

A STUDY OF HERPES ZOSTER PARTICULARLY IN ITS RELATIONSHIP TO CHICKENPOX

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INTRODUCTION

Since von Bokay (1909) first suggested an association between herpes zoster and chickenpox efforts have been made to prove the relationship between the two diseases in three main ways: by inoculation experiments, from immunity reactions and on epidemiological and clinical grounds. Thus Lipschutz & Kundratitz (1925) and Bruusgaard (1932), in human inoculation experiments with herpes zoster vesicular fluid, were able to obtain positive results in a proportion of their cases either in the form of a local reaction or by the production of a generalized vesicular eruption indistinguishable from chickenpox. Other workers, however, have carried out similar experiments with negative results (Lauda & Silberstern, 1925; Glaubersohn & Villfand, 1929).

Again, attempts have been made to show a relationship between herpes zoster and chickenpox by the study of serological reactions. Netter & Urbain (1924) found that convalescent serum from herpes zoster or chickenpox patients fixed, in the presence of complement, an antigen of saline extract of crusts obtained from either herpes zoster or chickenpox cases. Brain (1933) obtained a similar cross-fixation using vesicle fluid as antigen, but these results were not confirmed by Thomsen (1934) or Hassko, Vamos & Thoroczky (1938). Amies (1934) found a measure of cross-agglutination of elementary bodies and serum from patients with chickenpox and herpes zoster.

Lastly, evidence in support of the relationship between the two diseases has been adduced from the occurrence of chickenpox among herpes zoster contacts, and less commonly herpes zoster among chickenpox contacts. Numerous instances of such an association in individual cases have been recorded, while a similar association has been found in published studies of groups of cases in institutions ('Epidemics in Schools', 1938; Smith, 1931). It has been argued, however, that these occurrences are fortuitous, and Dahl (1946) has strongly supported this view on clinical and epidemiological grounds. More recently, the electron microscope has allowed a new approach to the problem, and morphological studies of the viruses of varicella and zoster have been carried out by Nagler & Rake (1948) and

Farrant & O'Connor (1949). The results, while generally supporting the identity of the two viruses, cannot be regarded as conclusive.

There are at present, therefore, two main views on the question of the relationship between herpes zoster and chickenpox. One that the two diseases are separate and distinct entities due to different causal agents, the other that in all, or at least in a proportion of instances, zoster and chickenpox are only different manifestations of infection by the same virus.

Herpes zoster is not a notifiable disease, and therefore most records have referred to individual patients or have been studies of cases occurring in hospitals or institutions. Patients attending hospital may not be representative of the disease in the general population, because it is recognized that only a comparatively small proportion attend in this way. This fact, which was commented upon by von Bokay (1928), is illustrated by the patients reviewed in this paper, only 16% of whom had attended as in-patients or out-patients at hospitals in Edinburgh.

Cowie (1925) carried out an inquiry among 813 notified cases of chickenpox, and found only nine, or 1.1%, with a history of previous association with herpes zoster. No other large field survey has been reported.

PRESENT INVESTIGATION

The present investigation was undertaken, therefore, to collect information on herpes zoster as it occurs in the population as a whole, and in this way to attempt to ascertain the incidence of the disease, its epidemiological features, and in particular its relationship to chickenpox.

General practitioners in the city were asked to co-operate by intimating cases of herpes zoster coming to their notice, and similar information was requested for patients attending hospital. A special form was drawn up and the doctors were asked to complete this form or, alternatively, to permit the necessary details being obtained by visitation of their patients. For reasons which can be readily appreciated an investigation on these lines is attended by difficulties, and a complete record of herpes zoster in the city was not achieved. It is believed,

however, that most of the information obtained is applicable to the population as a whole.

General incidence. The inquiry commenced in January 1947 and ended in June 1948—a period of 18 months. During this time 246 cases of herpes zoster were reported: 145 in 1947 and 101 in the first 6 months of 1948. It is calculated that the patients in 1947 represented the incidence of the disease in 15% and those in 1948 in 20% of the total medical practices in Edinburgh. If these practices—and they covered all areas in the city—be accepted as a sample of all practices in Edinburgh then approximately 970 cases of herpes zoster occurred in 1947, or 2 per 1000 of the population, and approximately 500 cases in the first 6 months of 1948. These figures suggest little difference in incidence in the 2 years.

The great majority of the patients were reported by general practitioners, only 28 being hospital notifications. Some of those intimated by their family doctors had, in addition, been referred for hospital advice, but from the information available only 16% of the patients attended in this way.

alone accounting for more than half the cases. There was no preference for either side of the body, the right being involved in 93 and the left in 91 patients.

