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Title:

Prevalence of Vernal Keratoconjunctivitis: a Rare Disease?

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Abstract

Objective(s): To determine the prevalence of vernal keratoconjuntivitis (VKC) in Europe.

Methods: A cross-sectional survey was mailed to 3003 ophthalmologists from 6 countries (Finland, France, Italy, the Netherlands, Norway, and Sweden) representing 151.9 million inhabitants. Results were analyzed per country and VKC prevalence for the 15 European member states in 2002 was extrapolated. Six hypotheses were used: disease duration (4 or 8 years) combined with 3 prevalence hypothesis for non-responding ophthalmologists.

Results: The response rate to the survey was 29.5%. The estimates of VKC prevalence in Western Europe (per 10,000 inhabitants) ranged from 1.16 to 10.55. The prevalence of VKC with corneal complications ranged from 0.30 to 2.26.
The VKC prevalence ranged per country: Italy 2.4–27.8, Finland, 0.7–8.4, Sweden 1.2–8.7, the Netherlands 0.6–4.6, France 0.7–3.3 and Norway 0.3–1.9. VKC with corneal complications were: Italy 0.4–4.8, Sweden 0.3–2.4, Finland 0.2–2.8, the Netherlands 0.2–1.6, France 0.3–1.4 and Norway 0.1–1.0.

Conclusions: Based on the most likely hypotheses concerning disease duration and non-responding ophthalmologists' VKC case rate, the best estimate of VKC prevalence in Western Europe is 3.2/10,000 inhabitants. The prevalence of VKC with corneal complications is 0.8/10,000 inhabitants.

Introduction

Vernal keratoconjunctivitis (VKC) is a severe form of ocular allergic conjunctivitis, occurring mainly in children. In addition to itching and grittiness usually observed in common ocular allergy, other highly specific symptoms are photophobia and tearing, which are particularly disabling. Palpebral thickening may result in pseudo-ptosis (1-4). The mucus discharge is thick and abundant and adheres to the giant cobblestones of the upper tarsus (5). Keratitis (that occur in up to 50% of cases (6, 7)) and shield ulcers are sight-threatening complications (8).

Two VKC forms occur: palpebral vernal is marked by cobblestone papillae on the superior tarsal conjunctiva and is more frequent in Europe and North America. Limbal vernal is marked by a broad thickened, circumferential gelatinous opacification of the limbus and by Horner-Trantas dots. It occurs more commonly in Africa and West India. Limbal and palpebral lesions may be combined (1, 3).

Symptoms occur before the age of 10 in 80% of cases (4, 9, 10, 11). Later and earlier onsets each account for 10% of cases. Boys are affected 2-4 times more frequently than girls (3, 11). Family atopy is very common as well as personal atopy: 40-75% of VKC subjects (2, 4, 9, 10, 12) have asthma, hay fever and eczema (4, 13).

Although VKC generally subsides with or after puberty, evolution towards atopic keratoconjunctivitis can be observed at an adult age. There is a risk of corneal complications or keratoconus (14, 15). Furthermore there are iatrogenic risks of cataracts or glaucoma due to the steroids (16). Around 6% of patients develop a visual impairment (16). VKC is a long-lasting disease, since most series confirm an average duration of 4-8 years (2, 4, 9, 11). The prolonged and recurrent VKC nature affects physical activity, psychological/social state and somatic sensation of the young patients.

A seasonal pattern is encountered in temperate countries, suggesting that atmospheric conditions promote flare-ups during spring and summer. The perennial form occurs more frequently in hot countries (11, 17-20).

VKC is a rare allergic conjunctivitis. However, no studies provide accurate calculations of VKC prevalence in the general population in European Union (EU) because epidemic characteristics were mainly described in case series. Therefore, to assess VKC prevalence, we performed a cross-sectional mail survey of ophthalmologists from 6 European countries.

Patients and Methods

Study population and methodology

The survey was performed in a few selected countries: Finland, France, Italy, the Netherlands, Norway and Sweden to have countries from north to south of Europe among the 15 member states in 2002.

Listings of practicing ophthalmologists were obtained (www.rosenwald.com). The type of practice (private/public; ambulatory/hospital) was available only for France, Italy and Sweden. A random sample of roughly 1000 professionals in France, of 1000 in Italy and of

1000 in Finland + Norway + Netherlands + Sweden were established on the basis of a hypothetical response rate of 30%.

A questionnaire and colour photographic documentation (see Figures 1 and 2) were mailed The questionnaire was provided in French in France, in Italian in Italy and in English to the Netherlands and the Scandinavian countries. Documents were mailed in June 2002 by the investigators from the INSERM SC11 Unit, and a reminder was sent in September 2002.

It was assumed that all VKC patients were referred to ophthalmologists (a reasonable assumption due to the obvious functional ocular signs involved) and that the VKC criteria are commonly applied by ophthalmologists.

Analysis
Responses were computed (double data entry). The analysed items were the overall number of diagnoses and corneal involvement (Stata® version 7).

Each country was analyzed separately, then, pooled to estimate the prevalence in the 15 EU countries. In 2002, we inferred the prevalence of southern countries (Spain, Portugal, and Greece) from the Italian prevalence, the prevalence of central Europe countries (Austria, Ireland, UK, Germany, Luxembourg, and Belgium) from France, and the prevalence of Denmark from Sweden. Demographic information in EU was derived from the 2001 Eurostat report (http://epp.eurostat.ec.europa.eu). Eurostat is the European Union (EU) official organisation, in charge of providing the EU with a high-quality statistical information service.

