The Parameters to Establish a New Corneal Dystrophy

GORDON K. KLINTWORTH

Because of the need for a worldwide standardized nomenclature for the corneal dystrophies, an international committee brought together the diverse literature on these disorders and recommended preferred names for each entity. Each corneal dystrophy needs a specific name because all of these entities do not affect the same parts of the cornea or have the same method of inheritance, pathogenesis, prognosis, or treatment. Like many other genetically determined diseases, knowledge about each corneal dystrophy passes through a continuum from clinical discovery, to a clinicopathologic characterization, to chromosomal mapping, to gene identification, and to the detection of mutations. As this knowledge advances over time, some designations gradually fall by the wayside and better terms are proposed based on clinical or clinicopathologic observations or an improved understanding of their cause, pathogenesis, and pathobiologic features. However, attempts to provide more accurate appropriate appellations often are unsuccessful. After an extended period of use, the names of some diseases become so ingrained in the literature that they are difficult to replace. For example, retinitis pigmentosa is a prime example of a misnomer, because inflammation of the retina (retinitis) is not a feature of this retinopathy. Nevertheless, despite attempts to replace this designation with the more precise name of pigmentary retinopathy, the old name lives on. Even corneal dystrophy is a misnomer because entities embraced under this umbrella do not arise from defective or faulty nutrition, as implied by the word dystrophy derived from the Latin term dystrophia. Particularly for the lay public, this is probably good because changes in nomenclature are not always easy to comprehend. To rename diseases frequently as knowledge advances may provide precision, as hematopathologists have done with the lymphomas, but for those who are not experts in particular diseases, the changes in nomenclature can create an aura of chaos.

At anyone point in time, all diseases are not known and new ones come to light, as occurred with the sudden emergence of retinopathy of prematurity, AIDS, and severe acute respiratory syndrome. If a new corneal disease is suspected, it is essential to determine that it has not been described previously. It is also necessary to make sure that the condition is not a variant of a known entity. The age of the patient, the duration of signs and symptoms, as well as the genetic background and other factors influence the phenotypes, sometimes making it difficult or impossible to establish a precise diagnosis on a single patient without additional information about other affected members of the family. As learned from the corneal diseases caused by mutations in the TGFBI gene, distinct clinicopathologic entities are not necessarily independent disorders, but may be fundamentally more similar than suspected.

When a new or previously forgotten corneal dystrophy is described, the discoverer has the opportunity to name the new disorder. Others encountering the same entity for the first time may be unaware of an earlier designation and may report their observations under a different term. Thus, the names of an entity may snowball, particularly when one of the original terms does not become established. Of all the conditions that affect the cornea, and indeed the eye, the record number of synonyms belongs to a disorder with multiple names that include chronic actinic keratopathy.

Recurrent corneal erosions occur in a variety of distinctly different corneal disorders, including Fuchs, lattice type I, Meesmann, and subepithelial mucinous corneal dystrophies, as well as in other conditions. Sometimes the recurrent erosions have an autosomal dominant method of inheritance and the erosions are the predominant feature of the condition. Albert Franceschetti (1896–1968), the renowned Swiss ophthalmologist, pioneered ophthalmic genetics and, together with 2 colleagues, published a comprehensive 2-volume book, Genetics and Ophthalmology, in 1961. Buried within the first volume of this text is a large 7-generation pedigree of a family with recurrent corneal erosions that he had published previously in 1928. The clinical features of affected individuals in this family originally were documented in a rudimentary way, and the Franceschetti paper was cited by Weiss and associates under the broad umbrella of epithelial recurrent erosion dystrophy (ERED). Somewhat similar cases have been named after the geographic location where the corneal dystrophy was discovered, as in the Swedish provinces of Sämland (Dystrophia Smolandiensis) and Hålsingland (Dystrophia Helsinglanica). These variants of ERED share features with relatively minor differences, and it is debatable whether they are indeed independent entities. Rigid geographic boundaries do not encase corneal dystrophies, and designations based on locations are unlikely to withstand the test of time, because the genetic pool of different mutations never remains entirely in a single community.

Commonly a new disorder is named after the first person known to describe it, but others are labeled after a
subsequent author. The disorder with recurrent corneal erosions that was documented by Franceschetti originally was dubbed *hereditary recurrent erosion of the cornea*, but it was later also referred to as *Franceschetti syndrome II*. Eponyms in nomenclature are common, and many eponymous corneal dystrophies are named after ophthalmologists: Ernst Fuchs (1851–1930, Fuchs endothelial corneal dystrophy); Arthur Groenouw (1862–1945, Groenouw corneal dystrophy type 1 and 2, currently known as *granular corneal dystrophy* and *macular corneal dystrophy*, respectively); Alois Meesmann (1888–1969, Meesmann corneal dystrophy); Frederick W. Stocker and L. Byerly Holt (Stocker-Holt corneal dystrophy); Max Bücklers (1895–1969, Reis-Bücklers corneal dystrophy); Hans-Jürgen Thiel (Thiel-Behnke corneal dystrophy); Walter F. Schnyder (1892–1980, Schnyder corneal dystrophy); and Hugo Biber (1864–1918), Otto Haab (1850–1931), and Friedrich Dimmer (1855–1926, Biber-Haab-Dimmer corneal dystrophy, currently called *lattice corneal dystrophy type 1*), and the list goes on and on.

At one time diseases, syndromes, and anatomic structures with eponymous names were referred to in the possessive form with an apostrophe, but this practice has fallen into disrepute and the trend of not using the possessive form has gradually gathered momentum in medical writing. With countless diseases having eponymous names, many individuals have difficulty learning and remembering the characteristics of the specific disorders, but a skill in recalling them is a distinct advantage for someone interested in trivial pursuit.

The human desire to compartmentalize diseases has spawned so-called splitters and lumpers, particularly among individuals studying genetic diseases. Those who are splitters regard each disorder with recurrent epithelial erosions, such as *Dystrophia Smolandiensis* and *Dystrophia Helsinglandica*, as distinct entities, but lumpers prefer to group all of these conditions together as variants of ERED. Although differences have been detected between the EREDs, an understanding of the basic defects in each of them remains unknown until the actual mutations in the responsible gene(s) have been identified. Until that time of reckoning, it will not be known whether these conditions are, or are not, variants of the same disease.