

## PRURIGO BESNIER (ATOPIC DERMATITIS) WITH SPECIAL REFERENCE TO THE ROLE OF ALLERGIC FACTORS

### III. The role of some factors in the course of the Prurigo Besnier

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In previous communications (93, 94) the author reported investigations into the effect of hereditary factors on the immediate skin test and presented an evaluation of the immediate skin test in Prurigo Besnier (PB). Distinction was made between patients with PB and PB patients also having respiratory manifestations. The patients were divided in 5 age groups: Group I: 0-6, Group II: 7-12, Group III: 13-18, Group IV: 19-45 and finally Group V: over 45 years of age.

The generally varying course of PB is well-known. However, the reasons are not yet elucidated why PB sometimes clears up or relapses whilst in other patients it shows an uninterrupted course. Free periods were seen in the course of PB in 28 per cent of young patients in a greater material (87). In 29 % of 330 cases it occurred before the puberty (98). Nexmand (78) found that the severity of the cases is not related to the incidence of symptom-free periods. After the age of 20 a tendency to spontaneous healing (123) (spontaneous desensitization? 39, 70) can be observed as years are passing. In the material of certain authors PB patients elder than 30 years are estimated to constitute a percentage of 5-17 (79, 18, 84, 89) and elder than 35 years to 20 % (77), whereas others have found only one such patient in the statistics of ten years (48).

There are several reports of subsequent examinations of patients with infantile eczema. Some suitable data for evaluation are summarized below:

No. of patients with eczema infantile	Years after hospital emission	Frequency of PB at the after-examination	Authors
33	18-20	19 patients	Boddin (14)
84	13-22	55 % by the age of 13	Vowles <i>et al.</i> (134)
		18-55 % by the age of 20	
93	15-21	15-28 %	Purdy (91)
64	10-40	7 patients	Schulthess (106)
67	"beyond infancy"	29 patients	Stransky & Weber (122)
818	"beyond infancy"	"minority"	Jordan & Kiefer (53)
311	17-38	18 %	Edgren (77)
53	5-15	22 patients	Clein (23)
200	7	20 %	Kesten (56)
71	7-10	27 patients	Nexmand (79)

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From the above data, it is clear that it is very difficult to evaluate uniformly these data which are so different from the point of view of the material collected, the time when the control examination was undertaken and in regard to the diagnostic criteria used. As regards the latter it is obvious that not all cases of infantile eczema can be classified as a preliminary stage of PB. Nexmand (79) opines that with typical clinical localisation in childhood a great number subsequently develops PB.

The following are some factors which may possibly influence the course of PB:

(i) *Seasonal dependence*

The seasonal course and estival improvement of a great part of PB patients have long since been described, although the data may vary due to different geographic climatic conditions. According to Hellerström & Lidman (43) among the cases with seasonal dependence only 16 of 187 deteriorated in summer whereas 23 of 24 patients became worse in spring. Of the 39 (16 plus 23) patients deteriorating during spring and summer, 13 were worse after sun exposure (2 had solar dermatitis). Nine of 12 other patients with spring and summer deterioration showed pollen sensitivity by history and skin tests. They mostly had respiratory manifestations.

Estival improvement was also noted in the majority of the cases by other Scandinavian authors (35, 70, 15, 84) as well as in reports from other geographical areas (87, 69, 85). Nexmand (79) found that 45 of 83 patients improved in the summer, whereas 24 cases became worse and 14 remained unchanged. Among those 45 patients the improvement was due to sun bathing in 20 cases and to sun- and sea-bathing in the remaining cases. Pollen sensitivity was shown in 17.8 % and many of the patients have had hay fever. Among the aggravated cases 6 became worse after sun exposure. The ratio of pollen positivity was higher in this group (62: 5 %).

Schnyder (104) found that 40 per cent of the PB cases aggravated in the winter, a further 18 % in the summer, 11 % in the spring and 10 % in the autumn. There was no difference in this regard between patients with and without respiratory symptoms or between patients with positive or negative immediate skin tests. However, the seasonal independence was three times greater in patients with positive skin tests. Thirty-two per cent of the pollen positives showed aggravation in winter time, 11 % in the spring and 17 % in the summer and 12 % in the autumn. Thus these incidences correspond to the values of the total number of PB patients in his series.

The causes of the estival deterioration are — according to the above authors and other literature data — sensitivity to pollen (97, 22, 99, 31), sunlight (39, 77) and molds (31).

The greatest part of PB patients deteriorate in winter. The cause of the winter deterioration cannot be dust because only 25 % of the dust positive cases and 75 % of the dust negative cases became worse in winter (104). Piriälä (89) found that the higher incidence of PB cases in Finland, as compared with Danish statistics (79), is in part due to the colder climate. He feels that the dark season (i. e. the short duration of daylight) plays a greater role in aggravating PB cases than low temperature itself. It is interesting, however, that in the

sunny and dry cold South African climate there is also winter aggravation in PB cases (69).

Deterioration in the spring (96, 39, 77, 133) and in the autumn (89, 133, 77, 55, 79) has been described by several authors. The proportion of PB cases showing no seasonal dependence is different as between different authors: 9.1 % (43), 21 % (104, 72) or in one-third of the patients (85). According to Wiener (136) there is rarely any seasonal dependence in infantile eczema cases; but other authors do not share this opinion (8, 121).

### (ii) *Environmental and climatic factors*

It is a common experience that certain environmental changes exert a beneficial effect on many PB cases. Nexmand (79) observed that 9 of 17 cases improved after change of residence, chiefly when the patients moved from damp to dry dwellings and in persons with allergy to dust and molds. This author adds that in other improved cases the number of the allergens used in skin tests was perhaps not adequate to find a possible environmental allergy.

Most PB cases improve during hospitalization. The cause of this is freedom from special environmental allergens and correct local treatment. However, other investigators state that the improvement is independent of local treatment (117, 111). According to Siemens (111) the regularity to spontaneous recovery in hospital in young as well as in adult cases speaks against the essential role of psychical factors on the course of PB.

Among the climatic factors sojourn at sea (96, 101, 35, 66, 85), stay in the highlands (55, 97, 77, 33, 73, 75) or in sunny climates (California, Florida and similar areas) (124, 87, 110, 29, 116, 113) are best known for their favourable effect on PB. The cause of these improvements is, however, not clear. The effects of sun- and sea-bathing have already been mentioned among the seasonal factors, and the effect of sun rays is used as heliotherapy (85) or in the form of general UV-therapy (79). Other authors opine that the improvement is due to relative freedom of allergens. No significant difference could, however, be shown in regard to climatic dependency of test-positive and test-negative cases (104). The effect on the circulation of the skin (59), increased activity of the adrenal cortex, a beneficial effect on the autonome nervous system (73) are also mentioned. So is the effect of relaxation, rest, psychological factors, and the improvement of sweat disturbances. Sulzberger (125) summarizes the effect of the sweat disturbances in PB as follows: in some cases the plugging of the pores is due to dry, hard keratin and the hydration helps to expel it. Such cases do well in moist heat. In other cases the sweat duct obstruction is due to the swelling of the horny layer and to edema of the tissues surrounding the duct. In such patients desiccation resulting from consistent low relative humidity and high environmental temperature as well as the effect of sunlight will relieve the condition.

The role of climatic factors is very complex. Although most cases do well during a stay in California for example, the incidence of PB is not lower there. In fact many of the cases improve if they leave this region (117). Not only changes from lowland climate to mountains may be beneficial, but in certain patients the opposite change has the same effect (76). The PB cases of non-

seasonal type react chiefly to climato-geographical factors (69). As disease eliciting factors in PB the following can be named: sudden temperature changes, moist climate, decreasing atmospheric pressure, intensity of wind (63, 89).

### (iii) *Sweat disturbances*

The role of sweat disturbances in PB has already been mentioned. According to clinical experience many PB patients start to itch when exertion, high temperature or excitement require secretion of sweat. The work of the Sulzberger and his group demonstrates that:

a) the number of sebaceous glands is smaller in young PB patients. It may be that the Prurigo process itself is injurious to the glands. The secretion of sebum is deficient. These facts are corroborated also by other workers (90, 60). Kochs (60) assumes that there is a hypofunctional factor in regard to sebum, associated with ichthyosis and transmitted mostly as a dominant gene.

b) in some cases of pseudohidrosis the sweat function is normal, but the dry, keratotic corneum absorbs the sweat immediately.

c) in rare cases a xerotic corneum becomes strongly hidratized and periosteal edema, parakeratosis and further keratin plugging follows in the sweat duct. According to another mechanism a periporal edema is the cause of the obstruction. In both cases a state similar to that in milia — a sweat retention-syndrome — develops. The sweat cannot evaporate and minute i. c. "injections" of the sweat — not infrequently containing allergens — occur into the tissues which acts as a pruritogen stimulus. The sebum and sweat are mutually influencing each other. The emulsifiers occurring in the sweat are mainly responsible for the delivery and spread of the sebum (46, 47, 126, 127).

