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DERMATITIS HERPETIFORMIS IN FINLAND

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Abstract. During a 3½-year period, 492 patients with dermatitis herpetiformis (DH) visited the dermatological departments of Finnish hospitals. The prevalence of DH in Finland was 10.4 patients/100 000 inhabitants, or 1/10 000. About 60 patients contracted DH each year, giving an incidence of 1.3 patients/100 000 inhabitants/year. These figures show that DH is a rather common disease in Finland—much more so in Finland than in Britain. Its incidence does not differ much from that approximated for coeliac disease in Finland.

DH occured in all parts of the country. The birthplaces of the patients were distributed evenly over the whole country, in contrast to the distribution pattern of rare hereditary diseases in Finland. No significant difference was found in the occurrence of DH in areas with differing levels of wheat consumption or iodine intake.

Key words: Dermatitis herpetiformis; Coeliac disease; Gluten consumption, Iodine intake

Dermatitis herpetiformis (DH) is a blistering skin disease which most commonly makes its appearance between the ages of 20 and 40. It is a highly chronic disorder which generally persists throughout life (1,6). The aetiology of DH is not clear. An association between dietary iodine and DH was suggested earlier, but today the importance of cereals (gluten) in DH is well documented (1, 5). Most patients with DH also have coeliac disease (CD), i.e. an enteropathy which responds to withdrawal of gluten, although only a few patients have clinical signs of malabsorption (5, 11). The rash can also be controlled by a gluten-free diet (6, 19).

The common factor which links DH to CD seems to be a genetic one. In both diseases most patients have the histocompatibility antigens HLA-B8 and HLA-Dw3 (21, 22). Moreover, family studies have shown that the relatives of patients with DH often have CD (12, 18). This is in agreement with the familial tendency of CD in which about 10–20% of first-degree relatives are affected (23).

In spite of the many common features, there are also some interesting differences between DH and CD. The male–female ratio is about 2 : 1 in DH, whereas the females outnumber the males in CD (1). The incidence of DH is obscure, in contrast to the many reports on the incidence of CD (14). In DH the only published figure is an estimate of the prevalence of 600–700 patients in Britain (25). In Finland, DH seems to be a rather common disease, and patient data were collected from the whole country in order to establish its prevalence. The geographical distribution was studied in order to ascertain if DH occurs in only limited areas, as is commonly the case with many rare hereditary diseases in Finland (16). An attempt was also made to determine whether the occurrence of DH correlates with consumption of cereals or iodine intake.

MATERIAL

Hospital records were collected concerning patients with DH who visited the out-patient and in-patient clinics of the dermatological departments of Finnish hospitals between January 1, 1973 and June 30, 1976. The hospitals were the university central hospitals in Helsinki (I), Turku (II) and Oulu (X), and the central hospitals in Tampere (III), Lappeenranta (IV), Joensuu (VI), Kuopio (VII) and Jyväskylä (VIII). The number of the corresponding province is given in parentheses (see Fig. 3). Central hospitals admit patients from the surrounding province; university hospital can also admit patients from other provinces, for example, from those without dermatological departments.

Before the diagnosis of DH was accepted, the data in the hospital records were studied. Only those patients who had shown a typical clinical and histological picture of the rash and had reacted favourably to dapsone or sulphapyridine were included in this study. IgA deposits in skin were present—constituting additional diagnostic evidence—in most patients in Helsinki and in some in Turku and Tampere.

The data on cereal consumption and iodine intake were taken from the study made by the Finnish National Pension Institute (7). The population data from various provinces in Finland were obtained from The Central Office of Statistics, Helsinki.

Table I. *The year of onset of dermatitis herpetiformis in patients visiting Finnish hospitals between 1.1.1973 and 30.6.1976*

	Before 1946	1946–50	1951–55	1956–60	1961–65	1966–70	1971–75
Patients (n=492)	10	9	17	22	67	116[a]	251[a]

[a] See Table II.

RESULTS

Prevalence and incidence

During the 3½-year study period, 492 patients with DH visited the dermatological departments of Finnish hospitals, 303 males and 189 females (ratio 1.6 : 1). The mean age at the onset of DH in men was 33.0±13 (range 3–75) and in women 30.6±13 (range 3–77). Finland had a total population of 4.7 million on January, 1, 1976. This gives a prevalence of 10.4 patients/100 000 inhabitants or about 1/10 000.