To prevent skewing data when using outliers with results far above the number of cases normally reported by the other ophthalmologists and also far above a realistic number expected with regards to the literature, we disregarded responses reporting 100 patients or more during the last 5 years. We counted them as non-responders since they certainly included misdiagnosed cases. Finland and Norway had no outliers while Italy had 14%. Overall 78 physicians reported 100 patients or more, and the data from 776 physicians were therefore considered. If a physician mentioned that his/her patients were also followed by another ophthalmologist, we divided the number of reported cases by 2.

To calculate the prevalence rate and 95% confidence intervals, 6 hypotheses were modelled with regards to the duration of the disease and the ophthalmologist non-responder status as follows

- Hypothesis 1: duration of the disease = 4 years and non responders have not seen any VKC cases
- Hypothesis 2: duration of the disease = 4 years and non-responders have seen half the number of VKC cases as responders
- Hypothesis 3: duration of the disease = 4 years and non-responders have seen the same number of VKC as responders
- Hypothesis 4: duration of the disease = 8 years and non-responders have not seen any VKC cases

- Hypothesis 5: duration of the disease = 8 years and non-responders have seen half the number of VKC cases as responders
- Hypothesis 6: duration of the disease = 8 years and non-responders have seen the same number of VKC cases as responders

Results

Response rate

We contacted 3003 ophthalmologists from 6 countries representing 151.9 million inhabitants. Table 2 provides the response rate by country. The overall response rate was 29.5%. The available data did not allow us to perform comparisons between ophthalmologist responders and non-responders. The results did not differ significantly by type of practice (private/public & ambulatory/hospital).

Table 2: Main features of the European questionnaire

Country	Population[1]	Number of ophthalmologists contacted / Total number of practicing registered ophthalmologists	P/H[2]	Number of responses analysed / Number of ophthalmologists contacted
Finland	5 181 000	249/576 (43%)	NK[3]	41/249 (16%)
France	59 521 000	1001/3318 (30%)	622/379	360/1001 (36%)
Italy	57 844 000	1000/5576 (18%)	511/489	170/1000 (17%)
Norway	4 503 000	157/363 (43%)	NK	43/157 (27%)
Netherlands	15 983 000	263/597 (44%)	NK[3]	69/263 (26%)
Sweden	8 883 000	333/768 (43%)	33/300	93/333 (28%)

[1] Source: Eurostat 2001.
[2] P/H: Private practice or Hospital
[3] NK: not known

The distribution of VKC number per physician is shown by country in Figure 3. The proportion of Italian physicians who had not seen any VKC was low (3.8% opposed to approximately 20% for other countries).

Prevalence by country

The prevalence rates per 10,000 inhabitants were calculated for each country and are presented in Table 3. Our results did not fully support the concept of a simple north-south factor for the prevalence of VKC. Among the Scandinavian countries (Norway, Finland, Sweden), in hypothesis 6, the prevalence rates per 10,000 inhabitants were 1.9, 8.4 and 8.7 respectively. The rate observed in Sweden (8.7) was also above that observed in the Netherlands (4.6) and France (3.3). Italy had the highest observed prevalence rate (27.8). The ratio between the highest prevalence (Italy) and lowest prevalence (Norway) was 14.8.

Table 3: Estimates of the prevalence of VKC per 10,000 inhabitants under several assumptions regarding non responders

	Disease duration (years)	Non-responder pattern	Finland	France	Italy	Netherlands	Norway	Sweden
Hypothesis 1	4	0[a]	0.69 (0.62-0.77)	0.73 (0.71-0.75)	2.37 (2.33-2.41)	0.60 (0.56-0.64)	0.26 (0.22- 0.31)	1.21 (1.14.-1,29)
Hypothesis 2	4	0.5[b]	2.45 (2.32-2.59)	1.12 (1.09-1.15)	8,14 (8.07-8.21)	1.45(1.39-1.51)	0.61 (0.54-0.68)	2.77 (2.66-2.88)
Hypothesis 3	4	1[c]	4.21 (4.03-4.39)	1.65 (1.62-1.68)	13,92 (13,82 -14.01)	2.29 (2.22-2.37)	0.95 (0.87-1,05)	4.34 (4.20-4.47)
Hypothesis 4	8	0[a]	1.39 (1.29-1.49)	1.19 (1.16-1.21)	4.73 (4.68-4.79)	1.2 (1.15-1.26)	0.52 (0.46-0.59)	2.42 (2.32-2.53)
Hypothesis 5	8	0.5[b]	4.90 (4.71-5.1)	2.24 (2.21-2.28)	16.28 (16.18.-16.39)	2.89 (2.81-2.98)	1.22 (1.12-1.32)	5.55 (5.39-5.70)
Hypothesis 6	8	1[c]	8.42 (8.17-8.67)	3.30 (3.25-3.35)	27.83 (27.69-27.97)	4.58 (4.48-4.69)	1.91 (1.78-2.04)	8.67 (8.48-8.87)

95% confidence intervals in brackets

a - 0 = Non-responders have seen no VKC cases

b- 0.5 = Non-responders have seen half the number of VKC than responders

c - 1 = Non-responders have seen the same number of VKC cases as responders

The prevalence of VKC with corneal complications was always much lower than the overall VKC prevalence (Table 4): 10-30% of VKC cases. Remarkably, there was less variation in the prevalence of corneal involvement between countries than prevalence of VKC. The ratio between the highest prevalence (Italy) and lowest prevalence (Norway) was only 4.6 for corneal involvement.

