

ASPECTS OF THE NATURAL HISTORY OF HERPES ZOSTER

A follow-up investigation of outpatient material

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Herpes zoster is a disease once named Ignis sacer (47). The segmental distribution of the rash was first recognized by Bright in 1831 (11), and the association with sensory ganglia first demonstrated by von Bärensprung in 1862 (16). The other main character, the association with varicella, was first noticed by von Bökay in 1888 (9). Many clinical and epidemiological investigations have later indicated that zoster is evidence of infection with varicella virus (1, 8, 12, 22, 34, 40, 53, 57, 59, 60, 63, 64). Much, however, concerning the pathogenesis of zoster remains unknown.

The prevalence in the total population is reported by Spitzer (55) to be 1:10,000 in Northern England and 1:25,000 in Madras. Dahl (17) gives a higher rate from the county of Viborg 11:10,000 and Hope-Simpson (32) gives 3.4 per thousand persons and McGregor (42) 4.8 per thousand persons concerning regions in England respectively Scotland. Other figures available are for the frequency of zoster in hospital materials consisting of skin diseases, which varies between 0.1 to 1.4 per cent (3, 6, 30, 36, 54). The incidence would probably be much higher if zoster sine herpette also could be added (39).

In most textbooks and papers dealing with the clinical picture of zoster it is pointed out that zoster occurs at all ages, but widely differing opinions are held with regard to further detail of the age distribution. The main opinion is, however, that zoster is a disease of older age. Considering the comprehensive literature on zoster,

comparatively rare attention has been paid to distribution according to age, the localization, prognosis related to sexes etc. The aim of this study was to investigate the actual situation of zoster by means of a follow-up routine.

Material and Method

All patients with zoster who attended the outpatient ward at the Department of Dermatology, Karolinska sjukhuset, Stockholm, during 1958-1967 were sent a questionnaire by post containing questions concerning previous history of chickenpox, age at onset and localization of the disease, the duration of the zoster lesions, the duration and intensity of the pains, relapse, presence of other disease and occurrence of zoster among close relatives.

During the given period of ten years a total of 706 patients (*total group*), 373 men and 333 women, attended the outpatient ward, representing 0.23 and 0.22 per cent respectively of all patients who attended the ward.

The diagnosis was in almost every case clinical, and in only a few cases was virus isolation or serological investigation undertaken.

The material has been processed by a punch-card routine.

Results

Sex and age distribution (age at onset) and localization of the lesions for the *total group* are shown in Table 1 and Figure 1.

Table 2 shows the prevalence of zoster by months.

Answers to the questionnaire were received from 339 persons, 48 per cent (*response group*), 161 men and 178 women. The non-response group thus consisted of 367 persons, of whom 45 were stated to be dead, 158 letters were returned by the postal authorities stamped "addressee unknown", and for 164 no information was received.

Sex and age distribution (age at onset) and localization of the lesions for the *response group* are shown in Table 3. Table 4 shows the duration of the zoster lesions and the occurrence of pain before the outbreak of the zoster lesions. The duration and the intensity of pain are shown in Table 5 and the incidence of postherpetic neuralgia in Table 6. The relapse frequency is given in Table 7 and the incidence of previous chickenpox in Table 8.

Discussion

Age and sex distribution

Zoster may appear at all ages, and the literature contains a number of data on the most usual age at onset. The distribution of the disease between sexes varies somewhat in different reports and is summarized in Table 9.

In the actual material the sex distribution was essentially even, 53 per cent men and 47 per cent women.

Concerning the age distribution most authors are in accord that zoster is a disease of older age. De Moragas and Kierland (44) found among 916 patients 2 per cent under 20 years of age, 13 per cent between 20 and 40, 37 per cent between 40 and 60, 30 per cent between 60 and 70, and 18 per cent over 70 years of age (the percentage calculated by the author). No difference between sexes are given. Söltz-Szöts (58) found among 806 patients 5 per cent younger than 20 years of age, 30 per cent younger than 50, 70 per cent older than 50, and 19 per cent older than 70 years of age. He does not give any difference between sexes either. Also Burgoon *et al.* (14), when correlating the incidence

in various age groups with the population distribution in those age groups of the investigated region state the increasing incidence of the disease with increasing age.

Ballarini (3) and Lang (36) seem to be the first authors who have paid attention to the distinction between men and women concerning the age distribution. In his material of 590 men and 286 women Ballarini found a distribution curve with two distinctly high points, the highest for the age group 10-20 and a less marked for the group 60-70. The curve for men and women follows largely each other, but the first rise is considerable less pronounced among women. Lang found an accumulation during the years of 45 to 65 among women and a more equal distribution among men from 15 to 65, but he also found a peak during the years of 20 to 25, although only among men. Björk (6) in a study of 233 cases found a high incidence for the lower age groups with maximum at 20-29, the rise is not so marked and maximum lies within an older age group than in Ballarini's record. When he divided the material in men and women, the high incidence was also found among men in age group 20 to 29, but the distribution among women was more even in the different age groups. However the female part of the material seems rather small. When he compared his entire material to the age distribution in the total population, on the other hand, he found not only the peak for the age group 20 to 29 but also a peak almost as high for the age group 70 to 79. Burckhardt and Széchy (13) in a study of 142 cases state a uniform distribution for the third to sixth decade among men and a maximum in the sixth decade among women. In a study of 666 cases Hellgren and Hersle (30) found the incidence of onset higher in both sexes in the age groups between 50 and 70 years of age, but there was an additional slight tendency for the incidence to rise between 15-19 years.