In order to obtain the incidence, the year of onset of DH in all 492 patients was analysed (Tables I and II). There were 61, 61 and 60 patients whose disease began in 1972, 1973 and 1974, respectively. This gives an incidence of 1.3 patients/100 000 inhabitants/year. The figures before 1972 were below 60 per year (Table II). This is obviously due to the fact that at least some of the patients who contracted DH before 1972 no longer visited the departments during the study period. For example, at the Department of Dermatology in Helsinki, there were 11 patients whose disease began in 1971 but who no longer visited the Department after 1972. The low figure in 1975 (Table II) means that only some of the patients who contracted DH in 1975 were still visiting the departments by the end of this study. For example, at the Department of Dermatology in Helsinki, 49 new patients with DH have been diagnosed during the 1½-year period since this study was concluded. Nine of these contracted the disease before 1972, two in 1972, four in 1973, six in 1974, ten in 1975, fourteen in 1976 and four in 1977. This shows that the time between the onset and the diagnosis of DH varies a great deal from one patient to another.

Geographical distribution

The birthplaces of the patients are indicated on the map in Fig. 1, which shows that DH is distributed throughout the whole country. The patient clusters on the map are restricted to urban communities and are in proportion to the local population. The birthplaces of the parents of 86 patients at the Department of Dermatology in Helsinki were also checked. No clustering was observed. Thus there is no clustering in certain limited areas of the country as occurs in rare hereditary diseases in Finland.

The patients' numbers within provinces were analysed both for birthplace and for domicile, since the whole population from the occupied southeastern parts of Finland was forced to move during the Second World War. In addition, during the last 20 years, urbanization has brought many people to the southern parts of Finland. In this study 40% of the patients were born in a different province from that in which they were living. One-fourth of these were from occupied areas. In the analysis of birthplaces, the population data from 1939 were used.

The patients born in the province of North Karelia (VI) were significantly over-represented (p<0.001) (Fig. 2). The number of patients living in this province was also higher in proportion to the population data than in other provinces, though the difference was not significant (Fig. 3). The numbers of patients living in the Vaasa (IX) and Lapland (XI)

Table II. *The year of onset of dermatitis herpetiformis from the last decade*

	1966	1967	1968	1969	1970	1971	1972	1973	1974	1975
Patients (n=367)	14	21	25	25	31	39	61	61	60	30

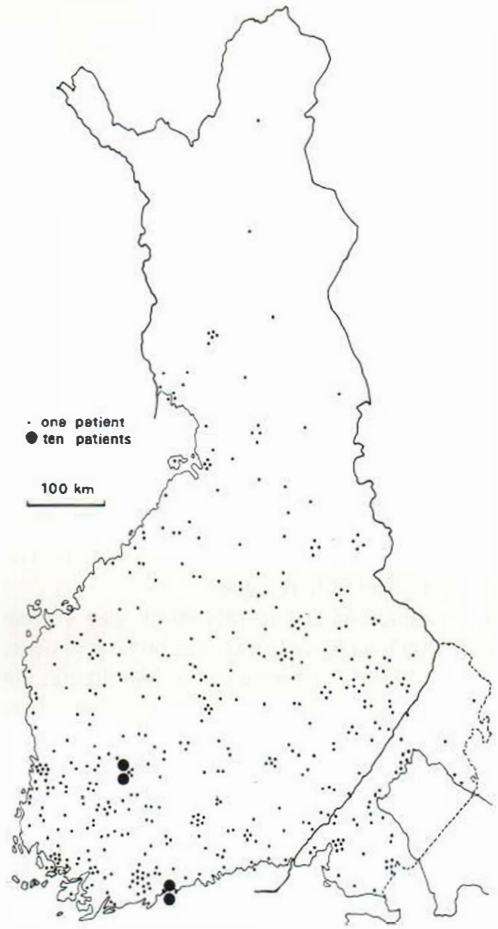

Fig. 1. Birthplaces of the 492 patients with dermatitis herpetiformis in Finland.