Table 4: Prevalence of corneal VKC complications

	Disease duration in years	Non-responder pattern	Finland	France	Italy	Netherlands	Norway	Sweden
Hypothesis 1	4	0[a]	0.23 (0.19-0.28)	0.30 (0.29-0.32)	0.39 (0.38-0.41)	0.21 (0.19-0.23)	0.14 (0.11-0.18)	0.34 (0.30-0.38
Hypothesis 2	4	0.5[b]	0.83 (0.75-0.91)	0.46 (0.45-0.48)	1.41 (1.38-1.44)	0.51 (0.48-0.55)	0.33 (0.28-0.39)	0.78 (0.72-0.84)
Hypothesis 3	4	1[c]	1.42 (1.32-1.53)	0.68 (0.66-0.70)	2.42 (2.38-2.46)	0.82 (0.77-0.86)	0.52 (0.46-0.59)	1.22(1.15-1.30)
Hypothesis 4	8	0[a]	0.47 (0.41-0.53)	0.49 (0.47-0.5)	0.79(0.77-0.81)	0.42 (0.38-0.45)	0.29 (0.24-0.34)	0.68 (0.62-0.73)
Hypothesis 5	8	0.5[b]	1.66 (1.55-1.77)	0.93 (0.9-0.95)	2.83 (2.79-2.88)	1.03 (0.98-1.08)	0.67 (0.59-0.75)	1.57 (1.48-1.65)
Hypothesis 6	8	1[c]	2.85 (2.7-3.0)	1.36 (1.34-1.39)	4.84 (4.79-4.90)	1.63 (1.57-1.70)	1.04 (0.95-1.14)	2.45 (2.35-2.55)

95% confidence intervals in brackets

a - 0 = Non-responders have seen no VKC cases

b- 0.5 = Non-responders have seen half the number of VKC than responders

c - 1 = Non-responders have seen the same number of VKC cases as responders

Prevalence in Europe overall

Table 5 shows the estimated European prevalence. The upper limit was 11.3 per 10,000 (95%CI, 11.2-11.4) calculated under the hypothesis 6 (disease lasted for 8 years, same frequency for non-responders and responders). The lower limit was 1.25 per 10,000 (95%CI, 1.22-1.28) calculated under the hypothesis 1 (disease lasted for 4 years; non-responders saw no cases).

Table 5: Estimated prevalence of VKC in European countries

	Disease duration in years	Non responder pattern	Prevalence per 10000 inhabitants with CI 95%
Hypothesis 1	4	0[a]	1.25 (1.22 -1.28)
Hypothesis 2	4	0.5[b]	3.41 (3.36 -3.46)
Hypothesis 3	4	1[c]	5.64 (5.58 -5.71)
Hypothesis 4	8	0[a]	2.34 (2.30 - 2.39)
Hypothesis 5	8	0.5[b]	6.82 (6.75 - 6.88)
Hypothesis 6	8	1[c]	11.29 (11.2 – 11.38)

95% confidence intervals in brackets
a - 0 = Non-responders have seen no VKC cases
b- 0.5 = Non-responders have seen half the number of VKC than responders
c - 1 = Non-responders have seen the same number of VKC cases as responders

Table 6 presents the European prevalence of VKC with corneal complications. The upper limit (hypothesis 6) was 2.52 per 10,000 (95%CI, 2.48-2.57). The lower limit (hypothesis 1) was 0.33 per 10,000 (95%CI, 0.31-0.34). Across all hypotheses, approximately 20-25% of VKC cases had corneal involvement.

Table 6: Estimated prevalence of VKC with corneal complications in EU 15 member states

	Disease duration in years	Non responder pattern	Prevalence with CI 95%
Hypothesis 1	4	0[a]	0.33 (0.31-0.34)
Hypothesis 2	4	0.5[b]	0.78 (0.76 -0.81)
Hypothesis 3	4	1[c]	1.26 (1.23 -1.29)
Hypothesis 4	8	0[a]	0.60 (0.58 -.0.62)
Hypothesis 5	8	0.5[b]	1.56 (1.53 -1.60)
Hypothesis 6	8	1[c]	2.52 (2.48 -2.57)

95% confidence intervals in brackets
a - 0 = Non-responders have seen no VKC cases
b- 0.5 = Non-responders have seen half the number of VKC than responders
c - 1 = Non-responders have seen the same number of VKC cases as responders

Steroid complications

Among the 613 ophthalmologists who reported at least one VKC, 3.5% of their patients were reported with major steroid complications (glaucoma or cataract). The distribution was very asymmetric, and its 95% confidence interval was 0-25%. Severe steroid complications showed moderate differences between the studied countries (Finland: 2%; France: 3%; Italy: 3.8%; Netherlands: 3.4%; Norway: 3.8% and Sweden: 4.1%).

Discussion

The aim of this study was to assess the VKC epidemiology in the EU population. An extensive literature review, over thirty years, failed to find epidemiological data, based on a population study. The largest survey (4) have enrolled 195 cases, over 13 years in a national Italian centre who have included patients originating from 3 Italian regions. This study is the only original study which provides information about the duration of the disease, estimated to be 62 months., The percentage of VKC patients in the literature were mainly reported among all ocular allergic patients and not in the general population: 46% in Central America (21), 16% in France (6), 8% in Italy (22), and 1% in United Kingdom (17). Studies on large cohorts of subjects were conducted outside EU and revealed that VKC is prevalent in approximately 5% of school-age children in endemic areas like Africa (3) (Somalia-3% (17), Cameroon -4% (23, 24), Turkey-4.6% (25), the Palestinian population in Jerusalem and the West Bank-10% (26)). In Morocco, India and Senegal it accounts for 6% of new ophthalmic referrals and up to 90% of the new ophthalmic referrals below the age of 15 (27). VKC is more prevalent in warm climates, particularly the Middle-East-Mediterranean region and North Africa, but also West Africa, Central America and some regions in India while being rare in most of North America and Western Europe (2, 8, 11, 12, 18, 28).