As it is shown in Figure 1 there is in the original material of 706 persons a marked difference in the age distribution between men and women. The frequency of young men is greater than young women, with a

peak in the third decade, which resembles that of Björk (6) and Lang (36). Below the age of thirty and forty it was found that $p < 0.001$, and over the age of sixty $0.01 < p < 0.05$. It has not been possible to correlate the studied material with the population distribution of the corresponding age groups in the region.

According to the prevailing theories about the pathogenesis of zoster suggesting that zoster is the clinical response to a second infection with varicella virus in partially immune persons (18) or that it is a reactivation of dormant varicella-zoster virus (32), most children in the first decade will be in the state in which they cannot be considered available for zoster, because they have no latent virus. Yet there are ten children under the age of 10 in this material, the youngest two boys of 1 and 3 and a girl of 2. Even younger ages have been described, the youngest seems apparently being a boy of four days and a girl of three weeks (21, 23, 41, 48, 65).

Localization

In Table 1 is also given the localization of zoster lesions.

As it is shown in the table, there are some obvious differences between the sexes. The engagement of the ophtalmic division is more frequent among young men than among young women ($p > 0.05$), so is also the engagement of the thoracal segments ($0.003 < p < 0.01$). In older age, however, the frequency of thoracic zoster is higher in women than in men ($0.01 < p < 0.05$). Concerning other locations there are no significant differences.

The distribution of the localization of the zoster lesions given by different authors are summerized in Table 10. Although the general tendency is the same some marked differences will be distinguishable. In none of these papers is there any difference mentioned between men and women not even if it is investigated.

In a study of 125 cases Bamford and Boundy (4) state the mean age of patients with cranial nerve involvement to be significantly lower than that of those with

other nerve groups involved. There was no patient over 60 years of age whose cranial nerves were affected. In his study Söltz-Szöts (58) states that among the cases with zoster lesions of the face, 78 per cent were more than 50 years of age.

Seasonal variations

Some reports have suggested a seasonal variation in the incidence of zoster. Ballarini (3) found an increase of zoster cases in the spring and the autumn, and Araki (2) most cases in the spring, less in the autumn and least in the summer and winter. Hellgren and Hersle (30) and Söltz-Szöts (58) on the other hand found an increase in the summer, and about the same frequency in other seasons of the year. Hope-Simpson (32) states that there is no perceptible seasonal effect. In his material zoster occurred in all months, the lowest figures being for March and December and the highest for July, but the differences are without significance. The same statement is given by Burgoon *et al.* (14), Falk (20) and McGregor (42).

In this material there is a peak in September among men but an essentially uniform distribution among women (Table 2).

Response group

Age and sex distribution in the *response group* (339 persons, 161 men and 178 women) does not differ essentially from that of the total group except that there is not the pronounced peak during the third decade among men (Figure 1). The youngest were one boy and one girl of 6 years. The oldest were one man of 87 and one woman of 89 years.

Distribution of localization of the zoster lesions in the response group is the same as that of the total group with one important limitation. The difference between young men and women concerning the engagement of the ophtalmic division and the thoracal segments are canceled, but there is still a perceivable difference among older men and women concerning the thoracal segments ($0.01 < p < 0.05$), Table 3.

Table 1. Total group: Age at onset and localization

Localization	Age at onset														Total							
	0-9		10-19		20-29		30-39		40-49		50-59		60-69		70-79		>80		♂	♀	%	%
	♂	♀	♂	♀	♂	♀	♂	♀	♂	♀	♂	♀	♂	♀	♂	♀	♂	♀				
V: I	—	—	6	1	5	6	4	1	6	12	13	20	26	19	11	19	3	6	74	20	84	25
V: 2, 3, VII	—	1	1	—	4	1	—	1	3	2	6	6	8	6	2	6	—	—	24	6	23	7
C	1	1	6	2	9	5	11	5	10	6	11	11	7	9	3	3	5	1	63	17	43	12
Th	3	3	20	16	35	12	19	10	21	17	20	19	15	29	11	15	—	4	144	39	125	38
L+S	—	—	7	5	8	4	11	8	7	5	8	11	6	9	8	8	—	3	55	15	53	16
Generalization	—	—	—	—	—	—	—	—	—	—	1	—	—	2	—	1	—	1	1	0.3	3	1
No information	1	—	2	—	2	1	1	—	2	1	—	—	1	—	2	—	1	—	12	3	2	1
Total	5	5	42	24	63	29	46	25	49	43	59	67	63	74	37	52	9	14	373	100	333	100
	10	—	66	—	92	—	71	—	92	—	126	—	137	89	—	23	—	706	—	—	—	—

