

EPIDERMOLYSIS BULLOSA HEREDITARIA - EPIDEMIOLOGY, DIAGNOSIS, COMPLICATIONS, PROGNOSIS AND MEDICAL MANAGEMENT

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INTRODUCTION

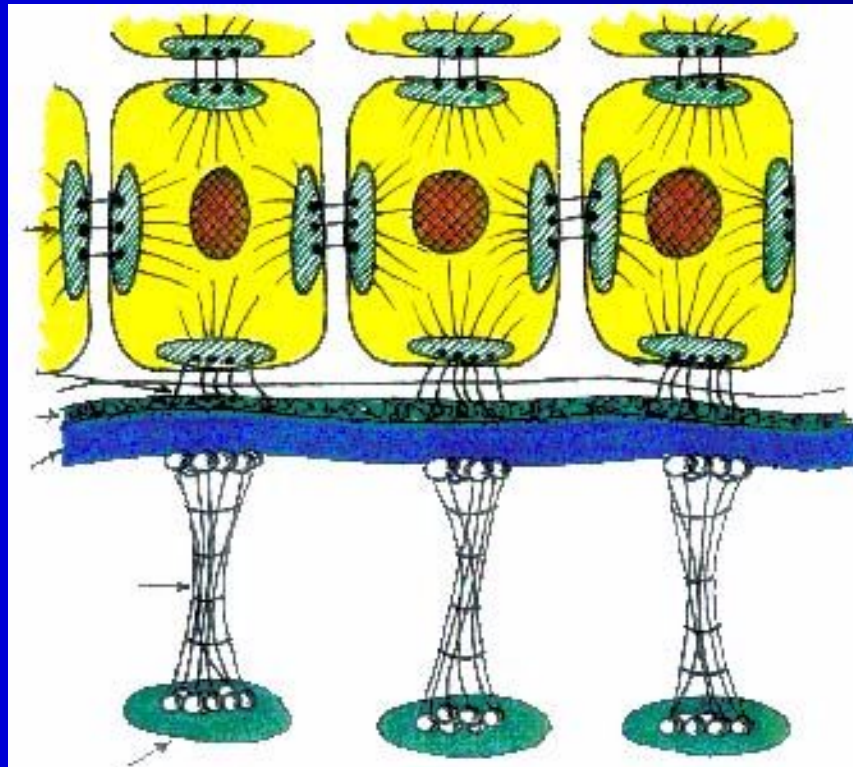
- Epidermolysis bullosa hereditaria (EBH) is a term which describes a group of genetic skin disorders manifested at or soon after birth with blisters and erosions of the skin and mucous membranes induced either by minimal mechanical traumas or arising spontaneously.
- The clinical features vary from small vesicular lesions to widespread blister formations, erosions and ulcerations leading to severe deformations of the fingers and toes, as well as disturbances in swallowing and resorption of food.

INTRODUCTION

- The disease is caused by **genetic defects** which lead to cleavage within or adjacent to the epidermal basement membrane.
- **Electron microscopic examination** still is the gold standard for classifying epidermolysis bullosa.
- According to the depth of the skin defects and the clinical manifestations **three major types** of epidermolysis bullosa hereditaria are recognized:
 - **epidermolysis bullosa simplex (EBS),**
 - **epidermolysis bullosa junctionalis (EBJ)**
 - **epidermolysis bullosa dystrophica (EBD)**

EPIDERMOLYSIS BULLOSA HEREDITARIA – ULTRASTRUCTURAL CLASSIFICATION

Basal keratinocytes
Desmosomal junctions
Anchoring filaments
Lamina lucida
Lamina densa
Anchoring fibrils



EB Simplex

EB Junctionalis

EB Dystrophica

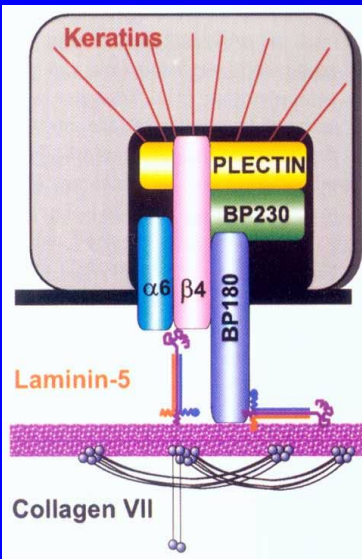
Anchoring plaques

EBH - 23 different clinical types

As a result of the recent progress in molecular genetics the different forms of epidermolysis bullosa have been linked to mutations in **10 distinct genes encoding the major structural basement membrane zone proteins**. This information has formed a basis for refined molecular classification with prognostic implications, improved genetic counseling, and prenatal and preimplantation genetic diagnosis.