We selected 6 countries representing 151 million European inhabitants. The proportion of northern and southern countries represents the demography of the overall European population including the 15 member states in 2002.

Our study design did not allow obtaining confirmation of cases and constitutes the first step in a complete epidemiological assessment with analysis of individual records.

There were possible biases that could overestimate VKC prevalence. Some individuals could have been recorded twice. Indeed, they may visit more than one ophthalmologist because the pathology is severe and does not always respond to treatment. False diagnoses could not be eliminated despite diagnostic information being sent with the questionnaire.

A large proportion of physicians did not answer our questionnaire (70.5%) and this may bias the results in unpredictable ways. However, it seems reasonable to suppose that physicians who responded see more VKC than physicians who did not answer the questionnaire *i.e.* there is some degree of responder bias.

Furthermore, given the rarity of VKC, it is possible that within a medical community certain ophthalmologists might attract significantly more than the average share of VKC cases because they become recognized as having VKC experience. In this case, the rarer the disease, the greater the fluctuations in VKC patient proportions between physicians, which in turn augments any existing responder bias.

In order to take into account these possible biases, the prevalence was calculated using 6 different hypotheses. This method leads to a wide range of prevalence, ensuring that the real prevalence can be found within the range.

Our results show that the proportion of VKC is much higher in Italy than in the other surveyed countries and this observation suggests a North-South gradient. However, the variation among the Scandinavian countries indicates that there are other important factors influencing VKC prevalence. The presence of the disease in some northern countries is

thought to be a consequence of the migratory movements of the susceptible population from the south, suggesting that both genetic and environmental factors are implicated (29). For example, in Sweden the varying VKC prevalence in different ethnic groups indicates a genetic predisposing factor since in a subgroup of children with VKC a significantly higher proportion of children with Asian and African origin were noted than that expected in the general population (30).

The prevalence of corneal involvement did not differ much between countries in comparison with the VKC prevalence in general. This is probably because the diagnosis of corneal complication in VKC is based on more easily identified objective signs than the diagnosis of VKC. The number of ophthalmologists reporting to have seen more than 100 VKC cases in the last 5 years suggests some confusion in diagnosing VKC even if reference centres may follow large cohorts of patients (29, 31).

Steroid complications

In VKC, steroids are often overused and adverse effects can be observed. In clinical practice, it is essential to adjust the lowest and shortest appropriate steroid treatment for the suitable level of anti-inflammatory effect. If needed, steroids should be prescribed for a limited time period, at high frequency with a slow tapering. Contrary to the rise in IOP, steroid-induced PSC is characterized by its slow development over a long period and its irreversibility in most cases, the only available treatment being surgery. Our study found that 3.5% of VKC patients had steroid complications. Therefore, a close ophthalmologic supervision with controlled discontinuous treatment according to the disease severity is essential to avoid self prescription and inappropriate or misused doses of steroids instilled.

Prevalence in Europe overall

We have inferred the European prevalence for the 15 European member states in 2002 from the observed prevalence rate in the 6 studied countries, attributing a North-South gradient. If all 6 hypotheses are considered, the prevalence of VKC in Europe ranged from 1.22 cases per 10,000 habitants to 11.38. If we modelled a disease-duration of 4 years, the VKC prevalence per 10,000 habitants in Europe varied between 1.25 and 5.64 depending upon the estimated VKC rates of non responder physicians. If we modelled a disease-duration of up to 8 years, the prevalence of VKC in Europe varied between 2.3 to 11.3. Considering that the available data suggests a duration of the disease of no more than 5 years (4) and considering that non responder physicians probably have a lower enrolment than responders, the most likely estimation prevalence of VKC in this European area should correspond to hypothesis 2 (4-year duration, non-responders have seen half the number of VKC cases has responders) which estimates a prevalence rate of 3.2/10,000 inhabitants. Under the same hypothesis the estimated prevalence of VKC with corneal involvement is 0.8/10,000 inhabitants.

Conclusion

VKC affects almost exclusively children and VKC is a severe disorder. The limitation of available epidemiological data prompts us to organise a survey among European ophthalmologists from 6 countries. Our survey provides some additional information about the epidemiology of the disease. This survey suggests that VKC may have a prevalence rate of 3.2 per 10,000 inhabitants in Western Europe.

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References

1. Leonardi A, Smith L, Secchi A. Vernal keratoconjuntivitis. In: Allergic diseases of the eye Ed. Mark Abelson 2000; 179-196.

2. Montan PG, Ekstrom K, Hedlin G, van Hage-Hamsten M, Hjern A, Herrmann B. Vernal keratoconjunctivitis in a Stockholm ophthalmic centre--epidemiological, functional, and immunologic investigations. Acta Ophthalmol Scand 1999: 77; 559-63.

3. Lee Y, Raizman MB. Vernal conjunctivitis. Immunol Allergy Clin North America 1997; 17: 34-51.

4. Bonini S, Bonini S, Lambiase A, Marchi S, Pasqualetti P, Zuccaro O, Rama P, Magrini L, Juhas T, Bucci MG. Vernal keratoconjunctivitis revisited: a case series of 195 patients with long-term follow up. Ophthalmology 2000; 107: 1157-63.

5. Leonardi A, Jose PJ, Zhan H, Calder VL. Tear and mucus eotaxin-1 and eotaxin-2 in allergic keratoconjunctivitis. Ophthalmology 2003; 110: 487-92.