Herpes generalisatus. A general vesicular eruption in association with herpes zoster occurred in 7, or 3.8%. The number of vesicles in 4 patients was sparse, only a dozen or more being noted, but in 3 a more widespread eruption was present. The relevant features are summarized, for convenience, in Table 2.

There was no sex distinction and no evidence that the generalized rash was more common in zoster of any particular site. The aberrant vesicles were noticed either simultaneously with the local zoster eruption, or within a few days of its appearance. Only in one case were they delayed as long as 7 days. This is in accordance with most published records. The previous history as regards chickenpox in most was doubtful, but one patient had definitely suffered from this condition in childhood, well-marked scars remaining.

None of the patients gave a history of association

Table 1. Percentage distribution of herpes zoster patients according to sex and in relation to area affected

Area affected	Males		Females		All cases	
	No.	Percentage	No.	Percentage	No.	Percentage
Supra-orbital	12	14.6	15	14.7	27	14.7
Facial	1	1.2	—	—	1	0.5
Cervical	20	24.4	17	16.7	37	20.1
Dorsal	40	48.8	58	56.9	98	53.3
Lumbar	6	7.3	11	10.8	17	9.2
Sacral	3	3.7	1	0.9	4	2.2
Total	82	100.0	102	100.0	184	100.0

As full investigation and observation were not possible in all cases the facts which follow are based for the most part on 184 patients who, through the courtesy of their doctors, were visited by the author and 'followed up' for a period of 3 months or longer.

There was no intentional selection of the patients described in the paper. Some of those notified by their doctors were not visited at the doctor's own request and, therefore, full details regarding them were not ascertained. In others notification was received some considerable time after the occurrence of the illness and it was felt that it would be undesirable to pay a visit. These again, therefore, did not have sufficient information to warrant their inclusion in the 184 cases. There was no evidence that any selection as regards age, sex or social class resulted.

CLASSIFICATION

The anatomical distribution of the herpetic eruption is shown according to sex in Table 1.

The dorsal, cervical and supra-orbital regions were affected in 88% of the patients, the dorsal region

with chickenpox before the onset of herpes zoster and only one case was related to the occurrence of a chickenpox condition in a contact.

Recurrent herpes zoster. A history of a previous attack of herpes zoster was given in 6, or 3.3%, of the patients. Information regarding these is given in Table 3.

Apart from one case in which the previous attack of herpes zoster occurred 7 years earlier, a period of 20 years or more elapsed between the two occurrences.

One patient suffered from advanced rheumatoid arthritis, chiefly affecting the small joints, but the others showed no clinical signs suggesting disease of the spine.

Motor paralysis. Motor paralysis occurred in only one case. The patient, a woman of 63, suffered from herpes zoster of the right upper lumbar region, and she developed paralysis of the quadriceps and adductor groups of muscles on the affected side. She suffered from osteo-arthritis, X-ray examination showing advanced disease of the lower dorsal spine. This patient died from cerebral thrombosis some 18 months after the onset of herpes zoster.

Table 2. *Generalized herpes zoster. Summary of cases*

Case	Age	Sex	Occupation	Site of herpes zoster	Month and year of onset	Period between local and general eruptions	Previous history of chickenpox	Nature of eruption
30	67	M.	Retired furnaceman	Cervical	April 1947	4 days	? Yes	Very widespread
31	52	F.	Housewife	Lumbar	April 1947	7 days	? No	Sparse
43	62	F.	Housewife	Supra-orbital	May 1947	Same time	? No	Widespread
46	66	F.	Housewife	Supra-orbital	May 1947	Indefinite	Unknown	Sparse
84	58	F.	Housewife	Upper dorsal	September 1947	4 days	Unknown	Widespread
111	40	M.	Ropemaker	Mid-dorsal	November 1947	Same time	Yes	Sparse
179	35	M.	Shop assistant	Lower dorsal	1948	Same time	Unknown	Sparse

Table 3. *Recurrent herpes zoster. Summary of cases*

Case	Age	Sex	Approximate site of herpes zoster		Period between attacks (years)	Previous history of chickenpox	Remarks
			Present attack	Previous attack			
4	68	M.	3rd left cervical	4th left dorsal	25	No	Scars of previous herpes zoster present
22	67	F.	2nd right sacral	11th right dorsal	20	Yes	—
28	51	F.	12th left dorsal	3rd left cervical	23	Unknown	—
44	70	F.	1st left dorsal	7th left dorsal	20	Unknown	Scars of previous herpes zoster present. Advanced rheumatoid arthritis
51	52	F.	4th right cervical	4th right dorsal	7	Unknown	—
153	60	M.	7th right dorsal	Lower dorsal? side	40	Unknown	—

Associated conditions. Herpes zoster is now generally regarded as a disease of virus origin but many cases have been described in which it appeared to arise in association with some other disease or circumstance. Careful inquiry showed that the majority of the patients included in this study were apparently well at the onset of the zoster condition, gave no clinical evidence of other disease and revealed no previous medical history which could be considered of aetiological significance. A number, however, had some disease or other condition associated with the onset of herpes zoster.