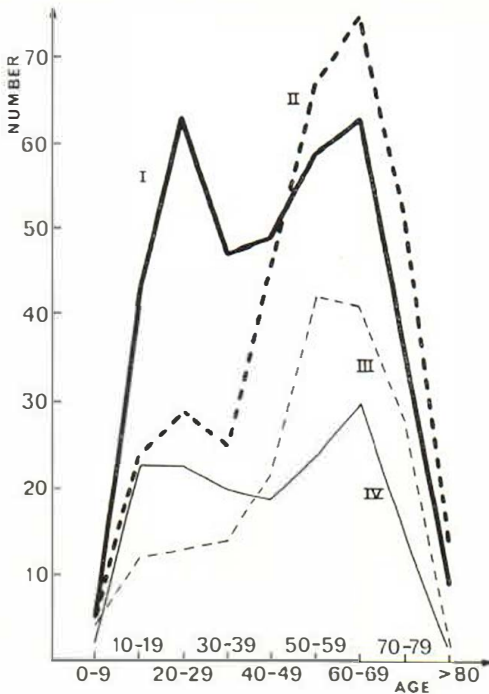


Fig. 1. Distribution of age at onset of zoster. Total group: I=males, II=females. Response group: III=females, IV=males.

Table 2. Total group: Prevalence by months in per cent

	♂	♀
January	8.3	7.2
February	6.4	6.2
March	6.2	8.2
April	7.6	9.7
May	7.5	10.5
June	9.4	9.8
July	9.4	10.7
August	8.4	9.1
September	11.8	7.4
October	7.6	9.5
November	9.8	4.6
December	7.6	7.1

Table 4 shows the duration of zoster vesicles and also gives the incidence of pain before outbreak of the zoster vesicles. 16 per cent stated pains during one or two weeks before the outbreak, and 3 per cent more than two weeks. There was no difference between men and women.

38-337-5619. Acta Derm. 49:6

The intensity of the pain as stated in the answers is presented in Table 5. Among them without pains the majority are men. All intensity-score groups are characterized by preponderance of older women. Those with severe pains had had engagement of the ophtalmic division and thoracal segments more frequent than those without or with only slight pains, these differences are not significant, however.

Table 5 also presents the duration of pain after the outbreak of the zoster vesicles.

Pains more than two months were reported by 14 men (12 per cent), and 31 women (19 per cent). Three of the men were less than 22 years old, ten of them more than 60. Seven had engagement of the ophtalmic division, one of a lower division of the trigeminal nerve, one of cervical segments, three of thoracal and two of lumbo-sacral segments. Twenty of the women were more than 60 years old. In sixteen of the women there was an engagement of the ophtalmic division, in two other trigeminal divisions, in three cervical, in nine thoracal and in only one lumbal segments. Those with severe pains had a significant longer pain duration than those without or with only slight pains. Those with severe pains also had a significant longer duration of the zoster vesicles, and conversely, those with a zoster vesicle duration of more than two weeks had a significant higher incidence of severe pains ($0.01 < p < 0.05$).

Postherpetic neuralgia defined as pains after the zoster vesicles are healed were stated by 68 persons (20 per cent of the response group), 23 men (14 per cent of the men) and 45 women (25 per cent of the women) Table 6.

Burgoon *et al.* (14) found healing of the skin lesions in 57 per cent in two weeks, in 25 per cent in two to four weeks. Postherpetic neuralgia occurred in 10 per cent, three quarters of them older than 60 years. Söltz-Szöts (58) mentions 5 per cent who had pains after the healing of the skin changes and more than six weeks after onset, nearly half of them had the lesions located to the head. Almost everyone were

Table 5. Response group: Intensity and duration (after debate of vesicles) of pain contra age at onset