6. Bloch-Michel E, Vérin P, Dibie, A. Observatoire des Allergies Oculaires. Enquête épidémiologique nationale sur les kératoconjonctivites allergiques saisonnières vues en ophtalmologie. Allergie Immunol 1995; 27: 182-9.

7. Bremond-Gignac D. The clinical spectrum of ocular allergy. Curr Allergy Asthma Rep. 2002; 2: 321-24.

8. Tabbara, K.F. Ocular complications of vernal keratoconjunctivitis. Can J Ophthalmol, 1999; 34: 88-92.

9. Buckley RJ. Allergic eye disease – a clinical challenge. Clin Exp Allergy 1998; 28; 39-43,.

10. Buckley RJ. Vernal keratoconjunctivitis. Int Ophthalmol Clin 1988; 28: 303-8.

11. Neumann E, Gutmann J, Blumenkrantz N, Michelson IC. A review of four hundred cases of vernal conjunctivitis. Am J Ophthalmol 1959; 47: 166-72.

12. Collum LMT. Vernal keratoconjunctivitis. Acta Ophthalmol Scand; 1999; 228: 14-16.

13. Buckley RJ: Long-term experience with sodium cromoglycate in the management of vernal keratoconjunctivitis. In Pepys J, Edwards AM, editor: The mast cell, London, Pitman Medical, 1980.

14. Totan Y, Hepsen IF, Cekic O, Gunduz A, Aydin E. Incidence of keratoconus in subjects with vernal keratoconjunctivitis: a videokeratographic study. Ophthalmology 2001; 108: 824-7.

15. Lapid-Gortzak R, Rosen S, Weitzman S, Lifshitz T. Videokeratography findings in children with vernal keratoconjunctivitis versus those of healthy children. Ophthalmology 2002; 109: 2018-23.

16. Bonini S, Lambiase A, Sgrulletta R, Bonini S. Allergic chronic inflammation of the ocular surface in vernal keratoconjunctivitis. Curr Opin Allergy Clin Immunol. 2003; 5: 381-7.

17. Bloch-Michel E, Helleboid L. Conjonctivites allergiques. Editions Techniques. Encycl Med Chir Ophtalmol. Paris France 1994; 21-130-E-10: 10 p.

18. Colby K, Dohlman C. Vernal keratoconjunctivitis. Int Ophthalmol Clin 1996; 36: 15-20.

19. Hannouche D, Hoang-Xuan T. Les conjonctivites allergiques. In: Inflammation chronique de la conjonctive. Hoang-Xuan T, Baudouin C, Creuzot-Garcher C, Hannouche D, Kantelip B, Robin H, Eds. Bull Soc Ophtalmol Fr 1998; 98: 93-124.

20. Duke-Elder S: Diseases of the outer eye, Part I. In Duke-Elder S (ed): System of Ophthalmology, p 476. London, Henry Kimpton, 1965.

21. Belfort R, Marbeck P, Hsu CC, Freitas D. Epidemiological study of 134 subjects with allergic conjunctivitis. Acta Ophthalmol Scand Suppl 2000; 230: 38-40.

22. Bonini S, Bonini S. Studies of allergic conjunctivitis. Chibret. Int J Ophthalmol 1987; 5: 212-22.

23. McMoli TE, Assonganyi T. Limbal vernal kerato-conjunctivitis in Yaounde, Cameroon. A clinico-immunology study. Rev Int Trach Pathol Ocul Trop Subtrop Sante Publique 1991; 68: 157-70.

24. Moukouri dit Nyolo E, Nyolo D, McMoli T, Ndombo K. Tropical endemic limbal conjunctivitis in Cameroon patients. Apropos of 819 cases in Yaounde. Bull Soc Pathol Exot 1993; 86: 120-124.

25. Saraclar Y, Yigit S, Adalioglu G, Tuncer A, Tuncbilek E. Prevalence of allergic diseases and influencing factors in primary-school children in the Ankara Region of Turkey. J Asthma 1997; 34: 23-30.

26. O'Shea JG. A survey of vernal keratoconjunctivitis and other eosinophil-mediated external eye diseases amongst Palestinians. Ophthalmic Epidemiol 2000; 7: 149-157.

27. Tuft SJ, Dart JK, Kemeny M. Limbal vernal keratoconjunctivitis: clinical characteristics and immunoglobulin E expression compared with palpebral vernal. Eye 1989; 3: 420-7.

28. Ehlers WH, Donshik PC. Allergic ocular disorders: a spectrum of diseases. CLAO J 1992; 18: 117-24.

29. Leonardi A, Secchi AG. Vernal keratoconjunctivitis. Int Ophthalmol Clin. 2003; 43: 41-58.

30. Montan PG, Ekstrom K, Hedlin G, van Hage-Hamsten M, Hjern A, Herrmann B. Vernal keratoconjunctivitis in a Stockholm ophthalmic centre--epidemiological, functional, and immunologic investigations. Acta Ophthalmol Scand. 1999; 77: 559-63.

31. Leonardi A, Busca F, Motterle L, Cavarzeran F, Fregona IA, Plebani M, Secchi AG. Case series of 406 vernal keratoconjunctivitis patients: a demographic and epidemiological study. Acta Ophthalmol Scand. 2006; 84: 406-10.

Figure 2: Color Documentation on VKC for the Ophthalmologists

Rare potentially serious clinical condition

1 PATIENTS

Children, most often boys.
Individual or family history of allergy.

2 EVOLUTION

Chronic evolution with bouts linked to UV exposure (aggravation frequent in spring and summer).
Frequent secondary infections and meibomitis.

Flattened polyhedric papillae under upper eyelid.