Associated disease. Twenty-seven patients suffered from some pathological condition at the time they developed herpes zoster, as follows: rheumatoid arthritis, 10; duodenal ulcer, 4; chronic bronchitis and asthma, 3; diabetes, 2; neurasthenia, 2; psoriasis, 1; oesophageal stricture of nervous origin, 1; nervous dyspepsia, 1; mitral stenosis, 1; pernicious anaemia, 1; and otitis media, 1.

In addition 1 patient had suffered some months previously from a condition diagnosed as alcoholic polyneuritis, and another developed zoster in the neighbourhood of a scar resulting from an operation for removal of a malignant condition of the breast 8 months previously.

Trauma. Only 5 patients gave a history of recent injury prior to the onset of herpes zoster. One had received a blow on the forehead 3 days before the

development of supra-orbital zoster in this region. Another, also a case of supra-orbital zoster, complained of injury to the eye 'by a fly' 3 days before the onset of the condition. A third patient gave a history of a severe blow to the chest followed 3 days later by herpes zoster of the 7th dorsal segment on the same side as the injury, while two others gave rather indefinite histories of injury to the back followed by herpes zoster of the thorax, the one 10 days and the other 2-3 weeks later.

Pregnancy. Two patients developed herpes zoster in relation to pregnancy, one 12 days after the birth of her child, and the other when 7 months pregnant. The children of both patients were apparently healthy and suffered from no obvious abnormality. Disease or other conditions did not seem to play an important part in the aetiology of herpes zoster.

EPIDEMIOLOGICAL FEATURES

Seasonal incidence. The dates of sickening of the 246 patients reported during the 18 months covered by this study are given in Table 4.

A somewhat different trend is shown in the two periods. The number of herpes zoster cases in 1947 increased from the beginning of the year to May, fell thereafter, to rise again in October and then diminished to the end of the year. Two peaks of higher incidence were observed, the one in May and

Table 4. *Incidence of herpes zoster by months*

Year	Jan.	Feb.	Mar.	Apr.	May	June	July	Aug.	Sept.	Oct.	Nov.	Dec.	Not stated	Total
1947	5 (233)	7 (230)	15 (220)	13 (133)	21 (149)	11 (210)	9 —	12 (10)	10 (32)	20 (73)	14 (103)	8 (201)	—	145
1948 (6 months)	19 (235)	19 (176)	20 (161)	16 (141)	16 (99)	9 (80)	—	—	—	—	—	—	2	101

Cases of chickenpox among school children in Edinburgh in brackets.

Table 5. *Age and sex distribution of herpes zoster*

	Age groups (years)												
	All ages	0-1	4-5	6-10	11-15	16-20	21-25	26-35	36-45	46-55	56-65	66-75	76-85
Males	82	—	—	—	3	1	4	17	13	10	14	16	4
Females	102	—	1	2	7	3	9	6	9	19	25	19	2
Total	184	—	1	2	10	4	13	23	22	29	39	35	6

Table 6. *Percentage age and sex distribution of herpes zoster in relation to that of general population*

Age groups	Males		Females		All cases	
	Herpes zoster (%)	Population (%)	Herpes zoster (%)	Population (%)	Herpes zoster (%)	Population (%)
0-15	3.6	23.9	9.8	19.9	7.1	21.7
16-45	42.7	45.8	26.5	43.9	33.6	44.8
46-65	29.3	21.7	43.1	24.8	37.0	23.4
over 65	24.4	8.6	20.6	11.4	22.3	10.1
Total	44.6	45.6	55.4	54.4	100.0	100.0

the other in October. During the 6 months' period in 1948, on the other hand, the incidence was relatively high at the beginning of the year and tended to decrease to June when the study ended. No deductions can be drawn from these figures. The numbers for each month are small and only a limited period was covered by the survey.

It has been suggested (von Bokay, 1928) that chickenpox and herpes zoster tend to show a similar seasonal prevalence. Figures for the monthly incidence of chickenpox among school children in Edinburgh have therefore been included, for completeness, in the table. They do not give a complete record, but in the absence of notification they are the only figures available. No conclusion can, of course, be drawn from these statistics.

