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Pterygium in an Isolated Population *

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According to the few studies that exist on its genesis, pterygium, a patch of thickened, usually fan shaped conjunctiva extending over a part of the cornea, has an autosomal dominant mode of inheritance.

Gutierrez-Ponce established 5 affected subjects in 3 generations, Armaignac 8 cases in a family of 22 persons, Newman 11 persons in 3 generations, Strebel 4 persons in 3 generations and Komai 9 persons in 6 generations. Pterygium was established by Enroth in a mother and 6 of her 7 children, by Kerkenezow in 2 families in one of which 8 persons had it in 3 generations and in the other 4 persons in 2 generations. Hilgers reported on 2 families in one of which 6 persons had pterygium in 3 generations and in the other 10 persons in 3 generations. Sedan established pterygium in 2 generations.

In one of Hilgers' 2 families both parents had pterygium and all 3 children were affected. In the other families the affection was demonstrated broadly speaking in a half of the children who reached maturity. Since the age of manifestation is high as a rule it is difficult without a long observation period to conduct a reliable genetic investigation covering 2 or several generations with affected members.

Study of twins also supports the theory that pterygium is hereditary. Weitz, Vogt and his co-workers, and Fulgosi observed pterygium in monozygotic twins.

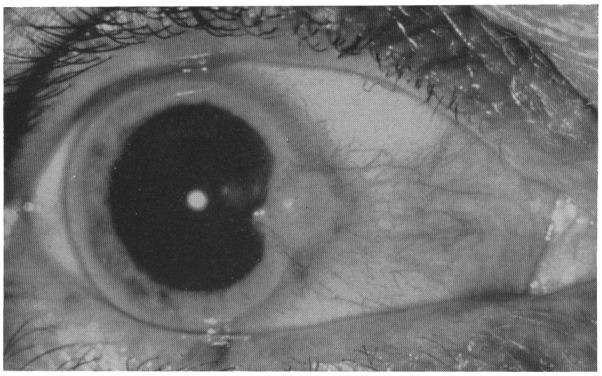
Vogt's series of elderly persons (58 pairs of twins, of which 30 pairs were monozygotic) included 3 pairs of monozygotic twins with what was presumed from the text to be bilateral pterygium, and a pair of alleged monozygotic twins and a pair of dizygotic twins with pterygium. The condition was established in one twin only in 2 pairs of twins, one monozygotic and the other dizygotic. It was held by Vogt and his co-workers that the mode of inheritance of pterygium was probably not dominant.

The frequency of pterygium varies greatly in the different parts of the world. However, it is difficult to ascertain how much of it is due to hereditary disposition

* This study was made possible by grants from the Sigrid Jusélius Stiftelse and Finska Lökaresöllskapet.

(racial characteristics) and how much is the consequence of external factors (peristasis). Certain racial differences speak for the significance of heredity (Hilgers). Other authors who have compared different races, e. g. Diponegro and Mulock Houwer in Batavia, have established racial differences which they attribute, however, to external factors.

As far as the sex distribution is concerned, men are in most cases but not always in the majority in he series published. Hilgers' statement that the incidence of pterygium is equally great for men and women in similar work appears convincing.



Pterygium corneae in a 53 year-old woman

Some 20 theories on the mechanism of manifestation of pterygium have been put forward. The theories which consider exposure to wind and dust and solar radiation to be the deciding factor have the most advocates. Opinions differ regarding the role of pingueculum, also called palpebral blotch and seen especially in elderly people as a yellowish spot of proliferation on the bulbar conjunctiva near the sclerocorneal junction, usually on the nasal side. Both pterygium and pingueculum seem, however, to be the same as regards localisation and pathological anatomy. Especially in regions where pterygium occurs frequently and forms rapidly, manifesting itself when the proband is young, as in Egypt (Kamel) or Australia (Kerkenezow), a pingueculum near the limbus has been seen to merge into a pterygium. Ophthalmologists in Central and North Europe where pterygium is less common have observed, however, pterygia without a trace of pingueculum (Friede, Forsius and Eriksson).

