



Climatic droplet keratopathy: is it really a degenerative human corneal disease related to climate?

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Key messages

What is known

- Climatic Droplet Keratopathy (CDK) is a degenerative corneal disease that develops in individuals who work outdoors, and as reported by previous studies is found in various parts of the world with dissimilar climates.

What is new

- Presently the pathophysiology of this illness is well known, and it is evident that CDK is not directly related to climate changes.
- Environmental multifactorial processes that activate the ocular inflammatory pathway, such as dietary intake, eye protection, and oxidative stress are the main causes of this human illness.
- Substitution of new terminology for this condition would be helpful to represent it clearly and prevent misleading ophthalmologists and others.

Dear Editor,

After 18 years of research about climatic droplet keratopathy (CDK), we compiled and reviewed papers on PubMed published on CDK, and the following is a focused opinion tempered by experience, viewpoints, synthesis of current evidence, and investigations by Dr. Serra's group. This opinion describes new insight into CDK pathophysiology and its major predisposing factors. This degenerative disease, first described by Baquis et al. [1] and later found in various

places around the world (Fig. 1A), was named with different terminologies based on its presumed etiology, deposit types, eponymous delineation, and clinical presentation [2].

Various clinical presentations and severities have been observed in world geographic areas with dissimilar climates. A few years ago, scientists from Dr. Serra's laboratory found moderate CDK in cold semi-arid Argentine Patagonia. In this area, advanced cases are accompanied by iris depigmentation and a marked decrease in corneal sensitivity, which correlate with abnormalities in the corneal nervous plexus [3]. Histochemical stains, SDS-PAGE, and proteomic studies of CDK corneas demonstrate the presence of protein globular deposits in cornea superficial layers [4].

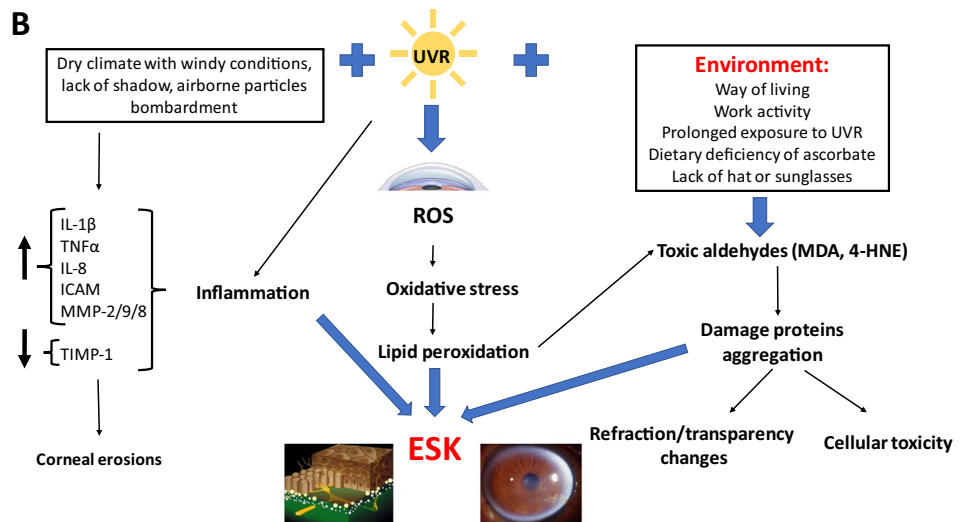
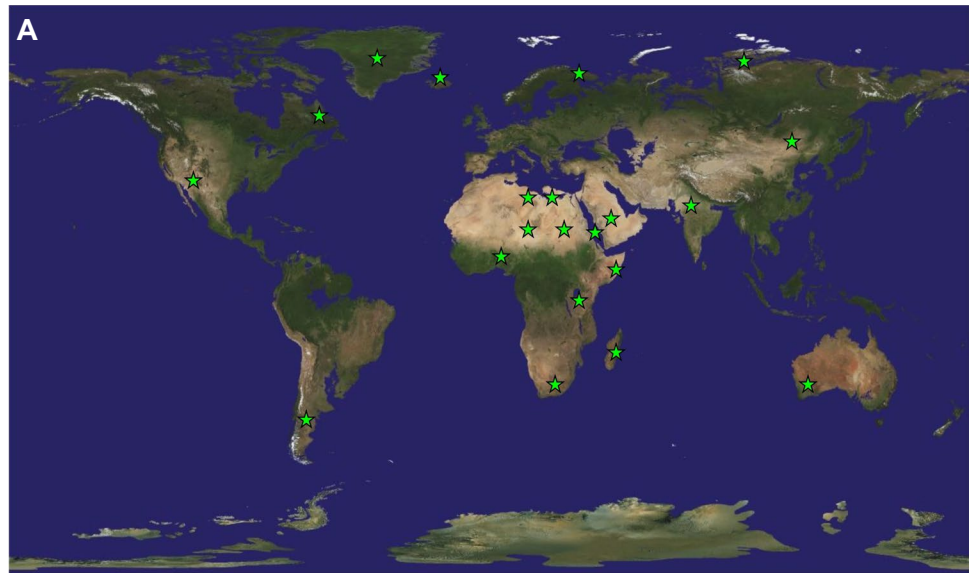
Although for many years CDK's origin has remained unknown, the climate has been considered the main reason for CDK onset; only recently have our investigations refuted that and provided more clear evidence of CDK's major risk factors. We have published data that reveal that environmental predisposing factors such as ocular inflammatory

