Summary

Observations in 107 patients with facioscapulohumeral disease (Landouzy-Dejerine's disease or facioscapulohumeral muscular dystrophy) enabled us to summarize this disease as follows:

- The mode of inheritance is autosomal dominant.
- The majority of our patients (82%) had presenting symptoms of shoulder girdle weakness. Symptoms, other than inability to whistle, suggesting facial onset were reported in 10% of the cases: 8% of the patients had presenting symptoms of foot extensor weakness. Presenting symptoms of pelvic girdle weakness have never been reported. Inability to whistle never was a complaint, although 50% of our patients never had been able to whistle and 12% lost this ability in the course of their disease. Four patients related episodes of shoulder pain to the onset of the disease.
- On physical examination 94% of the patients had facial weakness: in eight patients (7%) this was the only sign of the disease. Shoulder girdle weakness was present in 93%, foot extensor weakness in 67% and pelvic girdle weakness in 50% of the patients.
- The disease has a descending order of muscle involvement. It is probable that facial weakness is the earliest detectable sign in the majority of cases but as facial weakness rarely leads to complaints, only longitudinal studies could prove such a statement. The truncal or limb muscles first to become involved are the scapular fixators, the pectoralis major and the latissimus dorsi. On examination the cases presenting with symptoms of foot extensor weakness had shoulder girdle weakness as well. Early abdominal muscle weakness was common in our patients.
- The further spread of muscle involvement may occur in two ways. The majority of patients show early foot extensor weakness and,

subsequently, pelvic girdle involvement. In a few patients the reverse sequence is observed. Both sequences may be observed within one family.

- The course of the disease is steadily progressive in the majority of the symptomatic patients. The rate of progression is quite variable. Long periods of apparent arrest of the disease have been reported by our patients, but they do not occur frequently. Also, a very rapidly progressive course is rare and occurred in only one patient in this material. The average duration of spread from shoulder girdle to foot extensor involvement was 8.8 years (range 0-28 years), and from foot extensor to pelvic girdle involvement was 9.8 years (range 0-33 years).
- Thirty-two percent of the patients were abortive cases, defined as affected but asymptomatic patients. The difference between males (13 cases) and females (21 cases) was statistically not significant. It is probable that the majority of these cases will remain asymptomatic.
- The average age of onset, based on symptoms, was 17.0 years in our patients, which is in agreement with the findings in the literature. The difference between the age of onset in males (15.8 years) and in females (19.0 years) was statistically not significant. The age of onset varied from three to 44 years. Onset in infancy is possible and part of the disease.
- Asymmetric involvement of the shoulder and arm muscles was frequently observed. The right side was significantly more frequently more severely involved than the left side. This asymmetry was significantly correlated with handedness, but was not related to the body side.
- Pseudohypertrophy of muscles was rare. Calf hypertrophy with weakness was observed in two cases (2%).
- Ankle contractures were present in ten cases (10%). Contractures of other muscles are extremely rare.
- No evidence was found to suggest cardiac muscle involvement.
- Men and women were equally affected. There were no sex-differences in severity of involvement. The only significant difference between the sexes was observed in the number of

probands (15 males, 4 females).

- The penetrance was almost complete. Gene carriers that will not come to expression in a lifetime are rare, and probably do not exceed 2%.
- Fitness, judged by offspring, was normal in our patients with FSHD compared to their non-affected sibs.
- The prevalence of the disease in the province of North-Holland (The Netherlands) was at least 1 in 46.000 individuals. It is estimated that less than 45% of the kindreds have been found. This would bring the estimated prevalence in the province of North-Holland at at least 1 in 21.000 individuals.
- Disability increases with age and duration of the disease. Complete loss of the ability to walk occurred in 6% of our cases.
- The life span of the patients is probably not influenced by the disease.
- The serum creatine kinase activity was normal in 34% of the cases, and rarely exceeded four times the upper limit of normal. The level of the creatine kinase activity declined significantly with age and duration of the disease.
- Linkage between the locus for FSHD and the loci for 35 genetic markers has not been demonstrated. The highest lod-score (1.428) was obtained for GM at θ 0.20.
- Electromyography revealed no abnormalities in four patients (13%). A myopathic pattern was present in 23 patients (74%), and both myopathic and neurogenic features were recorded in three patients (10%). One patient (3%) revealed a neurogenic pattern due to a diabetic polyneuropathy. The neurogenic changes occurred in some family members and not in others, and are considered to be part of the disease.
- Histology was normal in six muscle biopsies (20%). The other biopsies all showed various degrees of myopathic changes. A low grade of necrosis and an even lower grade of regeneration are striking. Small cell infiltrations of various sizes may be present as well. Small angular fibres, possibly suggesting denervation, were present in six biopsies (20%). Occasionally groups of a few atrophic fibres were found and also moth-eaten

fibres occurred in groups. In addition to the moth-eaten fibres, histochemistry showed poor fibre type differentiation in four (13%) biopsies. The examination of the muscle biopsy may yield an extremely variable picture.

- In this material there were no grounds to assume that facioscapulohumeral disease, as described above, is genetically heterogeneous.
- The differential diagnosis is limited and includes autosomal dominant scapuloperoneal spinal muscular atrophy and autosomal dominant mitochondrial myopathy.
- The pathogenesis and cause of this disease are not known.