The incidence of pterygium is low in Finland — 0.64 ± 0.22 per cent in an ophthalmologist's private practice in Helsingfors (Forsius et al.).

Series and Methods

Kökar — a group of islands belonging to the Aland archipelago between the Baltic Sea and the Gulf of Bothnia — has a census-registered population of 578 and a population of about 400 resident throughout the year. Most of them are fishermen who also farm on a modest scale. The work is hard and the standard of living average. The authors examined 479 of the Kökar inhabitants (Table 1).

Well-preserved church registers permit a genealogical trace right back to the 17th century. The group of islands has been isolated for many centuries, which has

resulted in numerous intermarriages. There are several rare diseases of recessive inheritance.

The field studies which have been in progress during the summer for several years consist of a general ophthalmological examination, a clinical and hematological examination, chromosome marking with different blood group systems such as A_1A_2BO, ABH-secretor, MN, Rh(CDEc), P, Kell and Lewis, and with haptoglobins and Gm serum groups and phenylthiocarbamide (PTC) — taste test etc. In addition, a routine hematological examination was performed (erythrocyte sedimentation rate, blood count, hematocrit, bleeding time, B_{12}-vitamin in serum, serum cholesterol etc.).

Results

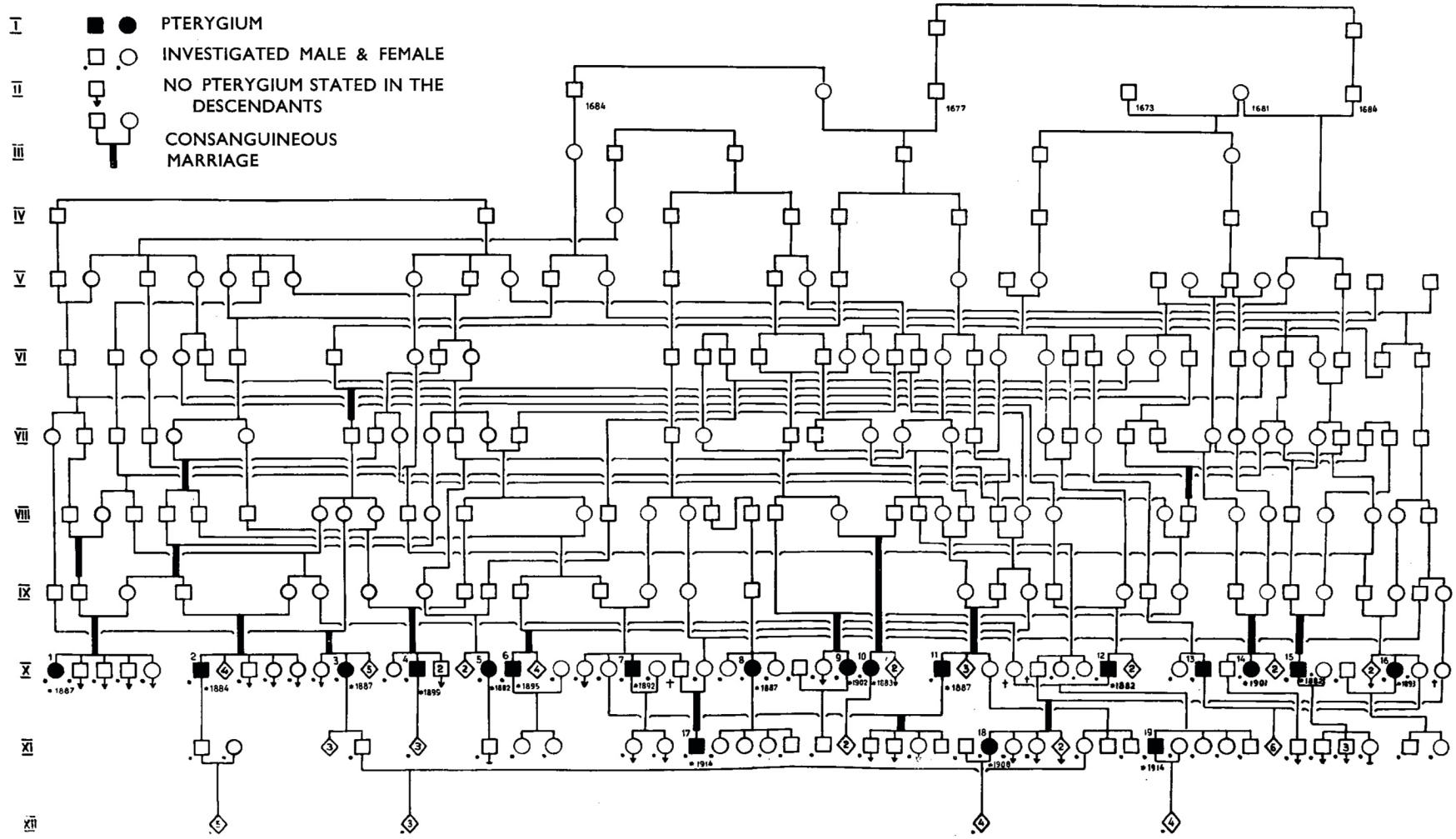
Of the 479 subjects studied at random, 19 (4.0 per cent) had pterygium. For those a full 40 years of age — no cases of pterygium were established among the younger age classes — the percentage rose to 7.8. Ten of the 19 affected subjects were men and 9 women (see Table 2).