EPIDERMOLYSIS BULLOSA HEREDITARIA - REFINED MOLECULAR CLASSIFICATION

EBH types	EBH subtypes	Target proteins
EBSimplex	EBS Weber-Cockayne EBS Koebner EBS Dawling-Meara EBS with musc. dyst.	KERATIN 5, 14 KERATIN 5, 14 KERATIN 5, 14 PLEKTIN
EBJunctionalis	EBJ Herlitz EBJ non Herlitz EBJ with pylor athresy	LAMININ 5 LAMININ 5, COLLAGEN XVII $\alpha 6\beta 4$ INTEGRIN
EBDystrophica	EBD dominanta EBD recessiva (Halopeau-Siemens) EBD recessiva (non Halopeau-Siemens)	COLLAGEN VII COLLAGEN VII COLLAGEN VII



*Epidemiological study on EBH in Bulgaria
for a period of 37 years (1970 – 2007)*

Aims of the study

- To document the number of patients affected by EBH and to create a National registry of the disease;
- To assign accurately the patients to a subtype and to provide genetic consultation (assign the mode of inheritance and the recurrence risk for the affected family members);
- To familiarize the society, relatives and medical staff with the nature and common complications of EBH and the necessary care for the patients.

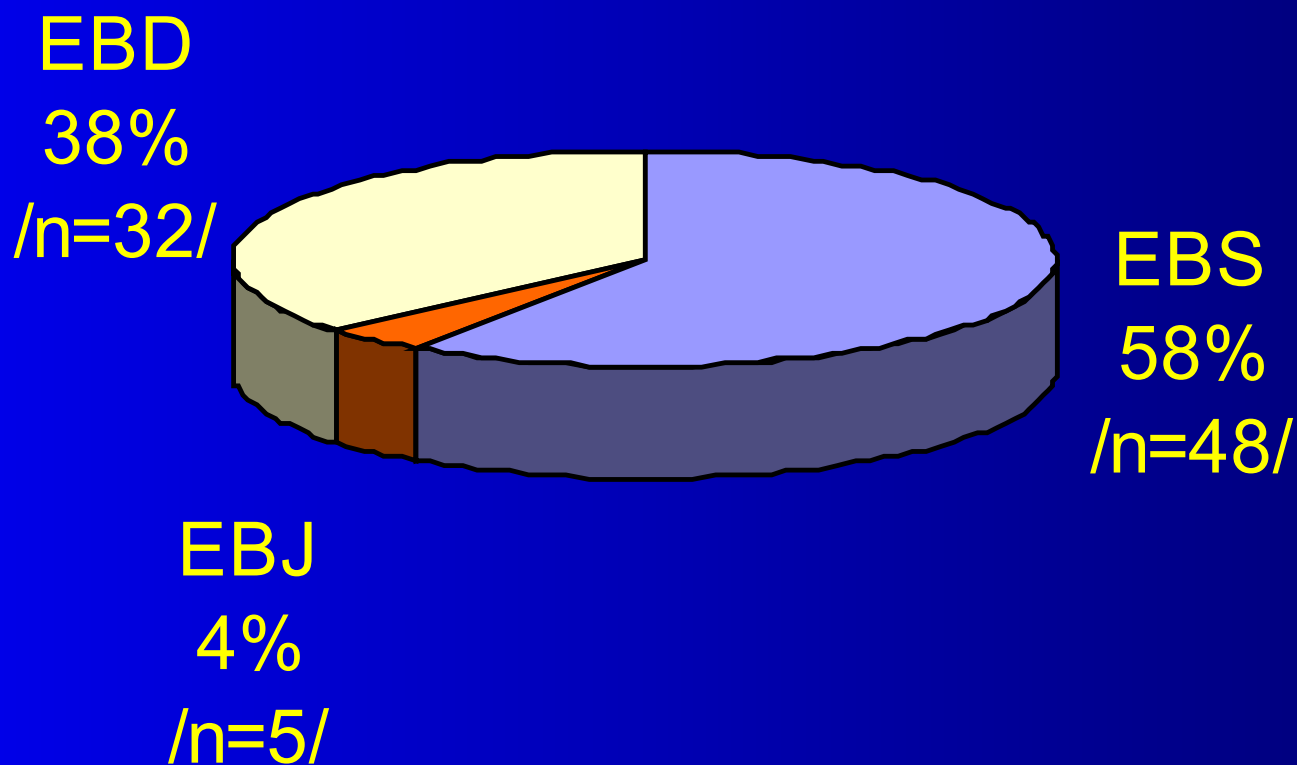
MATERIAL AND METHODS

- Cases of EBH were identified from the records of the Dermatology Clinics with the help of Association Epidermolysis Bullosa – Bulgaria (1994).
- The classification of EB subtype was made on the basis of clinical features and ultrastructural examination, using the criteria suggested by Fine et al. (2000).
- Genealogical analysis revealed the mode of inheritance.