Intensity:	Age at onset																	Total					
	0-9		10-19		20-29		30-39		40-49		50-59		60-69		70-79		>80						
	♂	♀	♂	♀	♂	♀	♂	♀	♂	♀	♂	♀	♂	♀	♂	♀	♂		♀				
No pain	—	—	8	2	6	—	5	3	5	3	5	3	5	3	6	2	2	1	—	42	26	18	10
Slight	2	2	3	4	6	5	6	2	7	8	6	10	6	10	1	4	1	1	—	38	24	48	27
Moderate	—	—	—	—	1	1	—	1	1	1	2	4	1	4	—	2	—	—	—	4	3	13	7
Severe	—	2	7	4	6	5	7	6	4	8	7	19	14	17	5	11	2	—	2	50	31	74	42
Very severe	—	—	1	—	—	1	—	2	—	1	1	1	4	6	1	8	—	—	7	3	19	11	11
Itching only	—	—	4	1	2	—	1	—	—	—	2	—	1	—	2	—	—	—	12	8	1	0.5	5
No information	—	—	—	1	2	1	2	—	2	—	—	3	—	—	—	—	—	—	8	5	5	2.5	—
Total	2	4	23	12	23	13	21	14	19	21	24	42	32	43	15	27	2	2	161	100	178	100	100
Duration:																							
<1 week	—	1	—	—	1	—	—	—	1	3	1	3	—	3	—	2	—	—	3	3	46	12	39
1-2 weeks	2	2	6	4	6	6	10	5	6	6	6	15	10	6	—	4	—	—	4	4	32	48	22
3-4 weeks	—	1	1	2	—	3	—	2	4	3	3	7	4	12	2	—	—	—	14	14	32	24	22
1-2 months	—	—	—	—	4	2	3	3	1	4	4	3	4	8	1	4	—	—	17	17	24	24	21
3-12 months	—	—	1	1	—	—	—	—	—	1	1	2	2	2	2	5	—	—	6	6	11	11	—
>1 years	—	—	—	—	1	—	—	1	—	1	—	4	3	4	2	7	1	—	7	7	17	12	—
No information	—	—	3	1	1	1	—	—	—	—	1	3	1	2	—	3	—	—	6	6	10	6	—
Total	2	4	11	8	13	12	13	11	12	18	16	37	24	37	7	25	1	2	99	100	154	100	100

Table 6. *Response group: Incidence of postherpetic neuralgia contra age at onset*

Age at onset	♂	♀	Total
0-9	—	—	—
10-19	2	2	4
20-29	3	1	4
30-39	—	5	5
40-49	1	6	7
50-59	5	9	14
60-69	7	9	16
70-79	4	13	17
> 80	1	—	1
Total	22	45	68

more than 60 years old. According to Burckhardt and Széchy (13) there was in their material 8 per cent with postherpetic neuralgia, 6 per cent of the patients under 40 and 9 per cent of those over 40 years old. In all but one case the pain did not last longer than six months. Bamford and Boundy (4) state postherpetic neuralgia in 21 per cent. It was rare in persons under 40 years but occurred in about 30 per cent above that age.

As the age increased, the number of patients in the material studied by de Moragas and Kierland (44) without pain diminished from 83 per cent in the age group less than 20 years to 9 per cent in the age group of 70 years or more. Simultaneously, the duration and severity of the postherpetic neuralgia increased from 4 per cent with pain for more than one year in the age group less than 20 years, to 48 per cent of patients in the age group of 70 years or more. The percentage of patients with pain for one month or more increased in direct proportion to the age.

As zoster occurs for the most part in grown-up or older people, a history relating to previous chickenpox is often unobtainable. In cases of zoster occurring in children, for whom information of this kind was more reliable, a history of previous chickenpox has been reported to obtain in over 70 per cent (43). Hope-Simpson (32) means that in the third decade of age almost all have experienced an attack of varicella. In this response group, 164 per-

sons (48 per cent) Table 8 gave an answer of a previous attack of chickenpox.

Incidence of chickenpox in close time relation to the zoster attack was stated by twelve persons in the response group. In human inoculation experiments there have been demonstrated a period of seven to fourteen days elapsing between the injection of herpes fluid and the production of a reaction (34) or exposition to chickenpox and the outbreak of zoster lesions (9, 24).

Relapses

An attack of herpes zoster is often considered to give rise to permanent immunity, so that subsequent attacks should be very rare. The supposition has according to many authors been a failing state of immunity because of other diseases. There are several reports of single zoster relapses in various material studied (13, 38, 51, 56, 62). Burgoon *et al.* (14) describe two cases among 206, Seiler (53) five among 184, Head and Campbell (28) three among 400, and Hope-Simpson (32) nine among 192 studied cases.

In the response group of this material as much as 26 persons (8 per cent) stated more than one attack of zoster, Table 7. Of these only 4 were men and 22 were women, most of them older than 50 years. Two of the women had two attacks, two had three attacks and one had four attacks. No men had more than two attacks. The time between the first and second attack is also presented in Table 7. In half of the cases there were a delay of more than ten years.

In half of the relapse cases the subsequent attack occurred in the dermatomes previously affected. The same relation was found by Hope-Simpson (32), who also states that the odds against this being a chance findings are very high. Of course it is very important in every case with a relapse to be sure it is not a zosteriform Herpes simplex (10, 37).

Heredity?

Zoster among the close relatives were reported by 91 persons (27 per cent), 35

Table 7. Response group: Incidence and localization of relapses contra age at onset