Clinical data corroborate these findings. Sometimes small, diffuse, symmetric, periporal papules develop in PB patients. The dry skin of the patients improves under conditions of a relative humidity above 60 % in cases of "plugging" sweat retention, whereas dry heat helps in periporal edema (see also under climatic factors). Dry heat with free evaporation of sweat is used for therapeutic purposes (sweat box therapy, 128).

Korting (62) also found oligohidrosis in PB cases and demonstrates a local hyperhidrosis during the time of flexural eruption in young patients. They are also other reports on hyperhidrosis (mostly local) in PB (cited by 63). Localized sweating in affected skin areas of PB patients after allergen inhalation was observed by Tuft and al. (132). Further, it was shown that PB patients react more slowly after thermal stimuli than do the controls (13).

### (iv) *Combination with other diseases*

#### a) *Atopic rhinitis and/or bronchial asthma.*

Combinations of PB with atopic rhinitis and/or asthma have already been described in a previous communication. In the author's material there were 557 cases combined with respiratory allergies out of a total of 1200 (93). As several workers have indicated there are more females than males in combinations of PB and respiratory symptoms (43, 105). Similar data were found in the author's material, where at the same time the onset of the respiratory symp-

toms in PB patients are described [Table 6 c (93)]. Mutual reactions in the form of an alternating course or flare-up are wellknown as between PB and asthma. In the case of coexistence the causes are mainly due to allergens capable of eliciting both symptoms. As Korting (63) mentions such allergens are: PPD, emetin, salvarsan, chinin, flour, persulfates,  $H_2O_2$ , ascaris, penicillin, chloroplatinic acid, cow hair. Exogenic allergens often play an important role in the etiology of bronchial asthma. The incidence of extrinsic asthma compared with non-allergic intrinsic cases is, however, very controversial. The percentages of extrinsic asthma (of all asthma cases) are mentioned from 17.9 % to 75 % (30 and others).

In regard to the occurrence of positive immediate skin tests in asthma these vary between 39.1 % and 95 % (107, 105). Schnyder (105) states that  $40 \pm 20$  % of asthma cases are test-negative. These cases can mostly be considered as intrinsic asthma patients.

#### b) *Ichthyosis.*

This genodermatosis exists along with skin diseases or other hereditary signs (36, 112), e. g. with cataracta (63). It frequently coincides with PB. This is known since 1877 (34) but the number of ichthyosis cases combined with PB is different, namely 7 of 38 (41), 7 of 29 (71), 7 of 83 (6), 6 of 100 (79), 8 of 330 (98) and finally 6 out of 15 patients who also had asthma (4). The explanation of these differences is presumably the difficulties in differential diagnosis between ichthyosis vulgaris and the ichthyiform xeroderma in PB cases. Hill & Sulzberger (48) state that a keratosis pilaris can be found in half of the PB cases. The functions of the ichthyotic skin are decreased — based on investigations of the alkali-neutralization, alkali-resistance and pH-conditions. This may be the cause of the frequent combination with eczema (140). Ichthyosis may also develop in asthma cases (16, 24) but there is no genetic relationship between asthma and ichthyosis (107).

#### c) *Cataracta.*

Cataracta and keratoconus may generally occur in PB cases in a frequency of 5 to 12 % (99, 19, 65, 115, 49, 9, 57, 61). However there are also reports of higher incidences (54, 52). Lenticular opacities are only to be found associated with severe cases of PB (19, 5). In regard to sex distribution it does not play a role. However there is a report of the preponderance in men (63). Most patients with these symptoms are adults. Kornerup & Lodin (61) found lenticular changes in 3 % in a diagnostically well controlled group of PB patients. By measurement of the corneal radius and corneal astigmatism not a single case of keratoconus was found.

#### d) *Gastroenteral disturbances.*

Gastroenteral disturbances, such as hypoacidity (28, 98, 92) or abnormal acid values (86), constipation (3) or dysbacteria (86) are not infrequently found in patients with PB. However gastroenteral disturbances in a patient with eczema (not specified) does not necessarily mean that causal relation exists (136). Korting

(63) could not observe a single case of colitis mucosa in his PB material. He found a low incidence of dysbacteria in his cases. Oppitz and Zelger (86) found 6 cases of infestations of 10 PB patients. This high incidence has, however, not been corroborated by other investigators.

c) *Epilepsy.*

The literature sometimes refer to a combination of epilepsy and atopic symptoms (107). While the incidence of epilepsy in a population is 0.4 % (58), Korting (63) found 0.99 % in his PB material.

(V) *Infections*

Microbial or viral infections as well as vaccinations can frequently elicit or exacerbate PB (129, 2). A deterioration followed infections of the upper respiratory tract in 39 % of the cases of Norrlind (84) and 23 % of Storck (119). Hellerström & Lidman (43) mention 47 % whereas Nexmand (79) reports only 5 % in his series. This deterioration may be due to an infective allergic mechanism. Thus a high incidence of immediate skin tests were found positive to bacteriae (84). The importance of the staphylococcic allergens in PB is very much discussed, as mentioned in a previous communication (94). The microbial skin flora in PB does not essentially differ from normal skin flora. Storck (119) did not observe differences in his groups with epicutaneous bacterial test technic. Beta-haemolytic streptococci were mainly found in the throat in 62 % and in a smaller percentage on the skin and in the nose of 44 children with infantile prurigo (44).

The decreased resistance to microbial (chiefly pyococcic) and viral infections is known by every clinician; but exact data fail to explain this circumstance. The antistreptolytic titers (AST) in PB patients are according to the literature contradictory. Helve et al. (44) found lower average values than in the controls, whereas other authors state an increase in 48 to 50 % (114, 139). Zezschwitz (139) considered titers above 200 Todd units as pathologic. Craps (25) found that 20.4 % of his PB patients had AST higher than 300 units. Hanson (38) notes that patients with various AST did not show differences in precipitating beta-haemolytic streptococci by the gel-diffusion method. The antistaphylolysin titer does not appear to be an indicator of staphylococcal antigen-antibody reaction in PB patients (11).

As mentioned in a previous communication (94), Nilzén (82) found thrombocyte fall in PB patients after the use of (polyvalent) staphylococcic extracts. Recently, Bergquist & Nilzén (11) used autogenous staphylococcal skin vaccine and thrombocyte tests in patients with PB. Immediate skin tests were all negative. However, a marked decrease was observed in the number of thrombocytes after injection of an autogenous vaccine.

Antibiotic therapy had no obvious effect on the duration of hospitalization of patients with infantile eczema (45). Storck (120) observed only 3 cases with improvement and 3 cases with questionable amelioration in 15 PB patients after serobacterin vaccine therapy.

On the other hand, several authors have noted a transitory beneficial effect

of infections associated with fever in patients with PB [i. e. Lomholt, 70, c. p. also Hollström & Feigenberg (50)].

(vi) *Hormonal influences in women*

The sex distribution of PB is important. The majority of investigators [with two exceptions (42, 85)] agrees that there is a prevalence of women among PB patients (18, 84, 79, 43, 60, 105).

Several authors describe relapses and exacerbations in the course of PB at the time of puberty (109, 6, 77). Furthermore, there is disclosed that about this period there are much more allergic diseases among women than among men (78, 110, 43). Others state, however, only slight or no difference between the sexes (62, 85), whereas Lomholt (70) has seen a tendency to healing of PB at the time of puberty. Horneck (51) found the first manifestations of allergic symptoms (including edema and idiosyncrasy) frequently around the menarche and refers to similar data in the literature. The menarche did occur somewhat later in patients with PB than in other persons, but the difference was not of statistical significance (89). The same author (89) found that the peak of the cases requiring hospitalization is between 15 and 16 years in women and between 17 and 18 years in men.

Many women with PB have skin deteriorations premenstrually and during menstruation (77, 12, 43). The assumed causes in skin diseases during menstrual exacerbations are: greater reactivity of the skin, disturbance in endocrine functions and liberation of toxic or allergic substances from the ovaries. The urticarial skin reaction is however strongest on the last day of the menstrual cycle (37). Seeberg (108) found (because of a more rapid absorption) a decreased reaction of the delayed type premenstrually and on the first menstrual day as compared to other stages of the cycle.