RESULTS

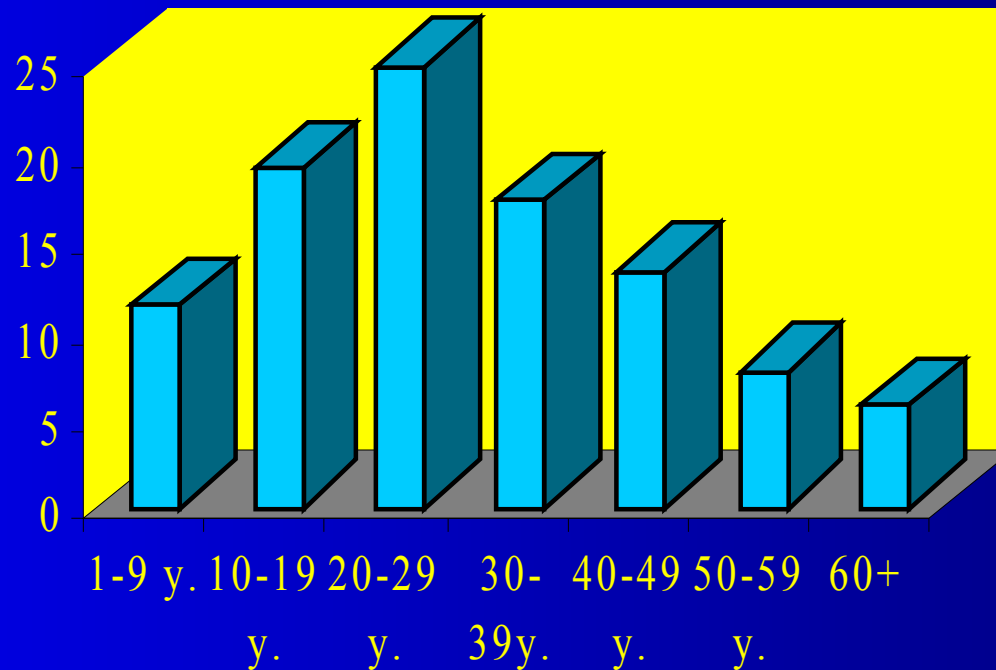
- Ninety seven patients – 49 men and 48 women, 0-77 years of age with EBH from 42 families were identified as suffering from EBH in Bulgaria and were assessed.
- The distribution of the major types of EBH was: EB simplex – 58 %, EB junctionalis – 4 %, EB dystrophica – 38%.
- The prevalence of all forms of EBH was estimated at 8.6/per million inhabitants. 75% of the patients live in towns, and 25% live in villages.

