Heritable disorders of connective tissue are an established cause of aortic disease. Genetic defects in matrix protein synthesis can lead to a critical reduction in tensile strength and predispose to aneurysm formation and dissection. Cystic medial degeneration is the common histopathologic expression of a number of such disorders, including Marfan and Ehlers–Danlos syndromes. Several other familial forms of thoracic aortic disease have been reported, and many other are suspected. In this chapter, we review the major features of the connective tissue disorders and their links with aortic dissection.

MARFAN SYNDROME

INTRODUCTION

Marfan syndrome occurs with a frequency of 2–3/10,000 persons and is transmitted in an autosomal dominant pattern with variable penetrance. Approximately 25% of cases occur sporadically as de-novo genetic mutations\(^1,2\).
The disorder involves chiefly the skeletal, ocular, and cardiovascular systems, but pulmonary, cutaneous, and dural structures can also be affected. Aortic disease confers the principal mortality risk and has been responsible for the large majority of the premature loss of life seen in this disorder. The survival of patients with Marfan syndrome has improved significantly over the last few decades, due in part to better cardiovascular imaging, prophylactic beta-blockade\(^3\), and the expanding indications for elective aortic root replacement in at-risk individuals\(^4\). The average life span of patients with untreated Marfan syndrome was 32 years in 1972\(^5\). Median life expectancy was reported at 41 years in 1993 and 61 years in 1996\(^6,7\). The majority of premature deaths are attributable to aortic dissection/rupture and heart failure owing to severe aortic regurgitation.

**HISTORY**

Marfan syndrome has been recognized for over one hundred years. It is interesting to review the landmark events that have shaped our recognition, understanding, and treatment of this challenging disorder.

- In 1896, Antoine Bernard Jacques Marfan, a renowned professor of pediatrics in Paris, described a syndrome of markedly long and thin extremities in a five-and-a-half-year-old child. His original description noted the presence of the skeletal abnormalities typical of the disorder but did not include recognition of its cardiovascular manifestations. The term that he gave to the disorder was *dolichostenomelia*, in recognition of the strikingly long extremities\(^8\).
- In 1902, Achard contributed the term *arachnodactyly*, meaning “spider legs”, to describe the long, thin extremities\(^9\).
- The first association of Marfan syndrome with cardiac abnormalities was reported in 1912\(^10\). The patient died at two and a half months of age. The postmortem observations included mitral leaflet degeneration and a patent foramen ovale. The next several decades focused attention on the associated cardiac abnormalities, in the early belief that congenital heart disease was a prominent feature of the disorder.
- In 1918, Bronson described the first association with Marfan syndrome with a vascular event, a ruptured aortic aneurysm in a child\(^11\).
- In 1931, Weve established that Marfan syndrome was an inherited disorder, transmitted in autosomal dominant fashion\(^12\).
- In 1943, Helen Taussig of John Hopkins University was the first to emphasize aortic involvement in Marfan syndrome\(^13\). Her report established aortic pathology as the principal cause of premature death in patients with this syndrome.