The course of PB during pregnancy is controversial. Thus Hellerström & Lidman (43) saw 11 improvements and 3 deteriorations during pregnancy. Nexmand (79) describes the unfavourable effect of pregnancy in three cases while one patient improved. On the basis of the similar course in the premenstruum and during pregnancy identical endometric alterations are assumed to be concerned. The cause remains, however, unknown and Nexmand considers the possibility of an absorption of toxic substances from the endometrium or endogenous allergic reactions.

(vii) *Working conditions*

The effect of working conditions on the course of PB has many sides. PB may occur in patients with widely different professions. The opinion of Korting (64) is that the profession only influences 3 per cent of the PB cases. Nexmand (80), however, mentions 44 cases where PB caused difficulties in the profession and 24 such cases where PB became worse by the work. In the latter instances dust was the cause in 8, sweating disturbances in 7, water, soap and external irritants in 5, temperature changes in 2 and finally contact with animals in 2 cases. A comparison between the influence of working conditions and skin testing showed agreement only in 4 cases. On this ground, the occupational allergy

seems not to play a decisive role in this disease. The skin testing is thus not an adequate method in elucidating such cases. Marchionini et al. (74, 75) report that 33 % of the PB patients were hindered by the disease in their profession and 20 % was obliged to change their work. Further 29.4 % had difficulties in their professional carrier owing to their PB. Schwartz (107) means that a person with atopic symptoms should not choose the following professions: baker, pastry cook, miller or professions where asthma may be an occupational disease, e. g. dyeworkers working with PPD. Textile factories or bakeries which are dusty working places are not considered suitable for PB patients (103).

#### (viii) *Drug reactions*

It is a common clinical observation that atopic individuals may frequently and strongly react to different drugs with allergic phenomena. Studies have shown — to quote Brown (17) that “drug sensitivity is three times more common in an allergic (atopic) as compared to a non-allergic population”. However, no investigations on a large scale could be found by the present author where the incidence of drug sensitivity was compared as between atopic individuals and normal controls. An exception is the study of Schnyder (105) who found no statistically significant difference in the incidence of medicamentall allergy as between 1525 patients with atopies and the controls. Among these atopics there were 78 PB patients and in this series not a single case of drug allergy occurred. In individuals with severe reactions to penicillin and where positive intradermal reactions were secured it was found that such reactions tend to occur in atopic individuals (1). Salicylates [which not infrequently elicit asthma — especially in patients with infective asthma — urticaria and general symptoms (68, 102, 32)] are considered to be histamine-liberators (135).

#### (ix) *Specific therapy*

It is an old ambition to attempt influencing the course of PB by specific therapy. However most results of hyposensitization in patients with PB are unfavourable (7, 137, 18, 130, 15). Bruun (20) who very clearly summarizes the principles and results of hyposensitization in allergic diseases recommend this therapy for PB patients only in the case of inhalants. Good results could be achieved in this field by Feinberg (31) in 8 of 14 cases and by Tuft (131) in 73 out of 95 cases. In the case of pollen Rowe (99) saw beneficial results in 27 out of 30 PB patients. In a recent communication Rowe Jr. (100) mentions 79 excellent and 21 good results after 2—8 years of hyposensitization in 100 PB-patients. The latter were all pollen sensitive according to skin tests or to case history. Rappaport (95) reports that a few cases of PB improved from pollen hyposensitization.

A detailed analysis is given in the communications of Nexmand (79) and Nilzén (83). They are as follows:

	Good effect	No effect	Problematic effect
Nexmand:			
Pollen	4	4	2
Housedust		4	1
Mold	1	1	1
Horse dander	1		
Nilzén:			
Pollen	6	4	
Animal dander	4	6	
Food	0	6	

The following aspects are not mentioned in the present communication among the factors which may exert an influence on the PB patients: social milieu (social groups, schooling, domicile), racial differences in the incidence, role of psychological factors, prophylactic measures and of nonspecific therapy.

#### *The author's investigations*

In Table 1 the incidence of PB with and without seasonal dependence are shown. The influence of spring on the course of PB and PB with respiratory symptoms is shown in Table 2 a and an analysis of the immediate skin test results of the cases showing spring deterioration follows in Table 2 b. The object of Table 3 a was the influence of the summer season on the course in PB patients as well as in patients with PB plus asthma bronchiale and/or rhinitis atopica. The summer course of patients with positive and with negative skin reactions are compared in Table 3. Skin reactions according to allergen groups are compared in PB patients showing improvement or deterioration respectively during summer. Table 3 d contains an analysis of skin tests of cases showing summer deterioration.

Table 1. *Immediate skin reactions and seasonal dependence<sup>1</sup> in the course of Prurigo Besnier.*

		Positive in immediate skin tests				Negative in immediate skin tests	
		Seasonal dependence	Seasonal independence			Seasonal dependence	Seasonal independence
Group I	25 patients	20	5	Group I	25 patients	19	6
Group II	25 patients	23	2	Group II	25 patients	21	4
Group III	25 patients	23	2	Group III	25 patients	24	1
Group IV	25 patients	24	1	Group IV	25 patients	24	1
100		90	10			88	12

<sup>1</sup> Cases showing seasonal improvement respectively deterioration.

Table 2 a. Influence of spring on the course of Prurigo Besnier in patients with Prurigo Besnier and Prurigo Besnier with respiratory atopies.

I. Prurigo Besnier	Course of PB during the spring			Seasonal independence	II. PB with Asthma and/or Rhinitis	Course of PB during the spring			Seasonal independence
	Improved	Deterio-rated	Unchanged			Improved	Deterio-rated	Unchanged	
Group I 25 patients	1	5	14	5	Group I 25 patients	—	7	12	6
Group II 25 patients	—	3	20	2	Group II 25 patients	1	3	21	—
Group III 25 patients	3	6	14	2	Group III 25 patients	1	5	15	4
Group IV 25 patients	1	5	18	1	Group IV 25 patients	3	4	16	2
100	5	19	66	10	100	5	19	64	12

Table 2 b. *Analysis of immediate skin tests in 50 patients with Prurigo Besnier showing deterioration in the spring (Groups II—IV).*

18 patients	positive to	"spring pollens"
3 patients	positive to	"summer pollens"
9 patients	positive to	series II (molds, bacteriae)
2 patients	positive to	series I (animal hair)
5 patients	positive to	series I—II
2 patients	positive to	several allergens
11 patients	negative in	immediate skin tests

Table 4 a shows the ratio of allergic and non-allergic rhinitis for patients with rhinitis and PB plus rhinitis. In Table 4 b is presented the rate of extrinsic-intrinsic-type bronchial asthma cases in patients with bronchial asthma and with PB plus asthma bronchiale respectively. The history of the onset of PB in relation to infections is given in Table 5 a. Table 5 b summarizes data of the relationship between the course of PB and infections in children with PB. The antistreptolysin and antistaphylolysin titers of PB patients are compared with that of controls in Table 5 c. The data obtained on school problems in young PB cases are considered in Table 6.

The incidence of symptomfree intervals in the different PB age groups are presented in Table 7 a as a comparison of the course of PB during the ages of 13 to 15 years in women and men respectively (Table 7 b). The years 13 to 15 were chosen according to the statement of Lennér (67) that the average menarchial age of Swedish women was  $14.485 \pm 0.034$  years in 1940, and that during the last fifty years this age has on an average reduced by some 10 days a year. In Table 7 c and 7 d are given the data of the effect of menstruation as well as of pregnancy on the course of the PB in women. Table 8 contains an analysis of male PB cases which aggravated during military service. The relationship between profession and PB is the subject of the survey in Table 9. The incidence of drug reactions in general and of salicylates according to their frequency in the patient material of the skin clinic is compared with PB patients in Table 10. Owing to the fact that most drug reactions occur in adults, only PB age groups III—V are considered in this connection. In Table 11 an evaluation of the results of hyposensitization of 30 PB cases are presented. The minimum time between the onset of the PB and the commencement of specific therapy was 7 years. Finally the data of PB patients elder than 45 years (Group V) are recorded in Table 12.

## *Results and Discussion*

### *Seasonal dependence*

The results in Table 1 show a seasonal dependency in about 90 per cent of the PB cases with positive or negative skin reactions. In the spring which starts in Scandinavia rather late, only 5 % of the patients show improvement independently of combinations with respiratory symptoms (Table 2 a). In analysing the positive skin reactions in this group as shown in Table 2 b a relationship may be assumed to exist in about one-third of the cases between deterioration of PB in the spring and reactions to spring pollens.

Table 3 a. Influence of summer on the course of PB in patients with PB and PB with respiratory atopies.