Geographical distribution. The patients with herpes zoster were widely but unevenly distributed throughout the city. Broadly speaking the incidence was heavier in the central than in the outer residential areas, but there were many exceptions to this generalization, and no correlation between incidence and density of population was apparent.

There was little evidence of grouping of cases in time and space, and in the few instances where this did occur careful inquiry failed to reveal a common aetiological factor or any contact between the different patients.

These facts suggest that crowding or density of

population was not of important significance, and that the disease occurred sporadically rather than in epidemic form.

Age and sex distribution. Details of age and sex for the 184 patients fully investigated are given in Table 5, while the percentage distribution in relation to the estimated population is shown in Table 6.

Female cases (55.4%) were more numerous than male cases (44.6%). This difference, however, is to be expected from the distribution of the two sexes in the population, and the facts do not indicate any sex differentiation in herpes zoster. Males have been found more commonly affected in most other investigations (Rivers & Eldridge, 1929; Araki, 1937; Bera-green & Schüller, 1938) but as these have been based largely on hospital cases the preponderance of the male sex may be due to the larger number of men attending for hospital treatment. The fact that in the present study 20% of male as compared with 13% of female patients had received hospital attention lends support to this view. Almost 60% of all patients were over 45 years of age, but the age distribution in the two sexes is different in certain respects. Thus more females were found in the earlier years, while 42.7% of males as compared with 26.5% of females were between 15 and 45 years.

Housing conditions. The housing conditions are shown in Table 7, the classification adopted being

that used in a recent social survey in the city. There is little difference between the types of houses occupied by zoster patients and those for the population as a whole.

Overcrowding, on the standard of the Housing

on the association with other cases of herpes zoster and with infectious disease generally.

The facts ascertained may be conveniently dealt with under three headings: (a) the association with other cases of herpes zoster; (b) the association with

Table 7. *Housing conditions of herpes zoster cases*

Type of house	Definition	No. of cases of herpes zoster	Percentage	Percentage for population as a whole
Tenement	A building of two or more storeys where the dwellings are entered from a common stair	123	66.8	64.8
Flatted	Two-story block containing four houses as a rule	21	11.4	13.9
Villa	Includes self-contained, semi-detached or terraced houses of two or more storeys	22	12.0	12.1
Bungalow	One-story self-contained house	12	6.5	7.6
Cottage	One-story house of rural type	2	1.1	1.3
Miscellaneous	Lodging houses, institutions, etc.	4	2.2	0.5
		Total	184	

(Scotland) Act 1935, was present in only 22, or 12%, of the families as compared with 14% in the population generally. There is no evidence to show that overcrowding or housing conditions generally influenced the spread of the disease.

Family history. A family history of herpes zoster was obtained in 30, or 16.3%, of 184 patients and in 8 of them more than one member of the family had suffered from the disease. In addition, the wives of two patients had suffered from herpes zoster 2 and 12 years previously. Only 8 of the relatives giving a previous history were in close contact with the herpes zoster patients and periods of 2–30 years had intervened.

Occupation. Of 184 patients specially investigated, 61 were employed in household duties only; 13 were at school; 17 had retired from active work and 3 were unemployed. A study of the occupations of the remaining 90 patients revealed no information of importance: commercial occupation, 15 instances; workers in transport and communication, 11; clerical workers, 10; persons employed in personal service, 9; and professional occupations, 7. These accounted for 58.9% of the total, which compares with 57.1% for the same five groups at the Census (1931). The order in which the groups occur are also very similar. There was, moreover, no evidence that herpes zoster was more common among any particular section of the community.

RELATIONSHIP WITH CHICKENPOX AND OTHER INFECTIOUS CONDITIONS

The investigation had, as its main object, the study of the relationship of herpes zoster and chickenpox, but the opportunity was taken to collect information

chickenpox, and (c) the association with other infectious disease.

(a) *Association with other cases of herpes zoster*

Eighteen patients gave a history of having been in contact with other cases of zoster, but in 7 the relationship was so remote or indirect that it is difficult to believe the occurrence was other than fortuitous. The facts in the remaining 11 cases are briefly summarized:

Case 35. Male, aged 64, developed supra-orbital herpes zoster 6 weeks after the onset of shingles of the neck and shoulder in his wife.

Case 67. Female, aged 67, developed herpes zoster of the lower dorsal region 3 months after her married son, who was recovering from a zoster of the neck and shoulder, came to live with her.

Case 76. Male, aged 27, developed herpes zoster of the mid-dorsal region 2 months after visiting his aunt, when she was suffering from a severe attack of shingles of the lumbar region.