3 FUNCTIONAL SIGNS

Photophobia sometimes inducing blepharospasm and liable to impair school performance.
Pruritus, lacrimation.

4 APPEARANCE ON EXAMINATION

Bilateral condition, usually symmetrical.

4.1 **Mucous hypersecretion** with:

- cord-like whitish discharge,
- infiltration of mucus between papillae or covering them,
- sometimes pseudomembranes.

4.2 UPPER TARSAL involvement visible on eversion of upper eyelid

- in the palpebral form: numerous highly enlarged papillae (or ‘cobblestones’, of diameter greater than 1 mm), packed together, producing a flattened polyhedric appearance,
- sometimes conjunctival fibrosis.

4.3 Limbal involvement

Limbal form

- limbal thickening, broadening or opacification,
- presence, especially on upper limb, of papillae, and of near-white Trantas dots,
- upper limbal pannus.

4.4 Corneal involvement in one quarter of cases

- most often superficial punctuate keratitis (SPK),
- erosion,
- typically single ulcer, oval or shield-shaped in the upper third of the cornea, sometimes covered by a mucoid plaque (**vernal plaque**) with risk of neovascularization and scarring.

5 Evolution

Onset usually before age 10 years.
Resolution in 2 to 10 years. Risk of after-effects (decrease of visual acuity in 27%) or evolution toward adult atopic keratoconjunctivitis.
Keratoconus often associated.

Enlarged papillae and corneal involvement

Figure 1: Extract of the Questionnaire on VKC for Ophthalmologists

INVESTIGATION ON THE INCIDENCE OF VERNAL KERATOCONJUNCTIVITIS

1. How many cases of **VERNAL keratoconjunctivitis**[1] have you followed over the **past 5 years**?

2. How many cases presented with **giant papillae**[2] **and/or limbal papillae?**

3. How many cases were associated with **corneal complications?**

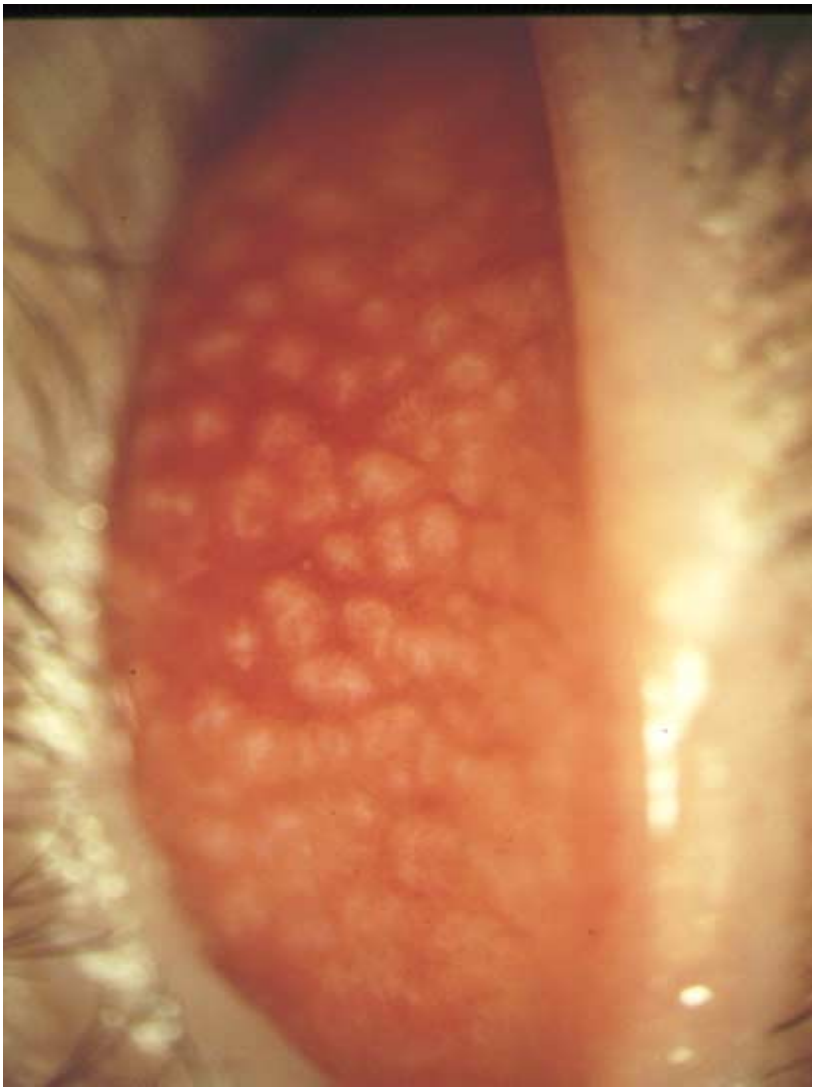
4. How many cases presented with iatrogenic **complications** due to **corticoids** (cataract, glaucoma)?