I Prurigo Besnier	Course of PB during the summer			Seasonal Independence	II PB with Asthma and/or Rhinitis	Course of PB during the summer			Seasonal Independence
	Improvement	Deteriorated	Unchanged			Improvement	Deteriorated	Unchanged	
Group I 25 patients	15	6	—	4	Group I 25 patients	14	5	1	5
Group II 25 patients	21	3	—	1	Group II 25 patients	20	2	—	3
Group III 25 patients	21	2	1	1	Group III 25 patients	19	4	—	2
Group IV 25 patients	19	3	—	3	Group IV 25 patients	22	—	2	1
100	76	14	1	9	100	75	11	3	11

Table 3 b. Correlation between skin test results and the course of Prurigo Besnier during the summer.

Positive in immediate skin tests	Course of PB during the summer			Seasonal independence	Negative immediate skin tests	Course of PB during the summer			Seasonal independence
	Improvement	Deteriorated	Unchanged			Improvement	Deteriorated	Unchanged	
Group I 25 patients	16	5	—	4	Group I 25 patients	11	8	2	4
Group II 25 patients	22	—	1	2	Group II 25 patients	21	—	—	4
Group III 25 patients	21	1	—	3	Group III 25 patients	20	2	1	2
Group IV 25 patients	20	4	—	1	Group IV 25 patients	22	1	1	1
100	79	10	1	10	100	77	11	4	11

Table 3 c. Correlation between allergen groups and the course of PB during the summer (Groups II—IV).

	Number of positive immediate skin reactions to:								Negative %		Total
	Series I %		Series II %		Pollen series %		Foods %				
I. 50 patients improved in summer <sup>1</sup>	12	14.8	20	24.7	14	17.3	10	12.3	25	30.9	81
II. 50 patients deteriorated during the summer <sup>1</sup>	14	16.9	24	28.9	24	28.9	10	12.0	11	13.3	83

<sup>1</sup> One patient has several positive reactions.

$\chi^2$  test and significance I to II in pollen series:  $p > 5\%$ .

Table 3 d. Analysis of immediate skin tests on 50 patients with Prurigo Besnier showing deterioration during the summer (Groups II—IV).

15 patients	positive to	"summer pollens"
8 patients	positive to	"spring pollens"
4 patients	positive to	series II (molds, bacteriae)
3 patients	positive to	series I (animal hair)
2 patients	positive to	series I—II
6 patients	positive to	several allergens
12 patients	negative in	immediate skin tests

Table 4 a. Type of rhinitis according to history and to immediate skin tests in patients with Rhinitis and in patients with Prurigo Besnier.

	Non-allergic type Rhinitis <sup>1</sup>	Atopic type Rhinitis
I. 50 patients with Rhinitis	13	37
II. 50 patients with Prurigo Besnier as well as Rhinitis	9	41

<sup>1</sup> Including Vasomotor rhinitis and Infective rhinitis according the classification of Duchaine (26).

$\chi^2$  test and significance I to II:  $p > 5\%$ .

Table 4 b. Type of bronchial asthma according to history and to immediate skin tests of patients with bronchial asthma and Prurigo Besnier with Asthma bronchiale.

	Intrinsic type Asthma <sup>1</sup>	Extrinsic type Asthma
I. 50 patients with bronchial asthma	30 = 60%	20 = 40%
II. 50 patients with Prurigo Besnier as well as bronchial asthma	18 = 36%	32 = 64%

<sup>1</sup> Including history of bacterial infections and immediate skin tests to staphylococci.

$\chi^2$  test and significance I to II:  $1\% < p < 5\%$ .

Table 5 a. *History of onset of Prurigo Besnier in relation to infections or vaccinations in 1200 patients.*

in 12	Cases onset after Variola vaccination
in 2	Cases onset after Vaccination with: Tetanus + Diphtheria + Pertussis vaccines
in 1	Case onset after BCG vaccination
in 4	Cases onset after Bacterial infections
in 3	Cases onset after Morbilli
in 1	Case onset after Pertussis
in 1	Case onset after Varicella

Table 5 b. *Correlation between infections and Prurigo Besnier. History of 100 children (Group I) with Prurigo Besnier according to infections.*

27	Cases: PB worse following infections of the Upper Respiratory Tract.
5	Cases: PB unchanged following infections of the Upper Respiratory Tract.
2	Cases: PB worse after Viral infection
1	Case: PB worse after Otitis media

Table 5 c. *Antistreptolysine and antistaphylolysine titers on 100-100 patients with Prurigo Besnier and with other skin diseases.<sup>1</sup>*

	Antistreptolysine titers in Todd units			Antistaphylolysine titer < 1 1-3 > 3
	under 200	between 200-500	over 500	
I. 100 patients with PB	66	34	—	— 100 —
II. 100 skin patients <sup>1</sup>	81	19	—	— 100 —

<sup>1</sup> Excluded: Pyodermias, furunculosis, acne, microbic eczema etc.  
 $\chi^2$  test and significance I to II in antistreptolysine titers: 10% < p < 5%.

Table 6. *Prurigo Besnier and school influences.*

40	observed cases
30	in the negative sense
7	worse during physical training (dust/sweat). Two had to be exempted from the lessons
5	teased by schoolmates owing to PB
4	concentration difficulties owing to itching
4	worse when going to school (mould, dust, and horse sensitivity)
2	sweating — itching at written examinations
2	often absent from school owing to PB
1	could often not write owing to bandaged hands
1	had to finish school owing to itching and asthma (dust, animal sensitivity)
1	exempted from chemistry lessons owing to deterioration during those lessons
1	obliged to eat food that did not suit him
1	did not get on well with his teacher
1	disabled from a school point of view (has even Asthma and Rhinitis)
10	in the positive sense
6	clever, got on well in school
4	good contact with schoolmates

During the relatively brief and mild Scandinavian summer, three quarters of the cases showed improvement (Table 3 a). There was no difference between patients with and without respiratory manifestations. The improvement in Table 3 a agrees well with the values noted in Table 2 a of the authors' previous communication (94). In that communication the improvement rates of patients positive to animal hair, dust and molds were between 56 and 94 %. The re-

Table 7 a. *Symptomfree intervals of more than one years duration in patients with Prurigo Besnier.*

		Symptomfree intervals	No intervals
Group I	50 patients	2	48
Group II	50 patients	9	41
Group III	50 patients	14	36
Group IV	50 patients	26	24

Table 7 b. *Course of Prurigo Besnier between 13 and 15 years of age in females and males.*

	Between the ages of 13 and 15 years						D	
	A		B		C			
	Continued course of PB %		Relapses of PB %		Symptomfree intervals of PB %		Onset of PB after 15 years of age %	
I. 200 men with PB	120	61.5	19	9.7	45	23.1	11	5.6
II. 200 women with PB	140 <sup>1</sup>	74.1	21	11.1	19	10.0	9	4.8

<sup>1</sup> 7 out of 140 showed strong deterioration.

$\chi^2$  test and significance I to II in A: 1% < p < 5%, in B and D: without significance, in C: p < 0.1%.

Table 7 c. *Effect of menstruation on the course of PB in 40 women.*

Better during the menstruation	in 10 cases
Worse during the menstruation	in 14 cases
Worse during the premenstrual period	in 13 cases
Worse during the postmenstrual period	in 3 cases

Table 7 d. *Effect of pregnancy on the course of PB in 25 women.*

Better during the pregnancy	in 14 cases
Worse during the pregnancy	in 11 cases

markable difference between spring and summer improvements depends on several factors which will be discussed below.

If the relationship between summer improvement and immediate skin reactions are considered, significant differences are not found between test-positive and test-negative groups (Table 3 b). The reactions according to allergen groups compared with the summer course of PB was the subject of the survey in Table 3 c. Between summer-improved and summer-aggravated PB cases there was no statistical difference in the incidence of pollen reactions. Table 3 d shows that 15 of 50 patients who became worse in the summer had sensitivity to summer pollens. In summarizing the data of the above tables and those of the previous communication (94) regarding the spring and summer course of PB it may be stated that:

Table 8. Analysis of 19 out of 100 male patients with Prurigo Besnier who showed deterioration in military service.

Ref. No.	Result of immediate skin tests				The patient suspects as deteriorating factors:	Other manifestations	Owing to the skin disease the patient was	
	Animal hair	Dust-mold	Food	Pollen			Others	placed in a lower class
53/111	+	+	+	+	dust, wool, straw, fumes	Rhinitis		
119		+			petroleum			
132		+						
136 <sup>1</sup>		n e g a t i v e						
183 <sup>1</sup>	+	+	+					
56/ 93		n e g a t i v e					+	
103		+						
108	+	+	+	+				
135	+	+		+		Rhinitis	+	
140		n e g a t i v e						
151	+				grooming			
57/ 79	+	+			dust, straw		+	
100						Rhinitis		+
104	+	+		+	straw, tidying			
111					blue navy uniform		2	
130					sweating			
58/ 86	+	+	+	+	heat, moisture, uniform	Rhinitis		+
87	+		+	+		Rhinitis		
89		n e g a t i v e		+				

<sup>1</sup> Had a recurrence of Prurigo Besnier in military service.