Case 103. Male of 33 years developed cervical herpes zoster 3 months after a lodger, who had just recovered from herpes zoster, came to reside in the house.

Case 125. Female, aged 10 years, developed herpes zoster of the lower dorsal region approximately 3 months after the onset of shingles of the neck and shoulder in an aunt living in the same house. This latter patient had completely recovered from a severe attack only 6 weeks before the child's shingles commenced.

Case 128. Female, aged 50, developed herpes zoster of the lower dorsal region 6 weeks after visiting her daughter-in-law, who was suffering from shingles of approximately the same region.

Case 150. Female, aged 18, developed herpes zoster of the mid-dorsal region 5 weeks after close contact with a fellow worker, who suffered from cervical herpes zoster.

Case 153. Male, aged 60, developed herpes zoster of the lower dorsal region 2 months after the onset of a severe attack of shingles of the lumbar region in a man who lived in the adjoining house and whom he visited almost daily.

Case 166. Male, aged 37, with herpes zoster of the mid-dorsal region, gave a history of contact with a fellow-worker suffering from a similar condition. The actual dates of contact were somewhat indefinite.

Case 171. Male of 42, developed herpes zoster of the mid-dorsal region 7 weeks after the occurrence of case 128 above, who lived in the same tenement and with whom he came in contact on a number of occasions.

Case 174. Female, aged 52, developed supra-orbital herpes zoster after frequent visits, during the 6 weeks before sickening, to a friend with herpes zoster of the dorsal region.

The relationship in some is suggestive, but in others it is difficult to rule out the possibility that the occurrences were merely due to chance. The fact that, after some months' observation, only 2 of 442 family contacts subsequently developed herpes zoster does not indicate that the disease is of a very infectious nature.

(b) *Association with chickenpox*

(i) *Previous history of chickenpox.* The information obtained of a previous history of chickenpox was as follows:

Previous history of chickenpox	No. of patients	Percentage
No	40	21.7
Yes	51	27.7
Doubtful	93	50.6
Total	184	

Many of the patients were of advanced years, and in the majority no confirmatory examination for scars of a previous chickenpox infection was possible. There were 43 patients, however, on whose history considerable reliance could be placed, and of these 15 (34.9%) had not had chickenpox, while 28 (65.1%) had suffered previously from the disease. The proportion with a positive history approximates closely to 66.6% found among a large sample of boys attending residential schools (M.R.C. Special Report, 1938).

The period elapsing between the occurrence of the two diseases varied from 2 to 45 years. Nine patients had suffered from chickenpox within 10 years and 2 within 5 years of the onset of herpes zoster.

(ii) *Chickenpox-herpes zoster association.* A history

of recent association with chickenpox prior to the onset of herpes zoster was given by 14 of the 184 patients, but in 8 the association was through a third party only. The relevant features concerning the other 6 patients is as follows:

Case 9. Female, aged 67, supra-orbital zoster, was in contact when visiting married daughter with boy who had chickenpox. Actual dates unknown but 'not long' before onset of herpes zoster.

Case 23. Male, aged 65, cervical zoster. Visited and in close contact on a number of occasions with his three grandchildren who developed chickenpox, two 30 days before, and the other 19 days before the onset of herpes zoster.

Case 44. Female, aged 70, thoracic zoster. In contact 48 hr. before onset of herpes zoster with grand-nephew who had chickenpox.

Case 66. Male, aged 52, developed lumbar zoster 20 days after last contact with children living in the same tenement who had chickenpox. Contact not very close.

Case 72. Male, aged 37, thoracic zoster, visited 4 weeks before onset a house where there was a child who had had chickenpox but was declared free from infection.

Case 145. Female, aged 12, thoracic zoster, visited 2 weeks before onset a family where two children had had chickenpox but were declared free from infection and had returned to school 1 week previously.

None of the patients was in contact with chickenpox among members of the immediate family circle, and in most the association was of doubtful significance, although in three (cases 9, 23 and 44) the circumstances were such as to suggest that the two conditions might have been associated.

(iii) *Association of herpes zoster and chickenpox.* A condition clinically indistinguishable from chickenpox occurred among the contacts of 10 or 5.4% of the 184 patients with herpes zoster. Twelve individuals were affected, and all but one were close family contacts. The relative information regarding these is given in Table 8.

With one exception, the affected contacts were young children and the eruption developed within the usual incubation period of chickenpox. None gave a previous history of that disease. Although in some the possibility of infection from other sources cannot be entirely eliminated, in all the association with herpes zoster is suggestive.

