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Geographical and temporal distribution of Ockelbo disease in Sweden

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SUMMARY

The incidence of Ockelbo disease and the prevalence of Ockelbo virus neutralizing antibodies were investigated in a sample of the Swedish population. The disease occurs throughout most of Sweden but with higher incidence and antibody prevalence rates in the central part of the country. It generally affects middle-aged men and women, with equal incidence between sexes, and is uncommon in people younger than 20 years of age. The disease occurs during a short period each year between the third week of July and the first week of October, with a peak during the second half of August. During the 8 years studied (1981–8), an average of 31 Ockelbo patients/year were diagnosed. The antibody prevalence rates in the oldest age groups were 20–40 times higher than the accumulated life-risk of being diagnosed and reported as an Ockelbo disease patient, which suggests that many cases are asymptomatic and/or unreported.

INTRODUCTION

Ockelbo disease was first observed in the 1960s, when, during late summer, several persons living in the vicinity of Ockelbo village in central Sweden experienced a syndrome with exanthema and arthralgia sometimes associated with fever. The arthralgia most often affected ankles, wrists, knees and hips, but less than 5% of the patients were hospitalized [1]. The disease was usually self-limiting, with recovery within a month, but 20% of the patients still complained of joint discomfort 3–4 years after onset of disease [2].

Ockelbo disease was shown to be caused by a virus related to Sindbis virus [3]. A candidate aetiologic agent was isolated by Niklasson and colleagues [4] from mosquitoes collected in central Sweden in 1982. This virus, designated Ockelbo virus, is serologically close related to, but distinguishable from, Sindbis virus [4–6].

The majority of patients with laboratory-confirmed Ockelbo disease in 1981 and

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1982 lived in central Sweden. Based on the area of residency for these patients and an antibody survey among healthy blood donors, the area between the 60th and the 63rd parallel was suggested as the main endemic area for Ockelbo disease in Sweden [1].

Illnesses clinically similar to Ockelbo disease and also caused by viruses related to Sindbis virus have been described in Finland (Pogosta disease) and in the Karelian part of the USSR (Karelian fever). In 1981 there was an outbreak with 36 laboratory-confirmed cases in Sweden, 200 in the USSR, and 300 in Finland [1, 7, 8]. Disease associated with Sindbis virus infections has been reported from South Africa and Australia [9, 10], including two epidemics in South Africa [11, 12].

The present study includes a seroepidemiological survey and summarizes the epidemiology of all serologically confirmed Ockelbo disease cases in Sweden between 1981 and 1988.

MATERIALS AND METHODS

Serosurvey

Regional health facilities in 21 towns in 11 Swedish counties were each requested to obtain 100–250 human sera from out-patient volunteers, independently of these persons' previous history of infectious disease. Information on the donors' age, sex and area of residence was collected. Age-standardized antibody prevalence rates were calculated for each county of Sweden on basis of the 1983 national census [13]. Serum samples were obtained in 1981–7, and were sent to the National Bacteriological Laboratory (NBL) and stored at −20 °C until tested for antibodies.

Serological confirmation of Ockelbo disease in Sweden is provided only by the NBL. A case of Ockelbo disease was defined as a patient with symptoms compatible with Ockelbo disease and with seroconversion or a significant rise in titre ($\geqslant$ four-fold) between acute and convalescent serum specimens by an indirect immunofluorescence test (IFT). Information on age, sex, date for onset of symptoms, and area of residence was collected for each Ockelbo disease patient between 1981 and 1988.

Incidence rates were calculated for each county (per year and per 100000 population) on the basis of population estimates as of 31 December 1983 [13].

The accumulated risk of contracting Ockelbo disease (clinical disease and serologically confirmed) during a lifetime was calculated for central Sweden (zone III in Fig. 1) by addition of age-group specific incidence rates.

Patients living south of the 60th or north of the 63rd parallel (see Fig. 1) were interviewed over the telephone by one of the authors (J.O.L.) to determine whether the infection could have been contracted outside the proposed endemic area.