For iris and hair colour the proportions were the same as in the rest of the population. Two persons had an allergic disease. Nine (6 with normal blood pressure)

Tab. 1. Age distribution of the patients and incidence of pterygium in different age groups

Age Years	Number investigated	Pterygium	
		Number	Percentage
1 - 10	43	—	—
11 - 20	87	—	—
21 - 30	48	—	—
31 - 40	54	—	—
41 - 50	70	2	2.9±2.0
51 - 60	72	2	2.8±2.0
61 - 70	52	6	11.5±4.5
> 70	53	9	17.0±5.3
Total	479	19	4.0±0.9

of the 19 pterygium probands showed increased capillary fragility (erythropermeability according to the Rumpel-Leede phenomenon), and increased capillary permeability for plasma (pathological fluorescein test according to Amsler-Huber) was established in one of 2 cases studied. Prolonged bleeding time on account of von Willebrand's bleeding disease (thrombopathia von Willebrand-Jürgens) was established in 5 of 13 subjects examined. No close linkage with the chromosome for sex, blood and serum groups etc. could be demonstrated.



https://doi.org/10.1017/S1120962300017844 Published online by Cambridge University Press

Arcus senilis was normal for age. The relationship between it and pterygium has been analysed in detail from a larger series (Forsius et al.).

The size of the pingueculum was assessed temporally and nasally in both eyes and the mean was calculated. Men appeared to have a more markedly developed pingueculum than women, and persons with pterygium seemed to have more pronounced pingueculum than the rest of the population even if the pingueculum on the pterygium was excluded. Two men and 2 women with pterygium, however, had a smaller pingueculum than normal.

Discussion

The hereditary factor would seem to be the essential element in the genesis of pterygium in the population on Kökar islands. Because the islanders are subject to a strong climatological influence, a number of pterygia have probably originated which would otherwise have remained latent on account of modification genes or low penetrance. A fisherman's life is moreover more likely to produce pterygia than other occupations (farmers). This view was put forward by Li and Yen.

Like pterygium, pingueculum occurs with increasing frequency in persons engaged in out-of-door work. In Kökar, too, pingueculum was more distinct in persons with pterygium than in the rest of the population; furthermore, it is probably an etiological factor of pterygium. It appears as if the number of degenerative eye diseases such as sclerosis of the ocular fundus, iridic atrophy, lens exfoliation, is more numerous in pterygium patients than in others. In a family with essential iridic atrophy Gedda et al. established 5 pterygia, 2 of them in successive generations (father and son).