At the same time, the number in relation to the total herpes zoster patients is not high. It is to be remembered, however, that many of the patients lived alone or with adults only, and a more satisfactory assessment is to be obtained by studying the question in relation to the contacts exposed to risk.

There were 442 family contacts, and details of their ages and susceptibility to chickenpox are given in Table 9.

Table 8. *Herpes zoster chickenpox association*

Patients with herpes zoster				Associated chickenpox condition in contacts					Remarks
Case No.	Sex	Age	Month of Onset 1947	Site of herpes zoster	Relation-ship to herpes zoster patient	Age	Interval between herpes zoster and chickenpox	Other susceptible contacts	
16	F.	35	April	Supra-orbital	Son	3 years	15 days	Nil	Child had just recovered from mumps when mother took herpes zoster
46	F.	60	May	Supra-orbital	Grand-daughter	10 years	26 days	F. 3 years	Child lived in adjoining house but visited grandmother frequently. No chickenpox in school or class
54	F.	42	May	Lower dorsal	Daughter	3 years	14 days	M. 6 years	Child slept with mother, but other unaffected child did not
68	M.	34	July	Lower dorsal	Son	6 years	10 days	Nil	Slept separately, but in same room with father
80	F.	23	Aug.	Mid-dorsal	{ Daughter Son	14 months 2½ years	17 days 3 weeks later	Nil Nil	Children slept separately, but in the same room with their mother. House small and overcrowded. Daughter attended Day Nursery but no chickenpox there
91	M.	31	Oct.	Cervical	{ Son Daughter	4½ years 19 months	16 days 17 days	Nil Nil	—
107	F.	44	Nov.	Supra-orbital	Son	4½ years	15 days	Nil	History of chickenpox in district, but not amongst children with whom son played
110	F.	14	Nov.	Cervical	Sister	4½ years	15 days	Nil	Sister attended Day Nursery, but no chickenpox infection there
1948									
150	F.	18	Feb.	Cervical	Brother	4 years	2 weeks	M. 19	Child with chickenpox condition not seen by doctor. Mother's diagnosis, but appears probable from history
159	M.	64	April	Lumbar	Female fellow-worker	38 years	10 days	—	Another adult, developed chickenpox 2 weeks later

Table 9. *Chickenpox history of herpes zoster contacts*

History of previous chickenpox	Ages of family contacts						Not stated	Total
	0-1	1-5	6-10	11-15	16-20	+20		
No	6	36	17	12	7	51	7	136
Yes	—	8	13	16	16	84	6	143
Doubtful	—	1	2	1	1	155	3	163
All cases	6	45	32	29	24	290	16	442
No. of family contacts developing chickenpox	—	9	2	—	—	—	—	11

When all family contacts are considered 2.5% developed a chickenpox condition, but limiting the question to those with no previous history of chickenpox the proportion rises to 8.1%, while among the 71 susceptible contacts under 15 years 15.5% were affected.

These calculations throw a somewhat different light on the question, particularly when they are considered with the results found in other investigations on the attack rate of chickenpox among contacts. Thus Stocks (1930) found that among 151 children aged 5-7 years in Paddington, who were excluded from school as contacts of chickenpox and were therefore presumably susceptible, 27 or 18% developed the disease within 3 months, as compared with 3 out of 296 or 1.1% of children of similar age excluded from school for some disease other than chickenpox. Again, in eight recorded school outbreaks of chickenpox the attack rate among susceptible contacts, the majority aged between 14 and 17 years, varied from 7.3 to 53.9% ('Epidemics in Schools', 1938). Taking these eight outbreaks together it is calculated that 270 cases of chickenpox occurred among 1499 susceptible contacts, giving an average of 18.0%.

It is of interest that a negative history of chickenpox was given by 30.8% of the contacts, which is very similar to the proportion found among the patients themselves.

(iv) *Concurrent chickenpox and herpes zoster.* There was one instance of concurrent herpes zoster and chickenpox. A brother and sister aged 50 years and 48 years respectively, residing in widely separated parts of the city, lunched together in a city restaurant having not met for some weeks previously. The sister developed zoster of the right buttock and thigh 21 days later, while at approximately the same time the brother developed a widespread vesicular eruption diagnosed by his family doctor as chickenpox. The two patients had not met again during the intervening period. If the occurrences were not fortuitous they suggest infection from a common source.

(c) *Association with other infectious disease*

Table 10 shows the prevalence of the common infectious diseases among school children in Edinburgh during the 18 months covered by the survey, and also gives the number of patients who gave a history of association, either before or after the onset of herpes zoster, with these diseases.

The numbers in each group are small and do not lend themselves to statistical analysis, but other common infections did not seem to occur as frequently among contacts of herpes zoster as did chickenpox.