<sup>2</sup> Placed in a lower class for scoliosis.

Table 9. *Profession and Prurigo Besnier in the material.*

Sensitization cases	Following number had to give up work	Cases due to irritation	Following number had to give up work
<i>Mold (dust)</i>		<i>Humid work</i>	
office employees	10	medical attendance	7
grocer's shop	4	maid-housewife	6
pork-butcher's shop	2	milkshop employee	1
bakery-confectionery	2	(female) swimming master	1
brewery	2		
textile	2	<i>Chemicals</i>	
housewife (baking)	2	metal workers	9
dusty and humid working place	15	(female) hairdresser	5
	2	employees in chemist's shop	2
<i>Confectionery</i>	3	others	4
<i>Forestry</i>	1	<i>Wool (+ chemicals)</i>	
<i>Contact factor</i>		textile workers	6
dental nurse	2		4
nurse	2	<i>Dusty work</i>	3
(female) hairdresser	1	<i>Warm working conditions</i>	3
textile worker	1	<i>Cold</i> " " "	1
Exceptions:		Exceptions:	
2 — dust-mold sens. could work in such a place of work		1 (female) spinner did well endure wool	

*Not fit for work*

Profession	Period	Other symptoms
Restaurant worker	1 year	
postman	5 years	A
housewife	5 "	A + R
engineer	1/2 year	R
groom	1 year	R
carpenter	for a long time	A <sup>1</sup>
office employee	" " " "	R
cement worker	" " " "	A
drawing master	" " " "	R + A
office employee	" " " "	R + A
paint factory worker	" " " "	A
painter		A + R

<sup>1</sup> Bad working possibilities. Retraining recommended.

A: bronchial asthma

R: Rhinitis atopica

*Inappropriate hobby*

grooming (13-year-old girl, till now not sensitive)  
developing work (hydrochinon-positive)

- Spring deterioration in PB patients occurs in 19 %. (Table 2 a.)
- Among the spring pollen sensitive patients 34 % aggravate in the spring (see previous communication, Table 5 a).
- The total incidence of pollen positivity (the average of groups II—V) is 20.1 % (calculated from Table 2 a, see previous communication).
- Among the spring-deteriorated cases 36 % are positive to spring pollens

Table 10. *Drug reactions in PB patients.*

During 1957—1959 the total number of skin patients in the ward of the Karolinska sjukhuset, the Department of Dermatology, was .....	4437
I. During this period the number of PB patients (Groups III—V) warded was	436 (9.8 %)
During this period the number of patients investigated for suspected salicylate allergy was .....	81
II. During this period the number of PB patients (Groups III—V) investigated for suspected salicylate allergy was .....	1 (1.2 %)
During this period the number of patients investigated for suspected allergy to various drugs was .....	83
III. During this period the number of PB patients (Groups III—V) investigated for suspected allergy to various drugs was .....	2 (2.4 %)

$\chi^2$  test and significance I to II 0.1 % < p < 1 %, I to III 1 % < p < 5 %.

(Table 2 b). The difference between the data of a and b is not statistically significant; as between c and d it is however statistically significant. Pollen sensitivity can thus play a certain role in spring aggravation of PB cases.

e. Summer deterioration in PB patients occurs in 11 % and 14 % (Table 3 a).

f. Among the summer pollen-sensitive cases 10 % aggravate in the summer (previous communication, Table 5 a).

g. The total incidence of pollen positivity (the average of groups II—IV) is 20.1 % (calculated from Table 2 a, see previous communication).

h. Among the summer-deteriorated cases 30 % are positive to summer pollens (Table 3 d).

i. Among the summer improved cases 17 % are positive to summer pollens (Table 3 c). Statistically significant differences do not exist between e and f, between h and i or between the data of g and h respectively. Summer pollens may thus play a slight role in eliciting summer exacerbations in PB cases. In the summer aggravation of PB cases (see Table 3 c) the role of skin reactions to pollens is not great. The same applies to immediate skin reactions in general. According to the author's opinion the summer improvement/deterioration in individual cases depends on the inter-relationship of several factors:

*Improvement may be due to*

Better sebum and sweat secretion  
Sun baths (IR-rays and sweating?  
UV-rays?)  
Sea bathing (keratolytic effect?)  
  
Reduced exposure to dust-mold  
indoors  
Intake of less spiced food  
Changes of environment (beneficial  
climatic and "allergen"-conditions)

*Aggravation may be due to*

Extreme sweating (strong heat)  
Increased sunlight exposure  
  
Irritation following sea bathing of  
long duration.  
Increased exposure to molds  
outdoors  
Increased intake of fruits, vegetables  
Changes of environment (un-  
favourable climatic and "allergen"-  
conditions)

Holidays (elimination of irritants, allergens, beneficial psychological influences)	Increased contact with animals, pollens
Non-use of woolen clothes	
Less danger of infections	
Metabolic changes (?)	

Most of the considerations in this list do not require special comments. The role of the light factor in PB and differences between PB cases and patients with prurigo aestivale should however be emphasized. The summer prurigo (prurigo aestivale), is generally included in the group of chronic polymorph light dermatoses (138, 88, 21, etc.). One can hardly find any differences in morphology between prurigo aestivale and PB which deteriorates in summer. Kochs (60) states, however, that a chronic liver lesion can always be found in the former disease. Stevanovic (118) describes 7 cases of PB which became worse in the summer when sunlight acted as a nonspecific localising factor. There were 8 cases in the author's material which showed sensitivity to a light test with an Osram Ultravitalux lamp with UV-A, UV-B and visible rays as well as IR rays up to 5000 m $\mu$ . It may be assumed that PB which shows summer aggravation and a verified sensitivity to light represent a transition to, or is a manifestation of, the prurigo aestivale-group.

#### *Environmental changes*

Most of the author's patients improved by sojourn at sea and when staying in the Swedish mountains. According to the patients, the former was mainly due to the sun and sea bathing. In this relation it may be mentioned that a smaller mold spore count was found in the Swedish mountains than e. g. in cities by Nilsby (81).

#### *Sweating disturbances*

Almost all the patients in the author's material — independently of skin test results — had a history of increased itching following high temperature, exertion or sweating. Many of the patients had similar complaints after excitement and several women had increased premenstrual pruritus. Similarly many patients did not tolerate well underclothes made of nylon, especially crêpenylon or perlon (prevention of sweat evaporation). According to the author's observation, the intolerance to wool (clothes) which was highly characteristic of PB patients, is possibly due to mechanic irritation by the wool fibers on the dry-keratotic skin. In certain cases only moist wool (e. g. after sweating) elicited itching.

#### *Combination with other diseases*

##### *a) Combination with rhinitis atopica and/or asthma bronchiale.*

The positive immediate skin reactions which are possibly due to rhinitis or asthma components in patients with PB plus respiratory symptoms have been

Table 11. Result of hyposensitization in patients with PB controlled clinically and by skin test after a minimum of one year.

No.	Allergens according groups. The patient was hyposensitized with:				Result of new skin test after hyposensitization:		New reactions to:		Period between the two tests in years	Results of hyposensitization	
	Animal hair	Mold dust bacteriae	Pollen	Food	Allergens the patient reacted to	Inhalants	Foods	Became better		Temporary improvement in years	No improvement
1					slight positive				3		
2	+			+	negative				1		+
3		+		+	unchanged				3		
4		+			unchanged				11	+	
5					unchanged				6		+
6		+		+	negative				1		+
7	+			+	negative				1		+
8	+			+	negative				7		
9		+			negative				2	++	
10	+	+			unchanged <sup>1</sup>				4	++	
11				+	negative				3		+
12		+			unchanged <sup>1</sup>				4		+
13				+	unchanged				2		+
14	+				negative				2	(+)	
15	+				negative				2		+
16		+			negative		+		1		+
17		+			unchanged				2	+	
18		+			negative				1		+
19		+			unchanged				7	(+)	
20	+			+	unchanged		+		1		+
21		+			unchanged				4	+	
22		+			unchanged <sup>1</sup>				4		+
23				+	unchanged <sup>1</sup>				4	+	
24		+			unchanged				2		
25	+				unchanged				4		+
26	+				unchanged				1		+
27		+			unchanged <sup>1</sup>				7	+	
28		+			unchanged				5		+
29	+			+	unchanged				7		+
30	+			+	unchanged				6		+
	12	20	11	12	became negative in 10 cases	new reactions in 17 patients	average: > 3 years	13 cases	17 cases		

<sup>1</sup> Certain reactions became neg.

demonstrated in several tables in the author's previous communication (94). The same allergens are possibly responsible for eliciting asthma bronchiale or rhinitis atopica in patients with these symptoms or in patients with PB plus these symptoms respectively. The incidence of allergic and non-allergic rhinitis based on history and immediate skin reactions shows no significant differences between cases with rhinitis atopica and cases with PB + rhinitis atopica (Table 4 a). If cases with asthma bronchiale and cases with PB + asthma are compared on the basis of history and skin tests (although a prevalence of extrinsic factors (extrinsic-type asthma) is found in the PB plus asthma group) the difference is statistically not significant (Table 4 b). The majority, i. e. 13 of 17 patients with PB plus asthma reacted to extrinsic allergens also in Bergman's (10) series.

