Dystrophy: a revised definition

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SUMMARY Dystrophy is defined as the process and consequences of hereditary progressive affections of specific cells in one or more tissues that initially show a normal function. The term abiotrophy was previously applied to these lesions, but has gone out of use. Degeneration is an equivocal term used for both acquired and hereditary disorders. Aging may or may not be considered as dystrophy. Dysplasias or dyshistogeneses are different from dystrophies. Dyshistogenetic tissues present with abnormal structure and function at birth in contrast to dystrophies, which are genetically programmed for later onset.

A precise nomenclature is helpful in the delineation of congenital anomalies as international communication depends on the agreement of such definitions. Discussions on nomenclature have been intense within the field of birth defects, but less so when postnatal events are concerned. In the latter we have felt the need for a definition of dystrophy.

Dystrophy derives from the Greek: dys—wrong, difficult, trophé—nourishment. In biology and medicine dystrophy is used mostly in describing affections of the eyes, skin, and muscles. The term was introduced by Erb to delineate progressive pseudohypertrophic muscular disorders from spinal muscular atrophy.

Twenty years ago, the common definition of dystrophy was a hereditary, symmetrical, congenital or later appearing, slowly progressive affection, presenting slight intrafamilial variation, and of unknown aetiology. It was suggested that conditions secondary to systemic factors should not be termed dystrophies, but others found it somewhat artificial to exclude entities with systemic manifestations from the definition.

We intend to show that current knowledge has made part of the definition redundant. The aetiology of dystrophic lesions is no longer quite as unknown as before. Distinct histopathological types of ocular and muscular dystrophies have been described and those lesions reflect abnormal cellular structure or function or both. Furthermore, a number of genetic disorders are now being understood at the molecular level and dystrophies are no exception.

Dystrophies appear in specific cells in otherwise normal tissues. Since dystrophies are the result of genetic disorders, all cells manufacturing the abnormal gene product may sooner or later express the variant morphology and function; these cells eventually will become dystrophic. The ground glass cornea in some mucopolysaccharidoses is therefore a dystrophy because the corneal cells store the abnormal mucopolysaccharide. Similarly, muscle cells from patients with Duchenne muscular dystrophy producing abnormal dystrophin are dystrophic.

The better the hereditary dystrophies are understood, the greater the likelihood of finding generalised defects in disorders that were previously regarded as isolated. Therefore, a subclassification of isolated dystrophies versus generalised disorders is not justified. Reduced ornithine aminotransferase and tubular aggregates in type II fibres of skeletal muscles in patients with gyrate atrophy, and abnormal bronchial cilia in some types of retinitis pigmentosa, serve as examples.

Abiotrophy

Other terms have been applied previously to define what are now called dystrophies. Abiotrophy, according to Duke-Elder, was a term introduced by Sir William Gowers (1902) to define lesions affecting nervous tissues characterized by a ‘defective vitality’ leading to their premature decay determined frequently by genetic influences. Sorsby defined abiotrophies as progressive hereditary cellular lesions with little intrafamilial but some interfamilial variation. He stressed symmetry and manifestations in tissues that had developed and functioned normally for some years. Examples were corneal dystrophies,
retinitis pigmentosa, and Huntington's chorea. Abiotrophy was used by Opitz\textsuperscript{16} in a similar way for apparently non-metabolic disturbances of function in an organ that was previously apparently normal. The term abiotrophy, however, has almost gone out of general use.

**Degeneration**

Degeneration was used by Duke-Elder and Leigh\textsuperscript{7} synonymously with dystrophy; Opitz\textsuperscript{16} defined degenerations as genetic disorders with specific biochemical defects in certain cells, leading to progressive loss of function. Others have used the term less discriminately for any loss of function.\textsuperscript{17} This is borne out by the use of the term in, for example, vitelliform degeneration of the macula, which is a dystrophy, Wallerian degeneration where the loss of function results from a separation of a nerve fibre from its trophic centre, and bandicular corneal degeneration, which is a corneal opacity owing to phthisis or chronic inflammation. In clinical medicine the term does not distinguish between acquired and genetic disorders.

**Acquired lesions**

Acquired lesions, resulting from inflammation, trauma, or tumour, are not dystrophies. They should be designated according to the tissue involved as keratopathies, retinopathies, myopathies, neuropathies, etc.\textsuperscript{13} For example, sympathetic reflex dystrophy, hunger dystrophy, and chronic actinic skin dystrophy are not dystrophies as defined here.

**Dysplasia**

Dystrophies are progressive disorders appearing in tissues with initially normal function. Few of the disorders termed congenital dystrophies are progressive and many of them are better termed dysplasias or dyshistogeneses, which are developmental abnormalities of tissue structure.\textsuperscript{1,2} For instance, asphyxiating thoracic dystrophy is a congenital dysplasia and not a dystrophy, since abnormal structure and function are present at birth. Congenital muscular dystrophy (Fukuyama) is not progressive and affected patients may even improve somewhat during childhood; this, therefore, is a dysplasia. Similarly, some congenital ectodermal dystrophies and congenital corneal dystrophies show no progression and should therefore be classified as dysplasias or dyshistogeneses.

Sorsby\textsuperscript{15} pointed out that there is no fundamental difference between a congenital defect (by which he meant dysplasia) and an abiotrophic malformation (by which he meant dystrophy) except that in a congenital defect the disorder has run its course before birth while in a dystrophy the genetic dysfunction is programmed for later onset.

**Deterioration**

Localised and systemic dystrophies may give rise to secondary impairments that are not directly the result of intracellular expressions of mutant genes. This may be termed deterioration, and although such impairments may be progressive they are not dystrophic. Examples are corneal scarring in the Riley-Day syndrome and posterior cortical cataract in retinitis pigmentosa.

Although dysplastic tissues show no progression of the dysplastic lesion, the patients may deteriorate because of secondary events. These may be termed dysplasia sequences or dyshistogenesis sequences to match the terminology of errors of morphogenesis, such as malformation sequences, deformation sequences, etc.\textsuperscript{1,2} Examples of dysplasia sequences are ocular phthisis resulting from retinal dysplasia, contractures resulting from congenital muscular dystrophy, and respiratory failure in asphyxiating thoracic dystrophy.

**Aging**

Affections resulting from aging are usually not termed dystrophies,\textsuperscript{10,17} presumably because everybody expects the occurrence of preprogrammed changes in genetic expression late in life. However, premature aging disorders may be termed dystrophies, such as, for example, Werner's syndrome, characterised by premature aging of skin, muscle, and bones, and premature cataract. There is no known difference between the histopathological changes in premature aging and in normal aging. It is therefore possible that it is the age or age related expectations of the observer that determine whether a disorder is termed a dystrophy or the process of aging.

**Conclusions**

It therefore follows that dystrophy may be defined as the process and consequences of hereditary progressive affections of specific cells in one or more tissues that initially had normal function. Implicit in this definition is that the time of onset is variable; intrafamilial variation resembles that observed in other hereditary conditions; and dystrophies may or may not be part of systemic disorders. Symmetry is the rule in hereditary condi-
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Dystrophies or dystrophies are characterized by a lack of progressive deterioration or dissemination. It is also implicit in the definition that congenital non-progressive disorders are not dystrophies but dysplasias or dyshistogeneses. Similarly, dystrophies should be distinguished from sequences of congenital birth defects, infections, traumas, and tumors.

Deterioration of dysthistogenetic disorders or impairment secondary to dystrophic lesions are not dystrophies. Changes occurring at the time when aging is expected may be called dystrophic by some and physiological by others.

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References


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