DISCUSSION

The facts obtained from the investigation as regards the relationship of herpes zoster and chickenpox are

Table 10. *Association of herpes zoster with infectious diseases*

Disease	No of children affected	No. of herpes zoster patients associated with infectious disease	
		Before onset	After onset
Mumps	3902	2	2
Measles and rubella	3837	2	2
Chickenpox	2486	6*	10
Whooping cough	1703	—	—
Scarlet fever	426	—	—
Diphtheria	71	—	—
Dysentery	—	—	1

difficult to evaluate. Only 6 patients out of 184 gave a history of direct contact with chickenpox prior to the onset of herpes zoster, and the circumstances in only 3 were such as to suggest that the two conditions might have been related. Other common infections such as mumps, measles and rubella occurred in approximately the same proportion which suggests that the chickenpox association might well have been fortuitous.

The appearance of a chickenpox condition following contact with herpes zoster, on the other hand, raises a more difficult question. This occurred in connexion with 10, or 5.4%, of the total patients, while 11, or 2.7%, of 442 family contacts were affected. These are not impressive figures, and by themselves would not justify the conclusion that herpes zoster and chickenpox were closely related. There are, however, other facts which deserve consideration.

Thus the clinical features suggested a close association between the two conditions. None of the affected patients on careful inquiry had been exposed to other known sources of infection, and the circumstances were more consistent with the transference of infection from the herpes zoster patients. With one exception, where 26 days intervened, the vesicular eruption appeared within the usual incubation period of chickenpox. If the occurrences were fortuitous it might have been expected that more cases would have shown longer or shorter intervening periods. Again, it has been shown that 15.5% of susceptible contacts under 15 years developed the chickenpox condition, a proportion not far below that found in other investigations among contacts of chickenpox in the general population and in residential schools. Finally, despite their higher prevalence in the general population, other common infections such as measles, mumps and rubella occurred less frequently among contacts of herpes zoster than did chickenpox.

These facts, it is suggested, are more in favour of

* See p. 6.

a real than casual relationship between the two conditions. If this be accepted a further question arises.

Most observers who believe that herpes zoster and chickenpox are closely related consider that they are both due to infection by the virus of varicella. While some of the facts from this investigation would favour such a view, there are others which are difficult to reconcile with it. It has been shown, for instance, that the patients with herpes zoster in this study gave a previous history of chickenpox in approximately the same proportion as has been found in other investigations for the population as a whole. If herpes zoster and chickenpox were due to the same infective agent it might be expected, even allowing for the more common occurrence of zoster in the later years of life, when the immunity from chickenpox might have waned, that a group of zoster patients would tend to show a higher proportion with a negative previous history than would be found in the general population. Again 9 patients, for whom accurate information is available, gave a history of chickenpox within 2–10 years of the onset of their herpes zoster. Cases showing a similar or shorter intervening period have been published (Wilson & Mitchener-Little, 1926; Crisp, 1940 and Allen, 1944). It is surprising that the two conditions should occur within such a short interval if they are due to the same virus. Lastly, if herpes zoster and chickenpox were of similar origin it would be expected that a history of association with chickenpox would be met as frequently before as after the onset of herpes zoster. This is not in keeping with the findings of the present survey.

In view of these difficulties the question might be asked whether the vesicular eruption found in contacts of herpes zoster might not be a generalized manifestation of the zoster virus somewhat analogous to the occurrence of generalized vaccinia among contacts of vaccinated persons. Such a view would account for some of the difficulties, while the occurrence of the eruption only among contacts with no previous history of chickenpox might be explained by the presence of a group immunity of allied conditions as, for instance, cowpox and smallpox. A difficulty is the occurrence of the eruption in more than one contact. In the present study there were two such examples. These may, however, be instances of true chickenpox because it is obvious that, having regard to the prevalence of other common infections among contacts of herpes zoster, chickenpox might also make its appearance.

It is not suggested that any definite conclusions are justified from the findings of the investigation. The numbers involved are small and are difficult to interpret statistically. It is believed, however, that the facts are consistent with the view that an eruption clinically resembling chickenpox may follow contact with herpes zoster, but that this may be a generalized

manifestation of the virus of zoster rather than true chickenpox. The whole question of the relationship between herpes zoster and chickenpox is complex, and the words of Bruusgaard (1932) are still true: 'it may safely be said that it is difficult with the data we possess to take up any fixed position'.

SUMMARY

The results of a field survey of herpes zoster over a period of 18 months are described and the difficulties of such a survey mentioned.

A total of 246 patients with herpes zoster, only 16% of whom had attended hospital, is reported. It is calculated that the yearly incidence in the population was approximately 2 per 1000.