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Fig. 1 Global distribution of ESK (A), scheme summarizing the origin of ESK (B)



pathways, dietary intake, eye protection, and oxidative stress play important roles in the pathogenesis of CDK.

Since corneal gelatinases participate in corneal wound healing and its inflammatory diseases, Dr. Serra's group studied

and found that CDK patients' specimens had higher levels of gelatinases and pro-inflammatory cytokines, whereas TIMP-1 gelatinase inhibitor levels were significantly lower than in the control subjects [5].

Table 1 Work activity, nourishment, use of eye protection, climate, and CDK existence in different regions of Argentina

Regions	Region 1	Region 2	Region 3
Factors			
The main source of livelihood	Sheep farming & shearing	Fruit production & associated industries	Sheep & Camelid farming
Food intake	Sheep meat & a little milk	Meat, vegetables, cereals, and fruit	Meat, quinoa, corn, potatoes, and a little milk
Use of eye protection	No	Hat & sunglasses	Winged hats
Climate	Cold semi-arid	Cold semi-arid	Cold semi-arid
^a ESK existence	Yes	No	No

az, Environmental Subepithelial Keratopathy

Ultraviolet radiation B (UVB) can damage the cornea through the generation of free radicals, lipid peroxidation, and DNA fragmentation. The reactive species can shift the redox status of cells towards oxidizing conditions, and lipid peroxidation causes the accumulation of reactive aldehydes. Two protective mechanisms against these attacks are mediated by ascorbic acid (AA) and aldehyde dehydrogenases (ALDHs). Humans do not have one enzyme necessary for AA synthesis, so they have to eat food containing AA to prevent its deficit. AA is transported from plasma to the cornea epithelium preventing the damage caused by UVB [6].

Rather than climate, environmental factors such as diet, labor activity, and appropriate eye protection play an important role in the pathogenesis of CDK (Table 1). Our results showed that CDK was found exclusively in people who worked outdoors in Argentine Patagonia, which has a dry climate and arid soil. Their food intake indicated a severe AA deficiency which correlated with low vitamin plasma concentration. Although other regions of the country have similar climates, soils, and work activities, their residents have a much more balanced diet including meats and vegetables which leads to efficient protection against CDK development. This study also highlighted the critical role of wearing winged hats and sunglasses in preventing CDK even in areas with similar dietary and work habits [7]. The fact that all phospholipid classes were lower in CDK-affected areas than in control areas indicated the occurrence of an oxidative stress process.

To summarize, individuals chronically exposed to hostile environments (long exposure to UVB, lack of vegetation/shade, dry climate with windy conditions, airborne particle bombardment, AA nutritional deficiency, lack of eye protection) experience an inflammatory process and oxidative stress in their corneas, which results in the development of ESK (Fig. 1B). The team headed by Dr. Serra confirmed that

CDK is not purely and directly related to climate but rather to other environmental multifactorial processes. Considering the negligible effect of climate, the present name for this illness—"CDK"—can be confusing for young ophthalmologists. Based on these remarks, it is imperative to start using an accurate name like "Environmental Sub-Epithelial Keratopathy (ESK)" that fits the most recent evidence related to its etiology.

Declarations

Conflict of interest The authors declare no competing interests.

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