#### b) *Other diseases.*

The incidence of combinations of PB with other diseases in the author's material of 1200 cases was:

ichthyosis vulgaris	2.5 %
cataracta	0.5 %
epilepsy	0.4 %
gastroenteral disturbances	0.9 %
infestation	0.3 %

Thus the incidence of ichthyosis was not high and the one of cataracta was rather low. The latter can mostly be explained by the fact that the author's series of patients comprises only cases which had undergone ophthalmologic examinations when eye lesions were suspected. In a series of 100 patients by Kornerup & Lodin (61) every single patient was examined ophthalmologically and an incidence of 3 % was then found.

The incidence of gastroenteral disturbances in the present series is mostly based on the history and not on laboratory investigations. The incidence of epilepsy agrees with that in the general population. Infestations are only associated in a low percentage with PB. This is in contrast to the findings of Oppitz & Zelger (86).

#### *Infections*

Since the results of immediate microbial skin tests are not satisfactory, anamnestic and clinical data in relation to possible infections are collected. According to Table 5 a a relationship can be assumed in 24 cases, i. e. in 2 % of the material between the onset of PB and the infections or vaccinations. It should, however, be noted that in vaccination-cases also other factors than living or killed microorganisms may play a role (e. g. animal tissue, formaldehyde, antibiotics etc.). The most likely explanation of the mechanism of the cases cited above is Urbach's (133) that an infection is a predisposing factor in allergy. Table 5 b shows that among hundred PB-children a deterioration of the skin disease after upper respiratory infections was mentioned in about one-fourth of the cases. This number is of course decreasing in elder PB age groups.

Table 12. Analysis of 25 patients with Prurigo Besnier older than 45 years of age (Group V).

Reg. No.	Age	Sex	Hereditary	Onset of PB at the age of:	Free intervals of PB at the ages of:	Rhinitis	Asthma bronchiale	Positive i. c. tests to series:			Remarks		
								I	II	Food			
3/234	48	m	—	2 years	2—20 years	—	—	—	—	—	+	Hyposensitization to mold was given	
235	47	w	PB	3 months	6—18 years	+	—	—	—	—	—	—	Lives in a wooden house
236	49	w	PB	1 year	none	—	—	—	—	—	—	—	Summer deterioration from pollen
4/362	48	w	—	under 1 year	20—30 years	+	—	—	—	—	—	—	Contact sensitive to Nickel and Chrome
363	46	w	PB	under 1 year	none	—	+	—	—	—	—	—	History of foods
364	60	w	—	9 months	none	+	—	—	—	—	—	—	Light-sensitive. Rhinitis better after pollen hyposensitization
365	60	m	—	childhood	12—50 years	+	—	—	—	—	—	—	Works with irritative substances (oils etc.)
5/187	49	w	PB	1 year	none	+	—	—	—	—	—	—	History of foods
188	46	w	PB,A	6 months	6 m.—4 y., 18 y.—44 y.	—	+	—	—	—	—	—	History of foods
189	48	m	Asthma	under 1 year	—	—	—	—	—	—	—	—	—
190	49	m	—	under 1 year	1—29 years	—	—	—	—	—	—	—	Tests results "better" after hyposensitization. History of foods.
191	47	w	—	25 years	none	—	+	—	—	—	—	—	Contact sensitive to formaldehyde
192	48	w	A,R	"after birth"	none	—	—	—	—	—	—	—	History of foods
193	49	w	—	childhood	none	—	—	—	—	—	—	—	Contact sensitive to p-phenylenediamine
194	46	m	PB,R	under 1 year	3—42 years	—	+	—	—	—	—	—	Hyposensitization to animal hairs and pollens was given
6/157	46	m	PB	under 1 year	"Sometimes"	+	—	—	—	—	—	—	Hyposensitization to animal hairs and molds was given
158	74	w	PB	childhood	none	—	—	—	—	—	—	—	Course of PB got worse after 58 years of age
159	49	w	R	2 years	2—16 y., 30—40 y.	+	—	—	—	—	—	—	—
160	61	w	—	44 years	none	—	+	—	—	—	—	—	History of foods. Clinical diagnosis PB

161	50	w	PB,R	15 years	none	+	+	—	—	+	+	+	+	+	+	+	Hyposensitization to molds and pollens was given
7/138	48	w	PB,A,R	childhood	6—13 years	—	—	+	—	—	—	—	—	—	—	—	Nurse, contact sensitive to formaldehyde
139	63	m	—	5 years	none	—	—	+	—	+	+	+	+	+	+	+	—
140	52	w	PB,R	childhood	23—44 years	—	—	+	+	+	+	+	+	+	+	+	Hyposensitization to molds was given. Worse at work in textile factory
141	54	m	PB,A	10 years	10—27 years	+	—	—	—	+	+	—	—	—	—	—	—
142	47	w	PB	4 months	4 m.—20 years	+	+	+	+	+	+	+	+	+	+	+	Hyposensitization to animal hairs was given
25			9:— 7:PB 6:PB+A/R 3:Asthma and/or Rhinitis		11:none		17	10+	17+	9+	9+	9+	9+	9+	9+	9+	

## Abbreviations:

w = woman

m = man

m. = month(s)

y. = year(s)

PB = Prurigo Besnier

A = Asthma bronchiale

R = Rhinitis atopica

According to the data of Table 5 c, the difference in antistreptolysin titers noted between PB and other skin cases did not show a statistical significance. The antistaphylolysin titers in the two groups showed no differences.

#### *School problems in young PB patients*

The information on 40 school children indicate some of the more frequent problems which concern behaviour at school of children with skin disease. The relation between PB and the school was in three-quarters of these cases of unfavourable nature; the school represents for most of the PB children a certain affliction. No similar data were found in the available literature.

#### *Hormonal influences in women*

The author's material consisted of 665 women and 545 men. In the Tables 6 b and 6 c of his previous communication (93) the onset of PB in different ages was presented. The onset between 11 and 15 years was 1.5 % of the total cases for men and 3.5 % for women. The incidence for the age group 6—10 years was 4.8 % versus 7.2 % and for 16—20 years 2.6 % versus 2.1 %. In either of these age groups there is a statistically significant difference between males and females in regard to the time of the onset of PB.

Table 7 a shows that the symptomfree intervals for the age group III (between 13 and 18 years) is on an average 28 % of the total cases. Table 7 b shows that around the average menarche time in Sweden (between the years 13—15) this incidence is somewhat lower. During this period, symptomfree intervals occur in men more frequently than in women who in certain cases show very accentuated exacerbations (7 of 140 cases of Table 7 b). The difference is of statistical significance.

Around the menstrual cycle an aggravation can be observed in about three quarters of the female PB cases according to Table 7 c. The conditions occurring during pregnancy in female PB patients are contradictory; the rate of improvement/deterioration is about the same. Sometimes improvement is observed up to a certain period by the pregnancy, following which the course of PB becomes worse. Or the reverse situation may occur. Cases have been observed where in different pregnancies their effect on PB was antagonistic. No parallelism could be found in the same person between the effect of premenstrual changes or of the pregnancy on the course of PB. Some cases showed improvement while others were aggravated after delivery (hormonal influences (?), increased contact with synthetic detergents (?). Similar findings have been mentioned by other investigators (e. g. Pirilä, 89).

#### *The effect of military service on the course of PB*

For male PB patients the military service causes frequent difficulties owing to changed home and working conditions, the presence of different allergens etc. About one-fifth of the cases showed a deterioration during military service and the causes of this are analysed in Table 8. It is difficult to evaluate the role of

the responsible factors in individual cases, but the following seem frequently to play a role: contact with animal hair, pollen, dust, strawmattresses, textiles (uniforms) as well as sweating after military exercises. No similar data were found in the available literature.