Serological techniques

In the antibody prevalence study, sera were investigated for specific neutralizing antibodies to Ockelbo virus strain Edsbyn 82/5 by a plaque reduction neutralization (PRN) test [4, 14]. An 80% reduction in plaques was used as the

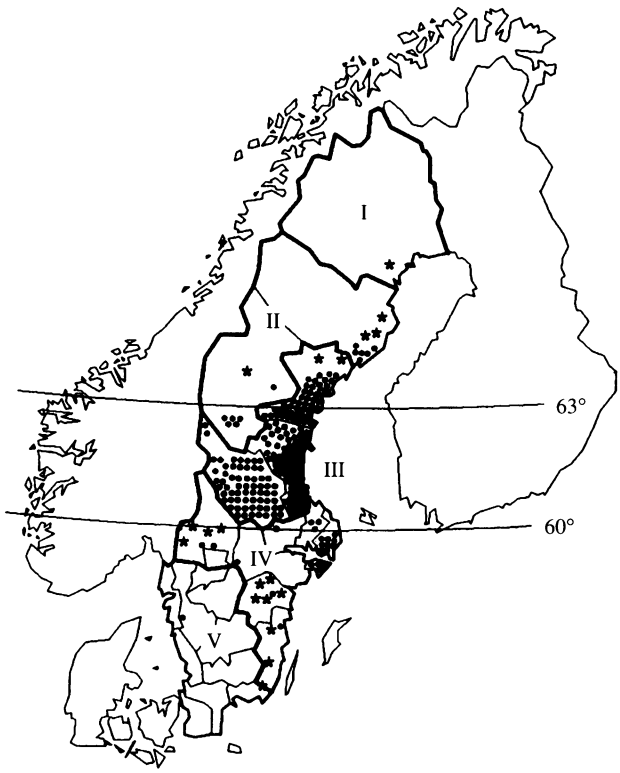

Fig. 1. The geographic location of patients with laboratory-confirmed Ockelbo disease in 1981–8. County borders are shown. The Swedish mainland is divided into five geographic zones based on county borders and the incidence of confirmed cases. ●, Ockelbo disease patient plotted in the area of residency; ★, patient who made no visits to the area between the 60th and the 63rd parallel within 4 weeks prior to onset of disease.

index for virus neutralization titre. All sera were first tested at a 1:10 dilution, and those found positive were retested at four-fold dilutions up to 1:640. Serum specimens with a titre of $\geqslant 10$ were considered positive.

Confirmation of clinical cases was performed by IFT using two-fold dilutions of serum starting at 1:5 [1].

RESULTS

Geographical distribution

In the serosurvey, a total of 3656 sera were examined, of which 91 possessed Ockelbo virus neutralizing antibodies. The highest antibody prevalence rates were found in three counties in central Sweden (zone III in Fig. 1, Table 1). Decreasing antibody prevalence rates were seen both north and south of this area, with rates $\leqslant 0{\cdot}2\%$ in both the northern and southern parts of the country.

Of the 91 sera with neutralizing antibodies to Ockelbo virus, 21% had titre of 10, 45% had titre 20–40, 30% had titre 80–160 and 4% had titre $\geqslant 320$.

Table 1. *Incidence of laboratory-confirmed Ockelbo disease and standardized prevalence of Ockelbo virus neutralizing antibodies in Sweden, by area of residency*

Geographic zone*	Population	Number of cases†	Disease incidence‡	Number of sera tested	Antibody prevalence§
I	264457	1	< 0·1	794	0·1
II	380198	16	0·5	427	1·0
III	841910	193	2·9	1286	3·6
IV	3493031	33	0·1	650	1·8
V	3350977	2	< 0·1	499	0·2
Totals	8330573	245		3656	

* See Fig. 1 for specification of geographic zones.
† Laboratory-confirmed cases 1981–8.
‡ Laboratory-confirmed cases per 100000 population and year.
§ Age-adjusted antibody prevalence rates in percentages.

A total of 245 Ockelbo patients was observed in 1981–8. Incidence rates of more than 2 per 100000 population were found in three counties (Västernorrland, Gävleborg and Kopparberg counties) in central Sweden (zone III in Fig. 1, Table 1). Incidence rates decreased to less than 0·1 in the northern and southern parts of Sweden.

Travel history was available for 37 out of 47 patients living north of the 63rd or south of the 60th parallel. Of these 37 patients, 19 had not made visits to the area between these parallels within 4 weeks prior to onset of Ockelbo disease (Fig. 1).

Seasonal and annual distribution

Information of time of onset was available for 244 of the 245 Ockelbo disease cases observed. All patients had onset between the third week of July and the first week of October, and the peak onset occurred during the third week of August (Fig. 2).

The number of reported cases of Ockelbo disease was 38, 66, 24, 18, 24, 14, 4, 57 for the years 1981–8, respectively.