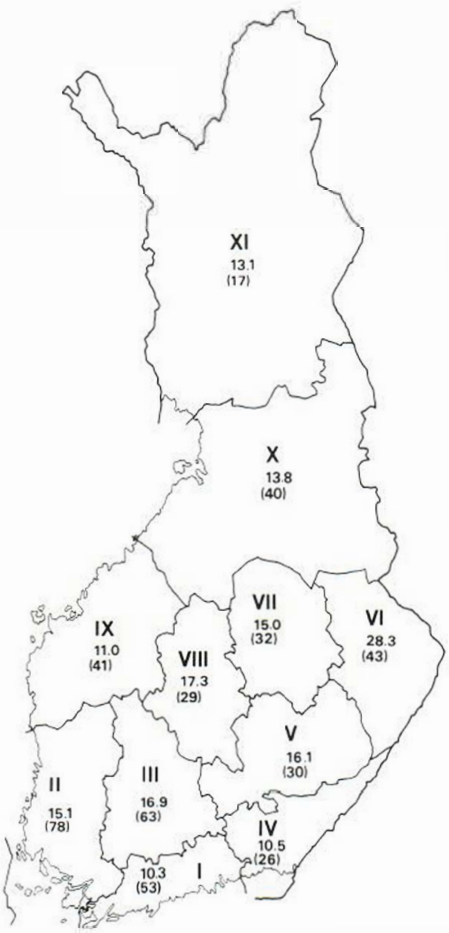

Fig. 2. The prevalence of dermatitis herpetiformis in different provinces per 100 000 inhabitants (birthplace). The numbers of patients are given in parentheses.

provinces were significantly lower than average ($p<0.001$).

Consumption of cereals and iodine intake

The total consumption of cereals in Finland now averages 300 g/inhabitant/day. Wheat and rye constitute 95% of this total; the ratio between them is 1 : 1. There are no regional differences in the overall cereal consumption within the country, but wheat outweighs rye in the western provinces; there the ratio between wheat and rye is 4 : 3. In the eastern provinces rye is the more important cereal. The numbers of patients in the provinces with high wheat consumption (II, III, IX) were compared with the numbers of patients with low wheat consumption, i.e. with high rye consumption (IV, V, VI, VII). The prevalences for birthplaces were 17.3 and 14.4 and for domicile 11.1 and 10.5, respectively. These differences are not significant.

In the 1950s, when the use of iodized table salt was very rare in Finland, the daily intake of iodine was low (50 μg) and the prevalence of endemic goitre high in the eastern parts of the country, whereas in western parts, iodine intake was higher (70 μg) and the prevalence of goitre was about one-tenth of the eastern figure (24). Today almost all table salt used in Finland is iodized. The daily intake of iodine has increased to 220 μg and geographical differences no longer exist (7). This only makes it possible to examine whether there are any differences between the numbers of patients born in the areas of low iodine intake (provinces IV, V,

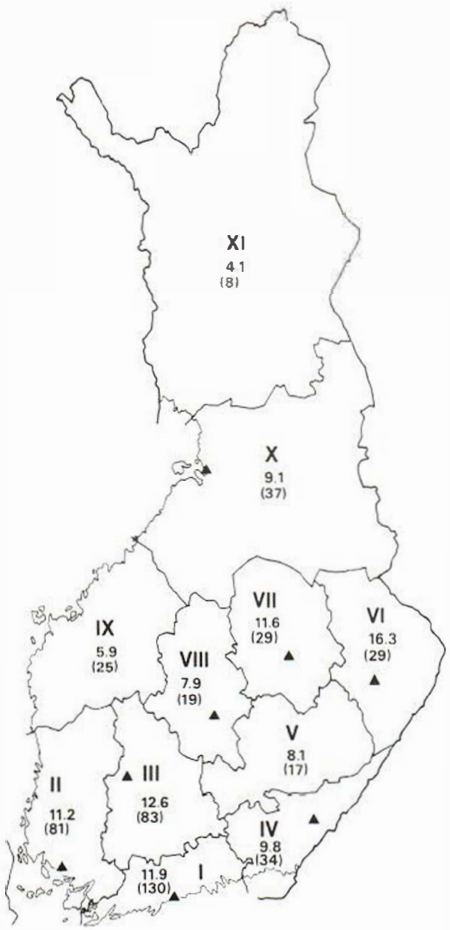

Fig. 3. The prevalence of dermatitis herpetiformis in different provinces per 100 000 inhabitants (domicile). The numbers of patients are given in parentheses. Triangles indicate dermatological departments.