### *Working conditions*

The most frequently occurring causes of aggravation of PB in various professions are enumerated in Table 9 according to allergic or irritative mechanisms. It should however be mentioned that besides the cases mentioned in Table 9 still more workers (e. g. house-wives) have problems following contact with water and detergents or with other irritative substances. The cause that the cases mentioned were not fit to work could also be explained by their respiratory allergic symptoms (except the first patient). In addition, it should be noted that most of the workers stopped with their work on medical advise whereas some others did this on their own decision.

Occupational advise to young PB patients with an obstinate course of the disease seems necessary. Although in most cases the disease becomes milder or ceases with time it is difficult to take this possibility into account at the moment of choice of occupation. Medical advice against choice of an intended occupation was given by the author, e. g. in the following PB cases:

- farmer — to a patient sensitized to animal hair and pollen
- confectioner — to a patient sensitized to mold
- teacher in domestic crafts — to a dust-sensitive person
- nurse — to a patient sensitive to dust, hair, metals and formaldehyde etc.
- cook — to a person sensitive to egg.

### *Drug reactions*

From the data of Table 10 it is seen that the incidence of drug allergies was rather low in the author's PB series. It is assumed these numbers are not free from errors (e. g. deficiencies in the history of the patients to drug reactions) but even so they seem to show that drug allergic episodes did not play a significant role in the course of PB. These results agree well with Schnyder's (105) statements on the whole atopic group. Statistically, there are significant differences between groups I and II whereas the difference between group I and III was not significant. The incidence of salicylate allergy in PB patients is thus very low, whereas the number of drug reactions in general corresponds to the incidence of this disease, but is not higher.

### *Specific therapy*

Table 11 shows 30 PB cases receiving specific therapy. The data were followed clinically and with repeated skin tests. In the repeated skin tests about two thirds of the earlier positive reactions remained unchanged. New sensitivities appeared in about half of the patients. (See also Table 7 of a previous communication, 94). There was no parallelism between clinical improvement

and the outcome of the repeated skin test. The average observation time was more than 3 years. The cases which were already investigated after one year showed no improvement (cases No 2, 6—7, 16, 18 and 26).

The allergens were mostly several inhalants or foods. It is therefore not easy to differentiate separate allergen groups. If one, however, compares the incidence of the allergen group-reactions in the improved cases and in the total number of cases, the following data appear: (I) food: 2 of 12, (II) animal hair: 3 of 12, (III) pollen: 5 of 11 and (IV) mold-dust-bacteriae: 10 of 20 cases. The effect of the hyposensitization was thus greatest in the pollen and mold-dust-bacteriae groups. On the whole, this finding agrees with the reports of other investigators, to which reference was made in the introduction (31, 131, 99, 100, 95, 79, 83).

The results could be classified as a temporary or quantitative improvement in more than one-third of the cases (in 13 of 30 cases). Complete, permanent cure which could be considered an effect of hyposensitization was not to be observed. The question of the practical benefit of hyposensitization in PB is very much discussed, as already mentioned in the introduction, and the majority of the investigators in this field are rather pessimistic. It would be useful to use placebo-injections instead of allergen extract in a group of PB cases to exclude possible psychological influences. This is, however, difficult to carry out. The author's opinion is that no more can be achieved by hyposensitization of PB patients selected according to strict criteria than a temporary relief of a certain improvement. Even the possibility of spontaneous reliefs and intervals should not be overlooked in evaluating therapeutic results in this disease (c. p. Table 7 a). Although the expected effect of a hyposensitization is not very great, it can be helpful in individual cases to exclude *one* of the possible etiologic factors in this complex condition. At the same time, it follows, however, that very severe criteria should be applied before recommending this tiresome type of therapy in the individual case. The patients should be informed of the outlook of the therapy so as to avoid false illusions.

Finally, it should once more be stressed that the foregoing refers to PB not combined with respiratory symptoms. In the combined cases, the situation is completely dissimilar.

#### *Patients older than 45 years of age (Group V)*

Table 12 shows the data of 25 patients with PB of more than 45 years at the time of the investigation. According to clinical and other data, these cases correspond to the diagnostic criteria of PB. They represent 2 % of the entire material. It would appear useful to analyse why the course of PB was so obstinate in these cases. The onset took place only in one case at the age of 44, whereas in most of the patients the PB started in childhood. In half the number of the cases there were no long interruptions in the course of the disease. The incidence of familial heredity corresponds to the data in the whole material whereas that of respiratory allergic combinations is higher. The results of immediate skin testing were negative only in 4 cases and in most of the cases the prevalence of mold reactions was observed. It should however be mentioned that 17 of 25 cases were PB cases combined with respiratory symptoms. In some

cases hyposensitization was tried without durable success. Six cases had a food history which could be corroborated by skin tests only in one patient. In summarizing the above considerations it may be said that even by analysis of these interesting cases it is not possible to approach the basic problems of PB any further.

### SUMMARY

The present communication is the third of a series in which some factors are discussed which may influence the course of Prurigo Besnier (PB) in a material of 1200 cases studied by the author. A seasonal dependence was found in 90 per cent of the patients. According to the data of the skin tests pollen sensitivity can play a certain role in the spring exacerbation but only a slight role in the estival deterioration of PB. The factors which may exert an influence on the estival course of PB are reviewed, including sweat disturbance which seems to be of importance. PB cases aggravating in summer and showing a verified sensitivity to light may represent a transition or belong to the prurigo aestivale-group. Some more cases of the exogenic-type were found in the patients with PB and asthma as compared to asthma-cases alone. This difference was however without statistical significance. There were no differences in the incidence of exogenic factors in patients with PB and rhinitis atopica and rhinitis atopica solely. The incidence of ichthyosis vulgaris and cataracta was not high and of gastrointestinal disturbances and infestations rather low in PB patients. The incidence of the combination PB and epilepsy did not exceed that for the average population.

In 2 per cent of the cases a relationship could be assumed between the onset of PB and infections or vaccinations. In three-quarters of the children with PB a deterioration in skin disease followed according to the history infections of the upper respiratory tract. The difference in antistreptolysin and antistaphylo-lysin titers in PB and control patients was not significant statistically.

Information was collected of school problems in children with PB. In three-quarters of the cases the information was of unfavourable nature. Symptomfree periods between 13 and 15 years occur more frequently in men than in women. The latter have in general menarche in this period. Related to the menstrual cycle an aggravation could be observed in about three-quarters of the female PB patients. The influence of pregnancy on the disease is very controversial. About one-fifth of the male PB cases showed a deterioration during military service. The possible causes of this are given. The most frequently occurring aggravating factors for PB patients in various professions are listed. The incidence of drug reactions was low in PB cases as compared to that in the controls.

Thirty PB cases receiving therapy were evaluated. In more than one-third a temporary relief or an improvement could be observed but no one case of complete or permanent healing was found. Therefore, the indication for this type of therapy should be strict. It should be kept in mind that one cannot achieve more by hyposensitization than to exclude *one* of many possible etiologic factors in this disease. Finally, the data of PB with a course of long duration were analysed in patients of more than 45 years of age.

## RÉSUMÉ

La présente communication est la troisième d'une série d'articles, dans lesquels sont discutés les divers facteurs susceptibles d'influencer l'évolution du prurigo de Besnier (PB), sur la base d'un matériel de 1200 cas étudiés par l'auteur.

Chez le 90 % des patients, il existe une influence saisonnière. Conformément aux résultats des tests cutanés, une sensibilité au pollen semble jouer un certain rôle dans l'éclosion des poussées printanières, alors qu'elle ne joue qu'un petit rôle dans l'aggravation estivale du PB. L'auteur passe en revue les facteurs susceptibles d'influencer l'évolution estivale du PB, y compris les troubles de la sudation qui semblent jouer un rôle important. Les cas de PB qui se péjorent en été, et présentent une sensibilité à la lumière certaine, peuvent représenter une forme de transition ou appartenir au groupe du prurigo estival. Le type exogène se voit plus souvent chez les patients qui présentent un PB associé à de l'asthme, que chez les patients atteints d'asthme seulement. Cette différence s'est cependant révélée sans importance statistique. Quant à l'incidence des facteurs exogènes, il n'a pas été trouvé de différences entre les patients atteints de PB et de rhinite atopique et ceux qui souffraient de rhinite atopique seulement. Chez les patients atteints de PB, le nombre des cas d'ichtyose vulgaire et de cataracte n'est pas élevé et le nombre des infections et troubles gastrointestinaux est assez bas. L'incidence des cas de combinaison de PB et d'épilepsie n'excède pas celle de la moyenne de la population. Dans le 2 % des cas, il a été possible d'établir une relation entre les poussées de PB et des infections et vaccinations. Dans l'anamnèse des  $\frac{3}{4}$  des enfants atteints de PB, on trouve que l'aggravation de la dermatose a été précédée par une infection des voies respiratoires supérieures. Les différences trouvées dans le taux des antistreptolysines et des antistaphylolysines entre les malades atteints de PB et les sujets de contrôle, s'est révélée sans importance au point de vue statistique. L'auteur s'est renseigné sur les problèmes scolaires des enfants atteints de PB. Dans les  $\frac{3}{4}$  des cas, les renseignements étaient de nature défavorable.