	Age at onset														Total						
	0-9		10-19		20-29		30-39		40-49		50-59		60-69			70-79		>80			
Relapse(s)	♂	♀	♂	♀	♂	♀	♂	♀	♂	♀	♂	♀	♂	♀	♂	♀	♂	♀	♂	♀	
2 or more	—	—	—	—	1	1	—	—	1	1	—	—	5	1	4	—	—	—	—	—	16
	—	—	—	—	1	—	—	—	—	1	—	—	1	—	1	—	—	—	—	—	6
Relapse within 2 years	—	—	—	—	2	1	1	3	1	2	—	—	6	1	5	—	—	—	—	—	22
2-10 years	—	—	—	—	1	1	—	—	—	—	—	—	—	—	—	—	—	—	—	—	4
> 10 years	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	5
No information about interval	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	5
	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	2
Relapse in the same dermatomes	—	—	—	—	2	1	1	3	1	2	—	—	6	1	5	—	—	—	—	—	4
not in the same dermatomes	—	—	—	—	1	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	22
	—	—	—	—	1	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	4
	—	—	—	—	1	1	—	—	—	—	—	—	—	—	—	—	—	—	—	—	5
	—	—	—	—	2	1	1	3	1	2	—	—	6	1	5	—	—	—	—	—	22
	—	—	—	—	1	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	4
	—	—	—	—	1	1	—	—	—	—	—	—	—	—	—	—	—	—	—	—	5
	—	—	—	—	1	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	5
	—	—	—	—	2	1	1	3	1	2	—	—	6	1	5	—	—	—	—	—	22
	—	—	—	—	1	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	4
	—	—	—	—	1	1	—	—	—	—	—	—	—	—	—	—	—	—	—	—	5
	—	—	—	—	2	1	1	3	1	2	—	—	6	1	5	—	—	—	—	—	22
	—	—	—	—	1	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	4
	—	—	—	—	1	1	—	—	—	—	—	—	—	—	—	—	—	—	—	—	5
	—	—	—	—	2	1	1	3	1	2	—	—	6	1	5	—	—	—	—	—	22
	—	—	—	—	1	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	4
	—	—	—	—	1	1	—	—	—	—	—	—	—	—	—	—	—	—	—	—	5
	—	—	—	—	2	1	1	3	1	2	—	—	6	1	5	—	—	—	—	—	22

Table 8. *Response group: Incidence of previous chickenpox*

Time between chickenpox and zoster	♂	♀	Total
Within 5 years	1	3	4
6-9	6	11	17
10-19	16	11	27
20-29	10	9	19
30-39	3	15	18
40-49	7	19	26
50-59	5	11	16
60-69	5	6	11
>70	—	2	2
No information about interval	13	11	24
	66	98	164

Table 9. *Distribution of Herpes zoster between sexes in different reports*

	Males	Females
Ballarini 1936 (3)	67 per cent	33 per cent
Burckhardt <i>et al.</i> 1954 (13)	63	37
Araki 1937 (2)	56	44
Hellgren <i>et al.</i> 1966 (30)	56	44
Burgoon <i>et al.</i> 1957 (14)	51	49
de Moragas <i>et al.</i> 1957 (44)	51	49
Hochleitner 1960 (31)	48	52
Lang 1938 (36)	47	53
Söltz-Szöts 1965 (58)	47	53
Actual material	53	47

Table 10. *Distribution of localization of zoster lesions in different reports, in per cent*

	V:1	Localization					S
		V:2, 3 VII	C	Th	L		
Ballarini 1936 (3)	15	—	19	48	3	—	5
Hellgren <i>et al.</i> 1966 (30)	20	—	17	45	—	27	—
Hochleitner 1960 (31)	26	4	21	33	14	—	3
Hope-Simpson 1965 (32)*	9	6	15	54	13	—	3
Rook <i>et al.</i> 1968 (49)	—	15	20	53	—	11	—
Söltz-Szöts 1965 (58)	30	7	6	29	—	27	—
Actual material	23	7	15	38	—	15	—

* the percentage calculated by the author

men (22 per cent of the men) and 56 women (31 per cent of the women). No marked accumulation was found in any age group. Among the men 13 of the relatives had been males and 28 females, and among the women 17 had been males and 49 females. Among 7 of the men and 13 of the women there had been more than one member of the family who once had had zoster attack. The incidence of zoster among close relatives was thus very high, and more pronounced among women. This was an unexpected finding. However, it is not possible on the basis of a disease having a familiar manifestation to postulate heredity.

Systemic disease

The factors determining the development of zoster are usually unknown, but some systemic diseases are associated with a significantly increased incidence (26, 49). Wright and Winer (66) found that zoster occurred in 0.22 per cent of patients admitted with non-malignant conditions, but in 0.85 per cent of those with malignant diseases. The high incidence in the lymphomas is believed to be due to an impaired antibody response (15, 25, 27). Nordén and Swahn (46) have described cases of chronic lymphatic leukemia complicated by zoster all having hypogammaglobulinaemia. In patients with other malignant diseases antimitotic drugs and other therapeutic agents may be partially responsible for the increased incidence of zoster (49, 50, 52).

In the studied material there were 39 persons (6 per cent of the total group) with malignant diseases known at the time for the zoster attack or afterwards. Thirteen were men, seven of them over 60 years of age, and twenty-six were women, eighteen of them over 60 years of age. Eight of the men and five of the women had engagement of the reticuloendothelial and lymphoid system (Hodgkin's disease, leukemia, lymphosarcoma, reticulocellsarcoma). Six of the women had mammary cancer and nine genital cancer. Only four of the men and eleven of the women an-

swered the questionnaire. This group with malignant diseases are small as compared with the total and response groups, but there are no striking discrepancies between the groups concerning the localization of the zoster lesions or the intensity or duration of the pains as compared with the corresponding age groups.