VII, in Fig. 2) and in those with higher iodine intake (provinces II, III, IX). The corresponding prevalences were 13.4 and 14.4 and thus there was no significant difference.

DISCUSSION

During the 3½-year study period, 492 patients with DH visited dermatological departments in Finland. This gives a prevalence of 1/10000. It is clear that this figure is a minimum for DH in Finland. There are patients who were diagnosed as having DH before 1973 but who no longer visited the dermatological departments during this study. Furthermore, no data were collected from private dermatologists. However, this source would not have added many patients to the total figure because the number of private dermatologists is so small and new patients suspected of having DH are usually sent by them to dermatological departments for further examination.

It seems reasonable to conclude that the number of patients was at least 550 in the summer of 1976. We cannot compare this figure with previous estimates. 1/500 dermatological attendances at one hospital in the USA, 1/800 in England, 1/80 in Norway and 1/160 in Sweden (1, 4). The total number of Finnish patients with DH is only 100 cases fewer than the figure Wyatt et al. (25) found in Britain. Finland has about one-tenth the population, which suggests that DH is much more frequent in Finland. However, Wyatt's study (25) was based on a postal survey, which means that a comparison of prevalences is not absolutely reliable.

The incidence of DH in this study was 1.3 patients/100 000 inhabitants/year, i.e. 60 new patients per year. To us, this seems a rather high figure, but no data from other countries exist. If we compare this figure with the incidence of childhood CD in Finland, which is about 1/1 000 births, or about 65 new patients per year (8), and estimate that there would be one adult case per four childhood cases, we find that the incidence of DH does not seem to differ much from the incidence of CD.

When the geographical distribution was analysed it was found that the number of patients born in the province of North Karelia (VI) was significantly increased. The reason for this is unclear. However, this difference no longer existed when the number of patients now living in that province was analysed. The low prevalence in the provinces of Vaasa (IX) and Lapland (XI) may result from the lack of dermatological services. These provinces have no dermatological departments and have only a few private dermatologists. The widespread emigration of young people from Lapland may also be a reason for the low prevalence.

In Finland, rare blood marker genes (gene frequency lower than 0.002) are found only in people living in or coming from isolated parts of the country, and the same is true of rare hereditary diseases (15, 16). The map in Fig. 1 shows that DH does not have this distribution pattern. If we generalize the results found for the distribution of rare blood marker genes to other genes, this would mean that DH-associated genes must be quite

common in the Finnish population, i.e. the gene frequency should exceed 0.002 (15). When we compare this figure (1/500), which can be taken as the lower limit of the frequency of DH-associated genes, with the prevalence of DH in Finland (1/10 000) we must assume that the number of people with these DH-associated genes greatly exceeds the number of patients with DH, i.e. the penetrance of DH is low. This tallies well with the occurrence of histocompatibility antigens in DH. In Finland 87 % of the patients with DH have HLA-B8, but this antigen is also common in the general population, where its frequency is 17% (17). However, it is clear that HLA-B8 itself is not responsible for DH, though it is evident that some genes situated in the major histocompatibility complex and closely linked with HLA-B8 are involved. Such a gene may be an "immune-response" gene, as immunological mechanisms seem to play a significant role in the pathogenesis of the diseases associated with HLA-B8 (DH, CD, juvenile diabetes, myasthenia gravis, etc.) (13, 20). The fact that the penetrance of DH seems to be low is also in agreement with the family studies in DH and CD. These have shown that not every member of the family carrying the disease-associated HLA haplotype is affected (18, 23).

It has been proposed that iodine intake is one of the exogenous factors affecting the manifestation of DH (1). In Norway, where DH seems to be common, seafish figures prominently in the diet (10). However, this study showed that DH is also frequent in a country where iodine intake has always been low and where, now that the use of iodized table salt is widespread, it is still lower (220 μg) than the corresponding figure (300 μg) in Norway (9).

The variation in gluten consumption may have an effect on the occurrence of DH. This has also been proposed for CD due to the geographical differences in its occurrence (14). In Finland, total consumption of cereals is high, on average 300 g per person per day (7). This means that the gluten load is at least 20 g per day, three times greater than the average intake (7 g) in England (2, 3). This could be one reason for the frequent occurrence of DH in Finland.

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