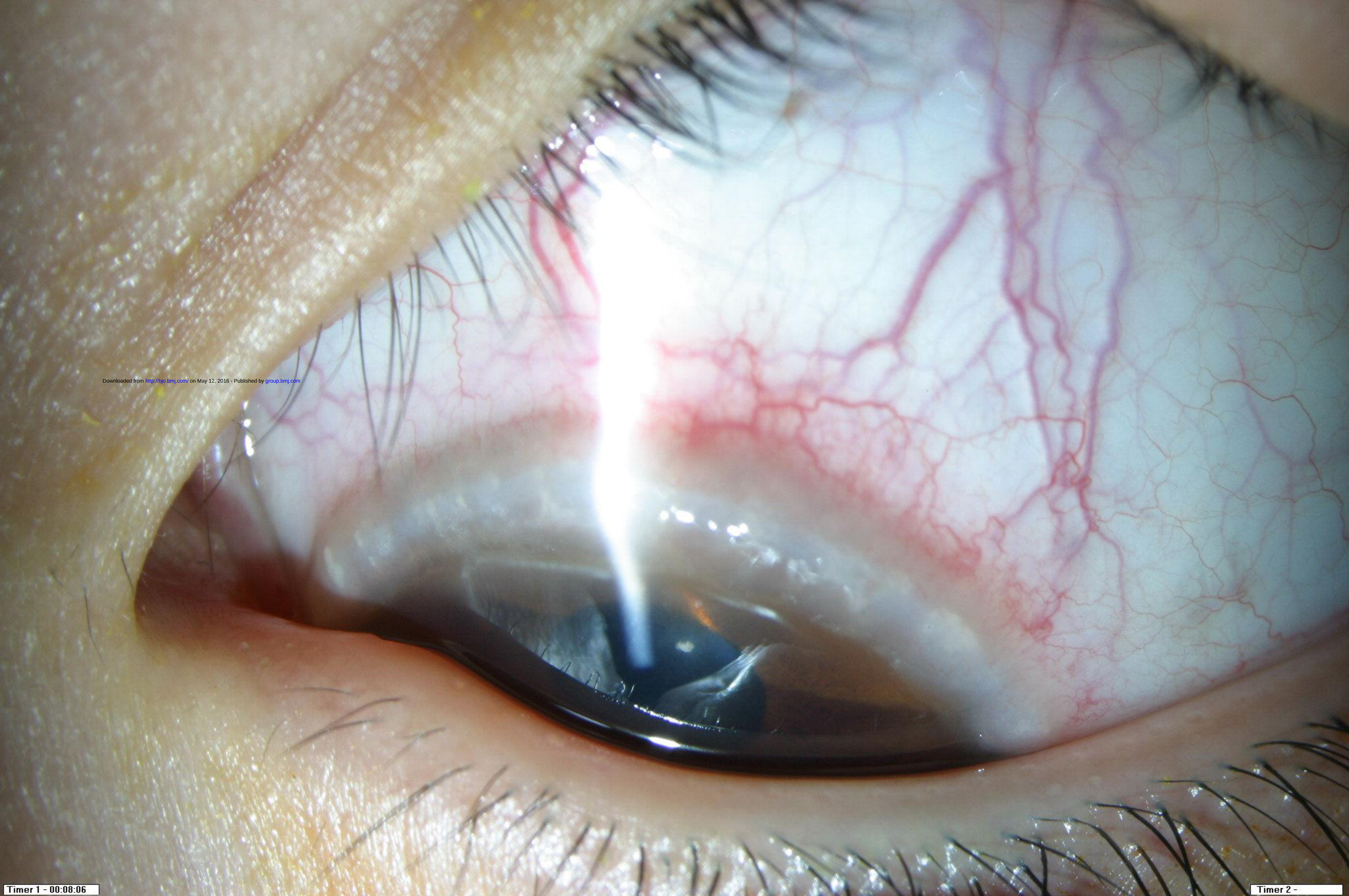
5. How many cases were co-followed by another ophthalmologist?

Thank you for sending back this questionnaire to the following address:

INSERM SC 11
102, rue Didot
75014 PARIS – FRANCE

[1] An enclosed form provided the clinical characteristics with photographs.
[2] Diameter more than 1mm.