Age and sex distribution

More than two-thirds of Ockelbo disease patients (Fig. 3) were middle-aged (30–59 years), while only 6% of the patients were younger than 20 years of age. The average age at onset of disease was 46 years for both sexes.

The age and sex distribution of antibodies to Ockelbo virus were studied for the area with the highest incidence and antibody prevalence rates (zone III in Fig. 1, Table 1). The antibody prevalence rates reached a peak in the age-group 60–69 for females and 50–59 for males (Fig. 4).

Life time risk of infection compared with diagnosed patients

Assuming that presence of neutralizing antibodies in sera are lifelong and that Ockelbo disease does not affect mortality, the antibody prevalence rates of 5–10% in the oldest age-groups in central Sweden reflects the accumulated risk of

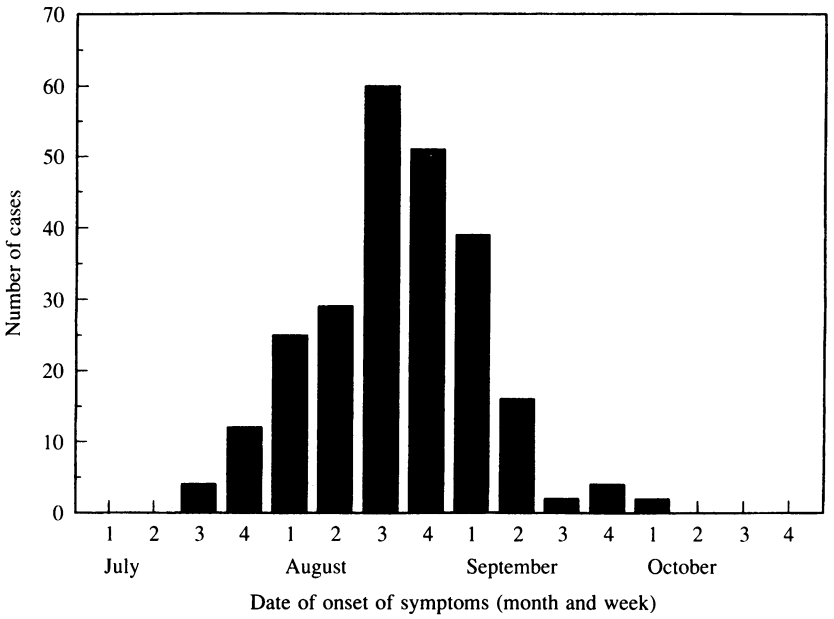

Fig. 2. The distribution of onset of disease by week for 244 of the 245 patients with laboratory-confirmed Ockelbo disease 1981–8.

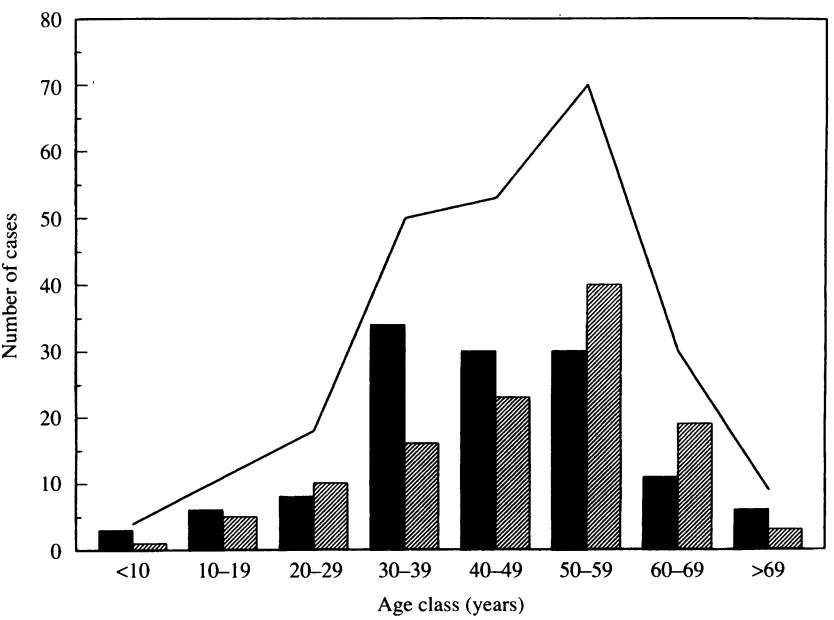

Fig. 3. Age and sex distribution of all patients with laboratory-confirmed Ockelbo disease 1981–8. ■, males; ▨, females; ——, males and females.

infection in this area during a life time. The accumulated risk of being diagnosed (and serologically confirmed) as an Ockelbo disease patient during a lifetime in the same area, is approximately 0·23%. This indicates that there are approximately 20–40 infected persons to each diagnosed case of Ockelbo disease.

