS

In this part of the study, the *farm* rather than the person was chosen the unit of observation, first of all because the intention was to pinpoint characteristics of minor *localities* with leprosy compared with localities without leprosy. The environmental variables to be studied were attached to the farm and not to the person.

Furthermore, elaborate calculations based on persons, e.g. calculation of risk ratios, would have been hampered by the lack of an exact denominator, viz. total number of persons at risk throughout the observation period. However, for the mere calculation of rates, e.g. total farm rate, an average total population was considered a satisfactory denominator. On the other hand, using the farm as the unit of observation, the exact denominator was known.

The possibility that the occurrence of leprosy could be *secondarily* associated with production/nutrition might hypothetically be the effect, on one hand, of a primary positive association between number of persons per farm and leprosy status of the farm and, on the other hand, of a primary negative association between number of persons per farm and production. Accordingly, one would expect a significantly lower production per person at farms with many inhabitants. Furthermore, one would expect only minor differences between total farm rates of farms with high and low production, because leprosy would occur particularly at farms with many inhabitants. However, no

significant association was found to exist between production per person and number of inhabitants, and also the rates were far higher at farms where production per person was low. In an additional attempt to avoid the bias, that a larger farm inevitably would have a higher risk of being a leprosy farm, solely due to a higher number of inhabitants, farms with more than 100 inhabitants were not included in the analyses. Besides, a general description with respect to environmental variables, of such a large farm as one entity, would hardly seem satisfactory. Accordingly, it may be concluded that the association demonstrated to exist between leprosy status of the farm and low production/malnutrition was not such a secondary association.

Obviously, the possibility should not be neglected, that a low production might represent the *effect* of leprosy and not a causal factor. This is, however, not very likely, because total number of patients present at any one farm at any time was rather small compared with total number of inhabitants, even at high frequency farms. E.g., even at the 2 farms with the highest total farm rates, 428·6 and 385·0 respectively, only 2 patients lived at the farms at the time of the census in 1865, and the total population was 27. Furthermore, the patients living at the farms were probably not much disabled; disabled patients were sent to hospital. Thus, the loss of labour, due to disabled patients living at the leprosy positive farms, lowering the production per person, was considered small.

The associations between leprosy status and farm indices for production were stronger and more significant than the associations between leprosy status and mere production per person. This implies that the variable 'production per person' at farm level in fact covered a wide range from the most wealthy to the most poor farm sections within one farm.

Even in an area with barter economy, leprosy did not appear to be associated with mere assets. This finding seems to affirm that the association between leprosy and production at the farms was less related to the economical value of the production than to its nutritional aspects.

The construction of the sphagnum index was based on two different components. The first was related to *conditions for growth of mycobacteria* in sphagnum vegetation observed at the farms today. The alternative, to relate this component to the occurrence today at different localities of specified mycobacteria in the sphagnum vegetation (Kazda *et al.*, 1979), might also be useful. However, the mycobacterial composition of the vegetation today is not necessarily the same as in the last century, while the conditions for growth apparently have not changed much during the last 100 years.

The second component, referred to in the construction of the sphagnum index, was *the inhabitants' access to the vegetation*.

From an ecological point of view, it was interesting to note that the most important variables in the stepwise analyses were related to different components, i.e. both components used in the sphagnum index appeared to be relevant in the analyses. Furthermore, in analyses based on a pool of all

sphagnum- and farm-variables, variables related to the two components were chosen as the most important, together with the variable for production.

The possibility is not very likely, that the positive association between sphagnum index and the occurrence of leprosy might be secondary, caused by primary negative associations, on one hand between sphagnum index and production, and on the other hand between production and occurrence of leprosy. On the contrary, the construction of the sphagnum index was based on conditions which would favour growth of vegetation in general (i.e. also production) as well as growth of mycobacteria in sphagnum vegetation.