**HISTORY OF NEPHROLOGY**

**HISTORY OF ANDERSON - FABRY DISEASE**

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**Introduction and Aims:** Anderson - Fabry disease is a hereditary lysosomal storage disorder caused by the partial or total inactivation of α-galactosidase A. This inactivation is responsible for the accumulation of glycosphingolipids in lysosomes, with subsequent cellular and microvascular dysfunction. Anderson - Fabry is a rare disease with an incidence of 1:40000; however, there are good reasons to believe that it is often seen but rarely diagnosed.

**Methods:** Historical data were collected from literature, textbooks, encyclopedias, scientific periodicals and laboratory experimental data.

**Results:** Anderson - Fabry disease was described for the first time at the end of the 19th century by two dermatologists, independently of each other: Johannes Fabry in Germany and William Anderson in England. In 1898 Fabry described a 13-year-old patient affected by nodular purpura and subsequent albuminuria and he classified this clinical case as angiokeratoma corporis diffusum. In the same year Anderson presented the clinical case of a patient aged 39 with angiokeratomas, proteinuria, fingers deformity, varicose veins and lymphedema and he suggested this was a case of systemic disorder.

In the first ten years of the 20th century other similar cases were described: in the 1912, Madden illustrated the clinical case of a young Egyptian patient with diffuse angiokeratoma; later, in 1915, Fabry reproposed this condition as "Angiokeratoma corporis naeviforme.

In 1947 Pompen began to suspect that the Anderson - Fabry disease was "familial", after the clinical case of two brothers died of the same disease. Right in 1964 the clinical features of the main two phenotypes of the disease, the classical form and the atypical variants, were already described.

Anderson - Fabry Disease is a multisystemic disorder caused by the build-up - inside lysosomes - of globotriaosylceramide or Gb3, which is the accumulated lipid material discovered in 1963 by Sweeley e Klionsky.

In the '70s the enzyme involved in the metabolism of Gb3 was found to be α-galactosidase A, whose functional deficit causes the disease. The enzyme is encoded by the GLA gene - described in 1974 - located in the long arm of the X chromosome (q21-22).

To date more than 1000 mutations have been described in the coding regions of the GLA gene.

Though many efforts were performed in past times to replace the lacking enzyme, only in the mid-1990s these efforts were successful and led to the enzymatic replacement therapy for Anderson - Fabry disease.

**Conclusions:** From the discovery of the disease, huge progresses have been achieved over one century about clinical, molecular and therapeutic knowledge of Anderson - Fabry disease, therefore we aim at exploring in depth the noteworthy features of this still growing course.