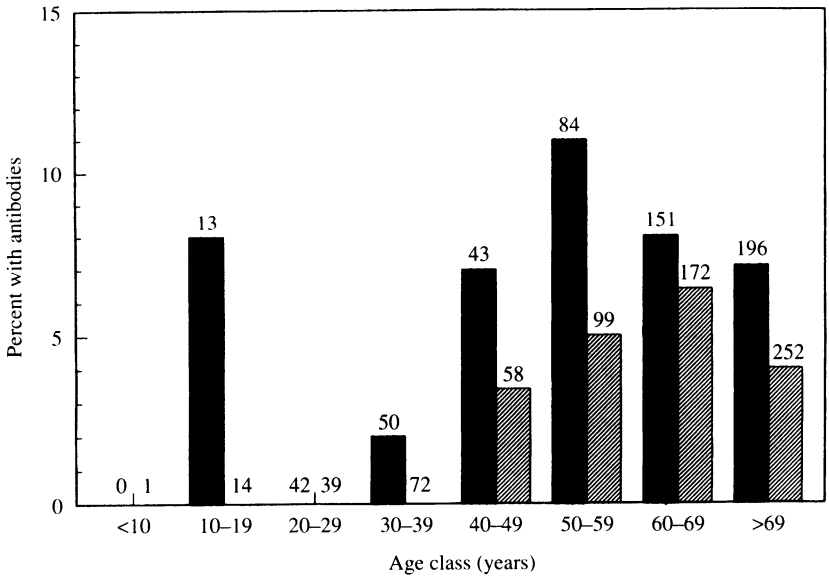

Fig. 4. Age and sex distribution of the population with Ockelbo virus neutralizing antibodies in the main endemic area in Sweden. The number of samples per group is shown above each bar. ■, males; ▨, females.

DISCUSSION

Both incidence of diagnosed Ockelbo disease patients and specific antibody prevalence rates show that the disease occurs mainly in three counties (Kopparberg, Gävleborg and Västernorrland) in central Sweden. However, a number of Ockelbo disease patients were infected outside this area which would indicate that Ockelbo disease occurs at a low frequency in most of Sweden. The concentrated geographical area with increased risk of disease together with the recurrence of Ockelbo disease within a similar area for 8 consecutive years shows that the disease is endemic at least in central Sweden.

Ockelbo disease is a mosquito-borne viral infection [14–16]. The virus has only been isolated from mosquitoes collected in July and August, with the highest rates of infection found in mosquitoes collected in August [14]. The seasonal timing of the disease therefore coincides with the occurrence of infectious mosquitoes.

The season for Ockelbo disease also coincides with the season for picking berries and mushrooms, and for hunting. These popular outdoor activities increase the number of people exposed to mosquitoes. In 1986 and 1987 Swedish national health authorities recommended that people should avoid eating berries and mushrooms due to radioactive contamination following the Chernobyl nuclear plant accident in 1986. The low number of diagnosed Ockelbo disease cases in 1986 and 1987 may thus have been due to the fact that fewer people were exposed to mosquitoes in the main endemic area. Outdoor activities such as mushroom- and berry-picking are very popular mainly among middle-aged people. A difference in the exposure to mosquitoes may therefore explain the increased risk of Ockelbo disease at the age of 30–59 years.

The life-time incidence of diagnosed Ockelbo disease patients in the most

endemic area was 0·23%. In order to compare this incidence with the antibody prevalence rates in the older age groups we must assume that Ockelbo disease does not affect mortality but does induce life-long antibodies detectable by PRN test. The antibody prevalence rates in the oldest age groups were 5–10%. If the above assumptions do not hold true, the ratio of infections per diagnosed case will be higher. An extrapolation from the ratio of infections per recorded case (approximately 30 cases/year) suggests that 600–1200 cases per year occur in Sweden. Although the calculations made above are based on approximations, they indicate the magnitude of Ockelbo infection in Sweden. It remains to be determined whether the clinical presentation in cases not diagnosed and reported are typical, atypical or asymptomatic.

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