Trauma as a noncausal trigger factor to precipitate zoster have been discussed by several authors (7, 33, 61). One case, a man of 24, will illustrate this phenomenon. He developed zoster lesions at just the same place as molluscum contagiosum had been treated by curettage two months earlier. As a whole six persons in the response group mentioned connection with trauma.

Other aspects on the pathogenesis of zoster in view of the answers in the questionnaire will be presented elsewhere (19).

There is no specific treatment for zoster. Therapy is symptomatic and is directed at relief of local discomfort and the control of secondary infection (29, 35, 45, 49, 58). The patients studied in this investigation have been treated in that way with different local remedies to prevent secondary infection and with analgesics. In about one third of the cases vitamins of the B group but in no cases systemic steroids have been prescribed. A critical evaluation of therapeutic approaches to the treatment of zoster is difficult because of the self-limited and variable nature of the acute process, as has been indicated in this paper.

SUMMARY

A follow-up investigation of an outpatient material with herpes zoster was carried out. The 10-year period covered by the investigation was from 1958 to 1967. The material consisted of 706 persons, 373 men and 333 women, who were sent a questionnaire concerning the duration of the zoster lesions, the duration and intensity of pain, relapse frequency, history of previous chickenpox, any concomitant disease and heredity. Answers were received from 339 persons 48 per cent, 161 men and 178 women.

The entire material was analyzed with regard to age at onset and localization of the lesions. In 34 per cent the onset was before 40 years of age, and in 35 per cent after 60 years of age. Youngest were three children under three years of age. In the age group under 40 years of age the frequency of zoster among women was only half of that among men. In older age groups there was a slight higher frequency of women than men. 25 per cent showed engagement of the ophtalmic division of the trigeminal nerve, 7 per cent of the other divisions and the facial nerve, 15 per cent of the cervical segments, 38 per cent of the thoracal, and 15 per cent of the lumbo-sacral segments. In 0.5 per cent the disease was generalized. The engagement of the ophtalmic division and of the thoracal segments was more frequent among young men than young women. In older age the frequency of thoracic zoster was higher in women than in men.

No seasonal variations were found.

In 30 per cent the duration of the zoster vesicles was less than two weeks, in 37 per cent three to four weeks, and in 24 per cent more than four weeks. In 16 per cent there had been pains during one or two weeks before the outbreak, and in 3 per cent in more than two weeks. No difference between men and women. 26 per cent of the men and 10 per cent of the women had no pains at all, 27 per cent of the men and 34 per cent of the women had slight or moderate pains, 36 per cent of the men and 53 per cent of the women had severe or very severe pains. All intensity-score groups were characterized by proponderance of older women. Pains less than two weeks after the outbreak of the vesicles were found in 35 per cent of the men and 34 per cent of the women, in two to four weeks in 11 per cent of the men and 19 per cent of the women. Pains more than two months occurred in 9 per cent of the men and 17 per cent of the women. Half of both men and women had an engagement of the ophtalmic division. Post-herpetic neuralgia were stated by 14 per cent of the men and 25 per cent of the women.

Cases with severe pains had a longer duration of pains and also a longer duration of vesicles than those without or with only slight pains. Those with a vesicle duration of more than two weeks had a higher incidence of severe pains.

More than one zoster attack were found in 8 per cent, most of whom were women, in half of the cases with a delay of more than ten years. The subsequent attack occurred in the dermatomes previously affected in half of the cases.

In 22 per cent of the men and 31 per cent of the women zoster had occurred among close relatives, of whom 72 per cent women.

In the whole material 6 per cent suffered a known malignant disease.

REFERENCES

1. Abrahamson, A. W.: Varicella and Herpes zoster: An experiment. *Brit. med. J.* 1: 812, 1944.
2. Araki, S.: *Jap. J. Dermat. Urol.* 97, 1937. Ref. in Seelentag, W.: Herpes zoster und Röntgenbestrahlung. Ein Beitrag zur Zoster-Ätiologie. *Strahlentherapie* 98: 582, 1955.
3. Ballarini, M.: Ricerche cliniche sulla topografia dell'Herpes zoster. *Arch. ital. Derm.* 12: 3, 1936. Ref. in *Zbl. Haut- u. Geschl.-Kr.* 55: 464, 1937.
4. Bamford, J. A. C., Boundy, C. A. P.: The natural history of Herpes zoster (Shingles). *Med. J. Aust.* 55: 524, 1968.
5. Bieling, R.: Die zwei Typen des Herpes zoster. *Dtsch. med. Wschr.* 77: 1611, 1952.
6. Björk, Å.: The incidence of zoster, particularly zoster ophtalmicus. *Acta dermat.-venereol.* 30: 34, 1950.
7. Blank, H.: Virus diseases affecting the skin. *Acta dermat.-venereol.* 29: 77, 1949.
8. Blank, H., Rake, G.: *Viral and rickettsial diseases of the skin, eye and mucous membranes of man.* Boston and Toronto: Little, Brown et Comp., p. 71, 1955.
9. Bókay, I. v.: Über den ätiologischen Zusammenhang der Varicellen mit gewissen Fällen von Herpes Zoster. *Wien. klin. Wschr.* 39: 1323, 1909.
10. Bremer-Anderson, E.: Diagnostic importance of punch biopsy and cytologic examination in herpes zoster and herpes simplex. *Acta dermat.-venereol.* 45: 262, 1965.
11. Bright, R.: Reports of Medical Cases [Lon-