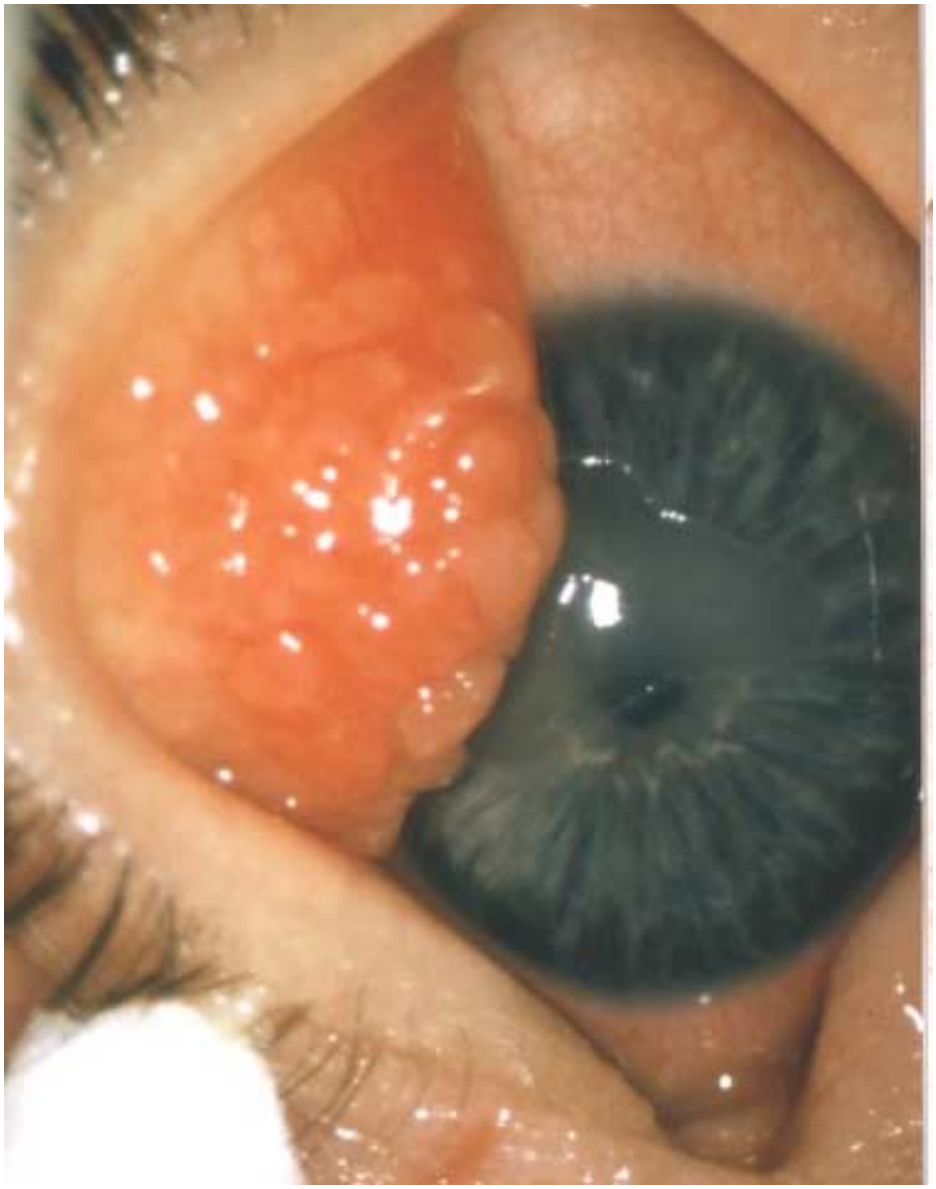
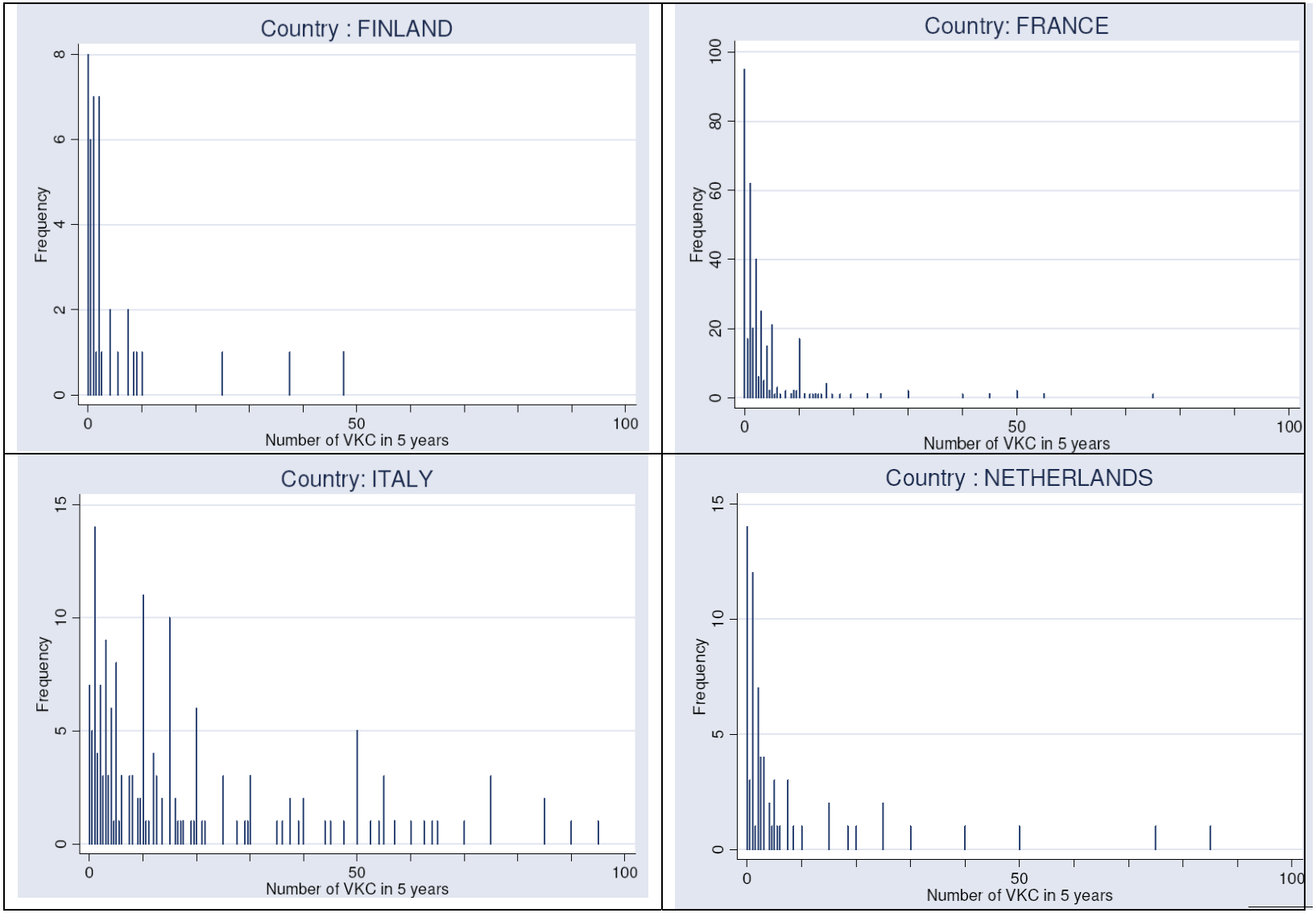


Figure 3: Distribution of Number of VKC cases per physician in the different countries



Prevalence of Vernal Keratoconjunctivitis: a Rare Disease?

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