Full investigation and 'follow up' was undertaken in 184 cases. These are classified according to the site of the zoster—the dorsal, supra-orbital and cervical regions being affected in almost 90%, the dorsal region alone accounting for 53·3%.

Herpes generalisatus occurred in 7, or 38%, of the cases, recurrent herpes zoster in 6, or 3·3%, while there was one case of motor paralysis affecting lower limb.

The majority of patients were apparently well at the onset of the zoster, but 27 had some associated disease; 5 gave a history of trauma prior to the onset and 2 were related to pregnancy.

The seasonal and geographical distribution is given and, while the numbers are too small for statistical analysis, the disease in 1947 showed two peaks of higher incidence, the one in May and the other in October. Crowding or density of population did not appear to be important, and the disease occurred sporadically rather than in epidemic form.

There was a higher proportion of female cases, but when related to the population as a whole no sex differentiation was observed. Of the patients 60% were over 45 years of age.

There was no evidence that housing conditions or occupation were of aetiological significance or that the disease was more common among any particular section of the community.

Eleven patients had been associated with other cases of herpes zoster before developing the disease, while 3* gave a suggestive history of prior contact with chickenpox.

A condition indistinguishable from chickenpox occurred among the contacts of 10 patients, 12 individuals being affected, and there was one instance of concurrent herpes zoster and chickenpox. Other infections such as mumps, measles and rubella, while as common in association with the onset of herpes zoster, were not so frequently found as the chickenpox condition amongst contacts of the disease.

The results of the survey as regards the relationship of chickenpox and herpes zoster are discussed.

* See p. 6.

It is considered that the evidence does not favour a significant association with chickenpox prior to the onset of herpes zoster, but that the facts are consistent with the view that a condition indistinguishable from chickenpox may follow contact with herpes zoster. It is suggested, however, that this may

be a generalized manifestation of the virus of zoster rather than true chickenpox.

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REFERENCES

- ALLEN, F. M. B. (1944). *Brit. Med. J.* **2**, 115.
 AMIES, C. R. (1934). *Brit. J. Exp. Path.* **15**, 314.
 ARAKI, S. (1937). *Jap J. Derm. Urol.* **41**, 97. (Annotation *Arch. Derm. Syph. Wien*, **37**, 1058, 1938.)
 BERAGREEN, P. & SCHÜLER, E. G. (1938). *Derm. Wschr.* **106**, 216.
 BRAIN, R. T. (1933). *Brit. J. Exp. Path.* **14**, 67.
 BRUUSGAARD, E. (1932). *Brit. J. Derm. Syph.* **44**, 1.
 VON BOKAY, J. (1909). *Wien. klin. Wschr.* **22**, 1323.
 VON BOKAY, J. (1928). *Jb. Kinderheilk.* **119**, 127.
 COWIE, J. M. (1925). *Brit. Med. J.* **1**, 642.
 CRISP, G. H. (1940). *Lancet.* **2**, 311.
 DAHL, S. (1946). *Schweiz. med. Wschr.* **76**, 343.
 'Epidemics in Schools.' (1938). *Spec. Rep. Ser. Med. Res. Coun., Lond.*, no 227. London: H.M. Stationery Office.
 FARRANT, J. L. & O'CONNOR, J. L. (1949). *Nature, Lond.*, **163**, 260.
 GLAUBERSOHN, S. A. & VILLFAND, R. A. (1929). *Ann. Derm. Syph.* **10**, 609.
 HASSKO, A., VAMOS, L. & THOROCZKAY, M. (1938). *Z. Immunforsch.* **93**, 80.
 LAUDA, A. & SILBERSTERN, E. (1925). *Klin. Wschr.* **4**, 1871.
 LIPSCHUTZ, B. & KUNDRATITZ, K. (1925). *Wien. klin. Wschr.* **38**, 499.
 NAGLER, F. P. O. & RAKE, G. (1948). *J. Bact.* **55**, 45.
 NETTER, A. & URBAIN, A. (1924). *C.R. Soc. Biol., Paris*, **90**, 461.
 RIVERS, T. M. & ELDRIDGE, L. A. (1929). *J. Exp. Med.* **49**, 899.
 SMITH, C. M. (1931). *Glasg. Med. J.* **116**, 115.
 STOCKS, P. (1930). *Proc. Roy. Soc. Med.* **23**, 1360.
 THOMSEN, O. (1934). *Z. Immunforsch.* **82**, 88.
 WILSON, C. R. & MITCHENER-LITTLE, J. H. (1926). *Brit. Med. J.* **1**, 697.

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