- don) 2, pt I: 383, 1831. Cit. by Hope-Simpson, R. E.: The nature of herpes zoster. *Proc. roy. Soc. Med. (London)* 58: 9, 1965.
12. Bruusgaard, E.: The mutual relation between zoster and varicella. *Brit. J. Derm.* 44: 1, 1932.
 13. Burckhardt, W., Széchy, H. v.: Beobachtungen über den Verlauf und Bemerkungen über die Therapie des Herpes zoster. *Dermatologica* 108: 295, 1954.
 14. Burgoon, C. F., Jr., Burgoon, J. S., Baldridge, G. D.: The natural history of herpes zoster. *J. Amer. med. Ass.* 164: 265, 1957.
 15. Bäfverstedt, B.: Herpes zoster generalisatus und leukämische Lymphadenose. *Acta dermat.-venereol.* 21: 60, 1940.
 16. Bärensprung, F. v.: Die Gürtelkrankheiten. *Ann. d. Charité-Krankenhause*, Bd 10: 57, 1862. Cit. by Hope-Simpson, R. E.: The nature of herpes zoster. *Proc. roy. Soc. Med. (London)* 58: 9, 1965.
 17. Dahl, S.: Herpes zoster, speziell im Hinblick auf mögliche Ansteckungswege. *Schweiz. med. Wschr.* 79: 436, 1949.
 18. Downie, A. W.: Chickenpox and zoster. *Brit. med. Bull.* 15: 197, 1959.
 19. Engström, J., Molin, L.: To be published.
 20. Falk, C. A.: Die Herpes Zoster und Pityriasis rosea-Fälle an der männlichen Hautpoliklinik des St. Göran in den Jahren 1931 bis 1935. *Acta dermat.-venereol.* 24: 271, 1944.
 21. Feldman, G. V.: Herpes zoster in a newborn. *Arch. Dis. Child.* 27: 126, 1952.
 22. Feyrter, F.: Über den Zoster. *Hautarzt* 5: 391, 1954.
 23. Freund, P., Rook, G. D., Gurian, S.: Herpes zoster in the Newborn. *Amer. J. Dis. Child.* 64: 895, 1942.
 24. Goldberg, L. C.: A clinical note on herpes zoster. *Arch. Derm. (Chicago)* 78: 392, 1958.
 25. Hallgren, B. E.: Herpes zoster och leukämi. *Nord. Med.* 44: 1475, 1950.
 26. Hauser, W.: Zum Problem der Lokalisation des Herpes Zoster. *Arch. klin. exp. Derm.* 222: 149, 1965.
 27. Hayhoe, F. G. J.: *Leukemia, research and clinical practice.* J. & A. Churchill Ltd., London, p. 265, 1960.
 28. Head, H., Campbell, A. W.: The pathology of herpes zoster and its bearing on sensory localization. *Brain* 23: 353, 1900.
 29. Hellerström, S.: *Hudsjukdomar.* Håkan Ohlsson, Lund, p. 270, 1962.
 30. Hellgren, L., Hersle, K.: A statistical and clinical study of Herpes zoster. *Geront. clin.* 8: 70, 1966.
 31. Hochleitner, H.: Beitrag zum Zosterproblemen. *Derm. Wschr.* 142: 1049, 1960.
 32. Hope-Simpson, R. E.: The nature of herpes zoster: a long-term study and a new hypothesis. *Proc. roy. Soc. Med. (London)* 58: 9, 1965.
 33. Klauder, J. V.: Herpes zoster appearing after trauma. *J. Amer. med. Ass.* 134: 245, 1947.
 34. Kundratitz, K.: Experimentelle Übertragung von Herpes zoster auf den Menschen und die Beziehung von Herpes zoster zu Varicellen. *Z. Kinderheilk.* 29: 516, 1925.
 35. *Lancet*, Ed. Annotation on Shingles. 1: 1242, 1968.
 36. Lang, J.: Über die Häufigkeit des Herpes zoster. *Arch. Derm. Syph.* 176: 515, 1938.
 37. Lausecker, H.: Über seltene Zosterformen. *Med. Klin.* 1: 149, 1952.
 38. Leurer, J.: A case of recurrent herpes zoster. *Brit. J. Derm.* 69: 282, 1957.
 39. Lewis, G. W.: Zoster sine herpette. *Brit. med. J.* 2: 418, 1958.
 40. Lipschütz, B., Kundratitz, K.: Über die Ätiologie des Zoster und über seine Beziehungen zu Varizellen. *Wien. klin. Wschr.* 38: 499, 1925.
 41. Lomer, A.: Herpes zoster bei einem 4 Tage alten Kinder. *Zbl. Gynäk.* 45: 778, 1889. Cit. by Hope-Simpson, R. E.: The nature of herpes zoster. *Proc. roy. Soc. med. (London)* 58: 9, 1965.
 42. McGregor, R. M.: Herpes zoster, chickenpox, and cancer in general practice. *Brit. med. J.* i: 84, 1957.
 43. Medical Research Council: Spec. Rep. Ser. med. Res. Coun., London No 227: 181, 1938. Cit. by Downie, A. W.: Chickenpox and zoster. *Brit. med. Bull.* 15: 197, 1959.
 44. Moragas, J. M. de, Kierland, R. R.: The outcome of patients with herpes zoster. *Arch. Derm. (Chicago)* 75: 193, 1957.
 45. Nasemann, Th.: Die Therapie der Viruskrankheiten der Haut. *Hautarzt* 6: 385, 1955.
 46. Nordén, A., Swahn, B.: Herpes zoster—Varicellae in cases of Leukemia. *Acta med. scand.* 170: 739, 1961.
 47. Plinii Secundi, C.: *Naturalis historia lib.* Bd. 26, cap. XI, p. 480. Frodenbuck, Basel. Cit. by Schönfeld, W.: Zoster und Herpes simplex. In *Handbuch der Haut- u. Geschlechtskrankheiten* von J. Jadassohn, Verlag von Julius Springer, Berlin, Bd VII: 1, p. 1, 1928.