The importance of the general condition, especially poor nutrition, was pointed out by Gerundo. The same point was made by Bartlett & Mumma who conducted a medical examination of 25 persons with recidivation of pterygium and established 11 different diseases among them. They stated, however, that a pterygium carrier is normally healthy. Dimitry considered pterygium to be a result of B-complex avitaminosis. Ascher thought that there was a nutritional factor (e. g. pellagra) in the etiology of pterygium. Block and Srinivasan did not agree with this view. Relatively low values on the average (mean 220 $\mu\mu$g/ml of serum) were established in the authors' pterygium probands in whom the vitamin B_{12} content was studied. This, however, is characteristic of the whole island population studied.

A distinctly elevated blood pressure (180/100 or higher) was established in 6 of the 19 pterygium patients. It was regarded as quite normal in view of the high mean age of the patients. The cholesterol level was normally up to 280 mg per 100 ml serum in these age groups with the method employed (Forsius), and was elevated in 5 cases. By way of comparison, it may be mentioned that Holt demonstrated an elevated cholesterol level in 10 of 50 cases with pterygium.

Pterygia are common in Eskimoes, a race which used to suffer from undernourishment and scurvy (Skeller, Norman-Hansen). We do not know whether capil-

lary fragility in scurvy increased the incidence of pterygium, but increased capillary fragility was demonstrable in 10 out of 19 of our probands in the form of a positive Rumpel-Leede phenomenon. One of the 2 cases studied had weakly pathological capillary permeability (Amsler-Huber fluorescein anterior chamber test). The etiological role that vessel defects such as increased capillary fragility (hemorrhagic diathesis, changes with age, high blood pressure, nutritional disturbances, etc.) or increased capillary permeability (e. g. allergic conditions) have in the manifestation of pterygium is not definitely established. Hilgers concludes that according to the pathology of pterygium degeneration caused by prolonged exposure to solar radiation is the main feature. Altered proteins may act as antigens leading to an interaction between antigen and antibody. These allergic inflammatory processes with vasodilation etc., probably also triggered by superimposed infections, may result in progressive pterygium, characterised by the presence of multiple small blood vessels (hypervascularity and sometimes hyperemia). All this might perhaps indicate that capillary defects may have a central role in the manifestation of pterygium. Defects in the blood vessels can, however, not explain the high incidence of pterygium in the tropics.

Inheritance

A recessive mode of inheritance seems the most plausible explanation, judging by the pedigree with the marked accumulation of intermarriages and the increased incidence of pterygium in the isolated population. It must be noted, however, that the marriage partners in the more remote ascendancy are often related in an isolated population. The increased incidence of pterygium in Kökar may be accounted for by the relatively large number of elderly people studied (cf. Table 1) and by the fact that in an outer archipelago community the environment contains more ultraviolet light, wind, spray and other agents conducive to the more ready manifestation of the hereditary disposition for pterygia.

Because of the high age of manifestation, only 2 of the parents of the 19 probands are alive. One of them has pterygium. Of the 19 cases with pterygium, 11 have 21 siblings not one of whom has pterygium. Families with only one child examined were omitted because variance in such families is zero, according to analysis by the Apert-Bernstein's aprioristic method. It can consequently be said that if the gene for pterygium is not recessive the dominant disposition has a low penetrance accompanied by a late age of manifestation, which adds to the significance of exogenous circumstances. The effect of all this is that the pathogenesis (mode of inheritance) of pterygium can hardly be determined definitely before the siblings and children of the probands have been given a systematic pathological examination as a family in the course of a generation. The occurrence of the predisposition in two successive generations and the mendelian segregation rate argue in favour of a dominant inheritance with low penetrance and variable expressiveness. This is confirmed also by the finding that both eyes had pterygium in only 4 out of 19 patients. It has been