Des périodes asymptomatiques de 13 à 15 ans surviennent plus souvent chez les hommes que chez les femmes. Les femmes ont leurs premières règles à cette période. Une aggravation en relation avec le cycle menstruel peut s'observer chez environ le  $\frac{3}{4}$  des femmes atteintes de PB. L'influence de la grossesse sur l'évolution de cette maladie est très controversée. Chez les hommes, le  $\frac{1}{3}$ ème des cas ont présenté une péjoration pendant le service militaire. L'auteur donne les causes possibles de ce fait. L'auteur a dressé une liste des facteurs susceptibles d'aggraver le prurigo de Besnier, que l'on rencontre le plus fréquemment dans diverses professions. Les réactions médicamenteuses sont rares dans les cas de PB, comparativement aux sujets de contrôle.

L'auteur a suivi 30 cas de PB qui recevaient un traitement. Dans plus d'un tiers des cas, une rémission passagère ou un soulagement a pu être observé, mais dans aucun cas, une guérison complète ou durable n'a été obtenue. Dans ces conditions, l'indication de ce traitement doit être sérieusement discutée. Il faut garder à l'esprit qu'on ne peut attendre de meilleurs résultats par une hyposensibilisation que par l'exclusion d'un des nombreux facteurs étiologiques de cette maladie. Finalement, les caractères du prurigo de Besnier ayant évolué pendant de longues années, ont été analysés chez des patients de plus de 45 ans.

## ZUSAMMENFASSUNG

Die vorliegende Mitteilung ist die dritte einer Serie, in der einige Faktoren diskutiert werden, die den Verlauf von Prurigo Besnier (PB) beeinflussen. Die Aussagen stützen sich auf ein vom Verfasser untersuchtes Krankengut von 1200 Fällen. Eine jahreszeitliche Beeinflussung fand sich bei 90 % der Patienten. Nach den Ergebnissen der Hautteste könnte die Pollenallergie eine gewisse Rolle bei der Frühjahrsexazerbation spielen, jedoch nur eine geringe Rolle bei der sommerlichen Verschlechterung des PB. Die Faktoren, die einen Einfluss auf den Verlauf im Sommer nehmen, werden dargestellt, einschliesslich der Schweißstörungen, die von Bedeutung zu sein scheinen. PB-Fälle mit Verschlechterung im Sommer und mit nachgewiesener Lichtempfindlichkeit stellen vielleicht einen Übergang dar, oder sie gehören zur Prurigo aestivale-Gruppe. Unter den Patienten mit PB und Asthma fanden sich mehr Fälle vom exogenen Typ als bei den reinen Asthmafällen. Dieser Unterschied war jedoch nicht statistisch gesichert. Es fand sich kein Unterschied in der Häufigkeit von exogenen Faktoren bei Patienten mit PB und Rhinitis atopica und Rhinitis atopica allein. Die Häufigkeit von Ichthyosis vulgaris und Katarakt war nicht hoch und die von gastrischen Störungen und Infektionen ziemlich gering. Die Häufigkeit der Kombination PB und Epilepsie überstieg nicht diejenige der Durchschnittsbevölkerung.

Bei 2 Prozent der Fälle konnte eine Beziehung zwischen dem Beginn der PB und Infektionen sowie Vaccinationen angenommen werden.  $\frac{3}{4}$  der kindlichen Fälle zeigten nach der Anamnese eine Verschlechterung der Hauterscheinungen im Anschluss an Infektionen der oberen Luftwege. Ein statistisch signifikanter Unterschied von Antistreptolysin- und Antistaphylolysin-Titern zwischen PB- und Kontrollpatienten liess sich nicht ermitteln.

Es wurden Informationen über Schulprobleme von Kindern mit PB gesammelt. Bei  $\frac{3}{4}$  der Fälle waren die Informationen ungünstiger Natur.

Symptomfreie Perioden zwischen dem 13. und 15. Lebensjahr waren beim männlichen Geschlecht häufiger als bei weiblichen Patienten, bei denen die Menarche in diese Zeit fiel. Etwa  $\frac{3}{4}$  der weiblichen Kranken wiesen während der Menstruation eine Verschlimmerung auf. Der Einfluss der Gravidität ist strittig. Bei ungefähr  $\frac{1}{5}$  der männlichen PB-Fälle verschlimmerten sich die Erscheinungen während der Militärzeit; auf die möglichen Ursachen dieser Beobachtung wird eingegangen. Die häufigsten beruflichen Faktoren mit ungünstigem Einfluss auf den PB werden aufgeführt. Arzneimittelreaktionen kommen bei PB-Patienten im Vergleich zu Kontrollfällen relativ selten vor.

Bei 30 PB-Patienten wurde das Therapieergebnis ausgewertet. Ein Drittel zeigte eine temporäre Besserung oder Symptombfreiheit, vollständige und anhaltende Heilungen wurden aber nicht beobachtet. Die Indikation für diese Art der Therapie sollte daher streng gestellt werden. Es sollte nicht vergessen werden, dass man durch die Hyposensibilisierung nur einen von vielen möglichen ätiologischen Faktoren dieser Krankheit ausschalten kann.

Abschliessend werden die Daten von über 45 Jahre alten PB-Kranken mit langem Krankheitsverlauf analysiert.

## RESUMEN

La presente comunicación es la tercera de una serie en la que se discuten algunos factores que puedan influir en el curso del Prurigo de Besnier (PB), en un material de 1.200 casos estudiados por el autor. En el 90 por ciento de los

pacientes se ha visto una cierta dependencia estacional. De acuerdo con los datos de pruebas de sensibilidad al polen puede explicarse un cierto papel en la exacerbación primaveral, pero una escasa importancia en el empeoramiento estival del PB. Se revisan los factores que puedan ejercer cierta influencia en el curso estival del PB, incluyendo las alteraciones sudorales que parecen tener importancia. Los casos de PB que se agravan en verano y muestran una comprobada sensibilidad a la luz pueden representar una transición o incluso pertenecer al grupo del prúrigo estival. Se encontraron algunos casos más de tipo exogénico entre los pacientes de PB y asma que en los de asma sólo. Sin embargo, esta diferencia carecía de valor estadístico. Tampoco hubo diferencias en la frecuencia de factores exogénicos entre los pacientes con PB y rinitis atópica y los que sólo tenían la rinitis atópica. La incidencia de ictiosis vulgar y catarata no fué elevada, y los trastornos e infecciones gastrointestinales eran más bien escasos en los pacientes de PB. La combinación de epilepsia y PB no fué más frecuente que lo usual en la población normal.

En un 2 por ciento de los casos pudo sospecharse cierta relación entre el comienzo del PB e infecciones o vacunaciones. En tres cuartas partes de los niños con PB la alteración de la piel enferma iba precedida de historia de infecciones de vías respiratorias superiores. La diferencia de títulos de antiestreptolisina y antiestafilolisina en enfermos de PB y controles carecía de valor estadístico.

Se recogieron datos acerca de los problemas escolares en los niños con PB. Tres cuartas partes de los casos proporcionaron informes desfavorables. Los períodos asintomáticos entre las edades de 13 y 15 años eran más frecuentes en varones que en hembras. Las mujeres tienen por lo general la menarquia a esta edad. Ha podido observarse una agravación del PB en las tres cuartas partes, aproximadamente, de las mujeres en relación con el ciclo menstrual. La influencia del embarazo sobre la enfermedad es muy discutible. Próximamente un quinto de los varones con PB tuvieron un brote durante el servicio militar. Se aportan las causas posibles de ello. Se da una lista de las causas más frecuentes de agravación del PB en diversas profesiones. La frecuencia de reacciones medicamentosas fué menor en los casos de PB que en los controles utilizados.

Treinta casos de PB y que recibieron tratamiento se valora éste. En más de un tercio pudo observarse un alivio temporal o mejoría, pero en ninguno se vió curación completa o permanente. Por tanto, la indicación para este tipo de terapéutica será limitada. Téngase presente que no puede conseguirse más por hiposensibilización que excluyendo *una* de las muchas causas etiológicas posibles en esta enfermedad. Finalmente, son analizados los datos de PB con curso de larga duración en pacientes de mas de 45 años de edad.

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