48. Poulsen, P. A.: Zoster ophthalmicus. Report of a case in a child of 15 month. *Acta med. scand.* 151: 131, 1955.
49. Rook, A., Wilkinson, D. S., Ebling, F. J. G., ed.: *Textbook of Dermatology*. Blackwell Scientific Publications. Oxford and Edinburgh, p. 763, 1968.
50. Rube, W.: Herpes zoster nach Röntgenbestrahlung. *Strahlentherapie* 97: 297, 1955.
51. Sayer, A.: Recurrent herpes zoster (femoralis). *Arch. Derm. Syph. (Chicago)* 33: 348, 1936.
52. Seelentag, W.: Herpes zoster und Röntgenbestrahlung. Ein Beitrag zur Zoster-Ätiologie. *Strahlentherapie* 98: 582, 1955.
53. Seiler, H. E.: Study of herpes zoster particularly in its relationship to chickenpox. *J. Hyg. (London)* 27: 253, 1949.
54. Serve, H.: Dissertation, München, 1951. Ref. in Seelentag, W.: Herpes zoster und Röntgenbestrahlung. Ein Beitrag zur Zoster-Ätiologie. *Strahlentherapie* 98: 582, 1955.
55. Spitzer, R.: Geographische Verteilung der Hautkrankheiten. In *Handbuch der Haut- und Geschlechtskrankheiten* von J. Jadassohn, Bd XIV, Teil 2, p. 301, Berlin, Springer, 1928.
56. Stern, L. S.: The mechanism of herpes zoster. *Brit. J. Derm.* 49: 263, 1937.
57. Strandberg, J.: The question as to the relationship between herpes zoster and varicella. *Acta dermat.-venereol.* 21: 401, 1940.
58. Söltz-Szöts, J.: Kritische Bemerkungen zur Klinik und Therapie des Herpes zoster. *Z. Haut- u. Geschl.-Kr.* 38: 123, 1965.
59. Tappeiner, J., Wolff, K.: Zoster. In *Infektionskrankheiten und ihrer Erreger*. Bd 10. Gustav Fischer Verlag, Jena, 1968.
60. Taylor-Robinson, D., Downie, A. W.: Chickenpox and herpes zoster. I. Complement fixation studies. *Brit. J. exp. Path.* 40: 398, 1959.
61. Tottie, M.: Trauma and herpes zoster. *Acta dermat.-venereol.* 31: 275, 1951.
62. Touraine, A., Golé, L.: Zona redux. *Bull. Soc. franc. Derm. Syph.* 42: 498, 1935.
63. Weller, T. H., Coons, A. H.: Fluorescent antibody studies with agents of varicella and herpes zoster propagated *in vitro*. *Proc. Soc. exp. Biol. (New York)* 86: 789, 1954.
64. Weller, T. H., Witton, H. M.: The etiologic agents of varicella and herpes zoster. Serological studies with the viruses as propagated *in vitro*. *J. exp. med.* 108: 869, 1958.
65. Winkelmann, R. K., Perry, H. O.: Herpes zoster in children. *J. Amer. med. Ass.* 171: 876, 1959.
66. Wright, E. T., Winer, L. H.: Herpes zoster and malignancy. *Arch. Derm. Syph. (Chicago)* 84: 242, 1961.