established in the last few decades that not only recessive traits but also dominant traits with low penetrance and a low natural selection rate can accumulate in isolated populations with high anidentity (« Ahnenidentitaet ») (Vogel 1961). Peristasis and possibly other hereditary factors such as pingueculum and capillary defects may have a role in the phenotypic manifestation of the predisposition to pterygium. However, as regards pingueculum it is difficult to decide whether this anomaly and pterygium show the same hereditary predisposition or whether the formation of a pingueculum, as an irritative factor, may increase the predisposition to the appearance of pterygium. However, not every pingueculum becomes a pterygium, and pterygia can originate without the presence of a pingueculum. According to Hilgers, pterygium can also originate as an acquired pathological condition excited by external factors.

Summary

The incidence of pterygium was studied in an isolated highly inbred fisher population. A clinical and hematological examination was performed and the blood chemistry was studied. Genealogical tables (pedigrees) were prepared for all probands and the degree of consanguinity in their parents stated. Of the total of 479 subjects studied by random sampling, 19 (4 per cent) had pterygium with a relatively high manifestation age. No linkage was detected between the genes for the blood group systems, serum groups etc. and the gene for pterygium. Increased capillary fragility was established in 10 probands. Capillary permeability was studied in 2 probands by the concentration in the anterior chamber of intravenously administrated fluorescein, and the test was found to be weakly pathological in one of them. The serum cholesterol level was elevated in 5 of the patients studied. Ophthalmological examination indicated the accumulation of degenerative eye diseases. Pingueculum showed a more pronounced development in 10 of the 17 subjects examined than in the rest of the population. The possibility of recessive transmission of the hereditary predisposition is discussed with reference to the high frequency of inbreeding and the accumulation of pterygium within the isolated population. According to the special frequency-raising peristasis conditions in an outer archipelago community and to the mendelian segregation rate, a not sex-linked, simple dominant gene, with low penetrance and no selective disadvantage for the pterygium seems to be the most plausible explanation. Because of the late manifestation age, pterygium was observed only in 2 generations. The expressiveness of the gene was unsteady and asymmetry of pterygium in the eyes of the probands is not uncommon.

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RIASSUNTO

È stato studiato il manifestarsi dello pterygium presso una popolazione isolata di pescatori, dove le unioni fra consanguinei sono molto frequenti. Sono stati fatti esami clinici e del sangue, sono stati studiati alberi genealogici ed è stato indicato il grado di consanguineità dei genitori. Dei 479 soggetti esaminati senza selezione, 19 (4%) hanno presentato una forma di pterygium a uno stadio relativamente avanzato. Non è stato trovato un nesso fra i geni dei gruppi sanguigni e dei gruppi del siero e fra i geni dello pterygium. Una aumentata fragilità capillare è stata costatata in 10 casi. La permeabilità capillare nella camera anteriore dell'occhio è stata studiata su 2 soggetti per mezzo della concentrazione di fluoresciна amministrata per via endovenosa. In uno dei soggetti il test è stato leggermente patologico. La sierocolesterina era aumentata in 5 dei 16 soggetti esaminati.

L'esame oftalmologico mostra un aumento di malattie degenerative dell'occhio. 10 su 17 soggetti esaminati hanno presentato delle pingueculae più pronunciate che nel resto della popolazione. È stata discussa la possibilità di una trasmissione recessiva della predisposizione ereditaria in considerazione delle unioni consanguinee molto frequenti e dell'aumento di pterygium nella popolazione isolata. La spiegazione più probabile dello pterygium sembra essere nelle condizioni speciali della peristasi e nell'aumentata frequenza nella comunità di un arcipelago appartato e nella proporzione della segregazione di Mendel nel gene non legato al sesso e di semplice discriminazione, con una bassa penetrazione e senza svantaggi selettivi. Per lo stadio avanzato della forma è stato osservato lo pterygium solo in 2 generazioni. La manifestazione del gene è instabile, e il comparire dello pterygium non è inconsueto.

