Clinical picture, evolution and peculiar molecular findings in a very large pedigree with Wolfram syndrome.

OBJECTIVES: a) To describe a very extended inbred pedigree with Wolfram syndrome (WS) (OMIM #222300); b) to report both the clinical picture and evolution in this large family and a peculiar mutation which has been reported hitherto only in Italian patients. DESIGN: The five-generation pedigree from Sicily was reconstructed through a proband with all the main manifestation of WS, born to a couple of healthy consanguineous parents. DNA examination was performed in both patients and healthy family members. RESULTS: In all seven patients we found a homozygous 16-bp deletion in exon 8 of the WFS1 gene that introduces a stop codon in position 454. CONCLUSIONS: This inbred pedigree is the largest with WS described in the literature. Its analysis definitively confirms the view of autosomal recessive inheritance in WS. The 16-bp deletion appears to be a relatively frequent mutation only in Italian patients. Before examining the entire coding region of the WFS1 gene a preliminary screening for the 16-bp deletion in exon 8 might be suggested when a new Italian case of WS is investigated.