ZUSAMMENFASSUNG

Das Auftreten des Pterygiums wurde in einer isolierten Fischerbevölkerung mit hoher Inzucht untersucht. Es wurde eine klinische, blutchemische und hämatologische Untersuchung durchgeführt. Stammbäume wurden für alle Probanden aufgestellt und der Verwandtschaftsgrad ihrer Eltern angegeben. Von insgesamt 479 Patienten, die ohne Auslese untersucht wurden, wiesen 19 (4%) ein Pterygium mit einem relativ hohen Manifestationsalter auf. Eine Koppelung zwischen den Genen für die Blutgruppensysteme, Serumgruppen etc. und dem Gen für das Pterygium wurde nicht entdeckt. Eine erhöhte Kapillarfragilität wurde bei 10 Probanden festgestellt. Die Kapillarpermeabilität wurde bei 2 Probanden durch die Konzentration von intravenös verabreichtem Fluoreszin in der vorderen Augenkammer untersucht.

Bei dem einen Probanden war der Test schwach pathologisch. Das Serumcholesterin war bei 5 der 16 untersuchten Patienten erhöht. Eine ophthalmologische Untersuchung zeigt eine Häufung von degenerativen Augenkrankheiten. Die Lidspaltenflecken waren bei 10 der 17 untersuchten Patienten stärker entwickelt als bei der restlichen Bevölkerung. Die Möglichkeit einer rezessiven Übertragung der erblichen Prädisposition wird im Hinblick auf die erhebliche Inzucht und die Häufung des Pterygiums innerhalb der isolierten Bevölkerung diskutiert. Nach den besonderen, die Frequenz erhöhenden Umweltbedingungen in einer abseits gelegenen Inselgemeinschaft und dem Mendelschen Aufspaltungsverhältnis scheint ein nicht geschlechtsgebundenes, einfach dominantes Gen mit niedriger Penetranz und ohne Auslesenachteile die überzeugendste Erklärung für das Pterygium zu sein. Wegen des späten Manifestationsalters wurde das Pterygium nur in 2 Generationen beobachtet. Die Expressivität des Gens schwankt, und einseitiges Auftreten des Pterygiums ist nicht ungewöhnlich.

RÉSUMÉ

On a étudié l'incidence du ptérygion dans une population isolée de pêcheurs, où des unions consanguines sont très fréquentes. On a effectué des examinations cliniques et hématologiques, étudié des arbres généalogiques et indiqué le degré de consanguinité de leurs parents. De 479 sujets examinés sans sélection, 19 (4%) présentèrent un ptérygion avec un âge de manifestation relativement avancé. On n'a pas trouvé un linkage entre les gènes responsables pour les systèmes des groupes sanguins, les groupes de sérum etc. et le gène responsable pour le ptérygion. Une fragilité capillaire augmentée fût constatée chez 10 probands. La perméabilité capillaire dans la chambre antérieure de l'œil fut étudiée chez 2 probands à l'aide de la concentration de fluorescéine administrée intra-veineusement. Chez l'un des probands le test était légèrement pathologique. La sérumcholestérine était augmentée chez 5 des 16 sujets examinés. L'étude ophtalmologique montre une accumulation de maladies dégénératives de l'oeil. 10 des 17 sujets examinés présentèrent des pinguéculae plus prononcées que chez le reste de la population. On a discuté la possibilité d'une transmission récessive de la prédisposition héréditaire en considération des unions consanguines très fréquentes et de l'accumulation du ptérygion dans la population isolée. En considération des conditions de péristase spéciales et augmentant la fréquence dans la communauté d'un archipel situé à l'écart et en vue de la proportion de ségrégation mendélienne, un gène non lié au sexe et de simple dominance avec une basse pénétrance et sans désavantages sélectives semble être l'explication la plus probable pour le ptérygion. A cause de l'âge de manifestation avancé on n'a observé le ptérygion que dans 2 générations. L'expression du gène est instable, et l'asymétrie du ptérygion n'est pas rare.