Distribution of the patients with EBH



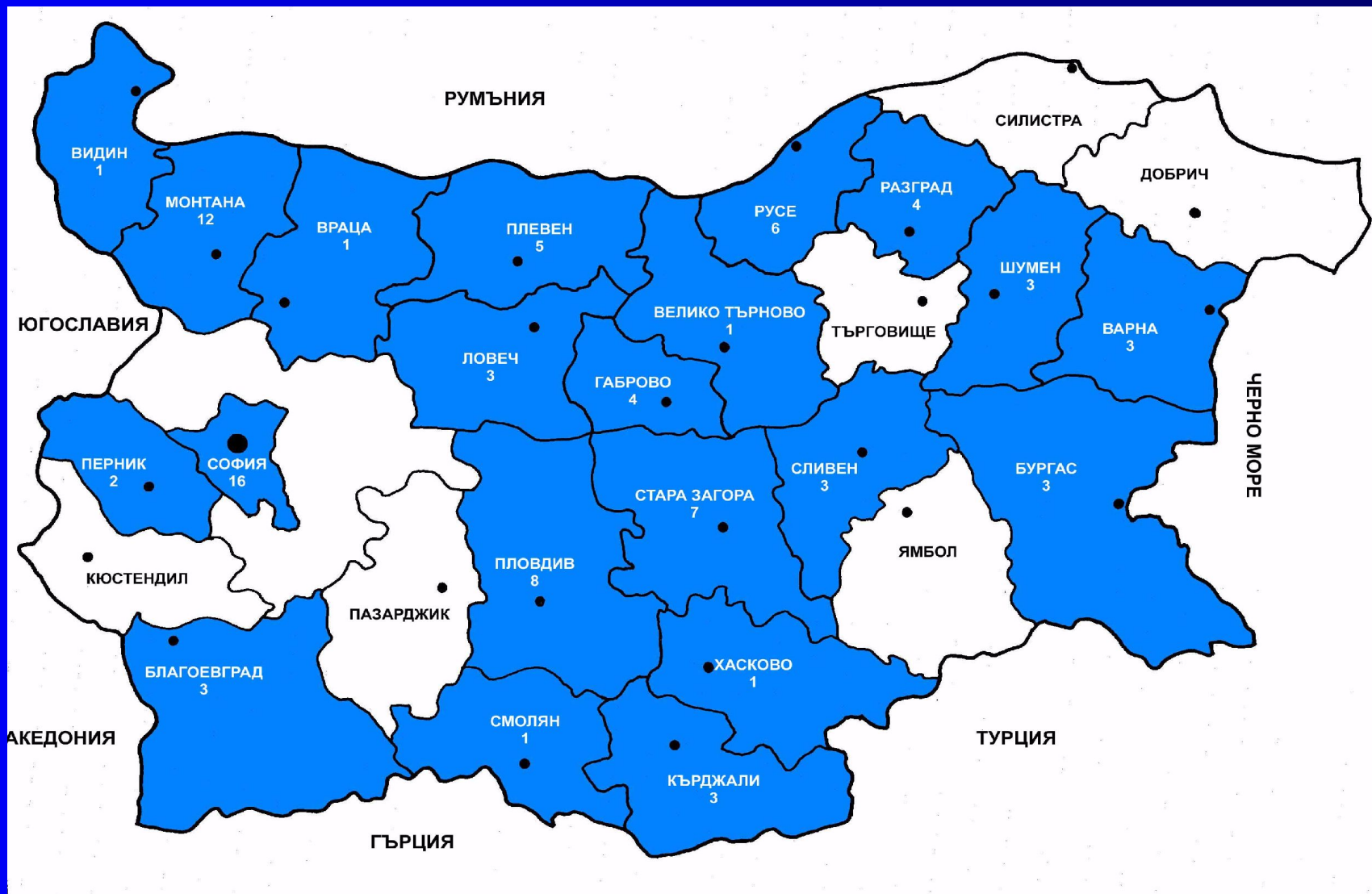
Distribution of the patients with EBH by age

Patients (%)



Years of age

Geographical distribution of the patients with EBH in Bulgaria

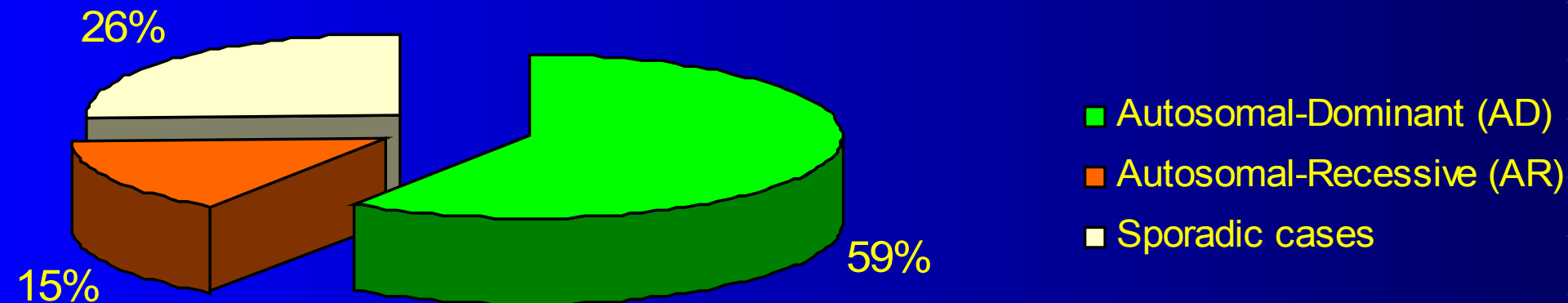


The prevalence of all types of EBH in Bulgaria (general population 7,973,671) up to 31 December 2007 is 8.6 cases/per million inhabitants;
of EBS – 5,3/mill; of EBJ – 0,1/mill; EBD – 3,1/mill

EBH	EBS	EBJ	EBD
8,6	5,3	0,13	3,1

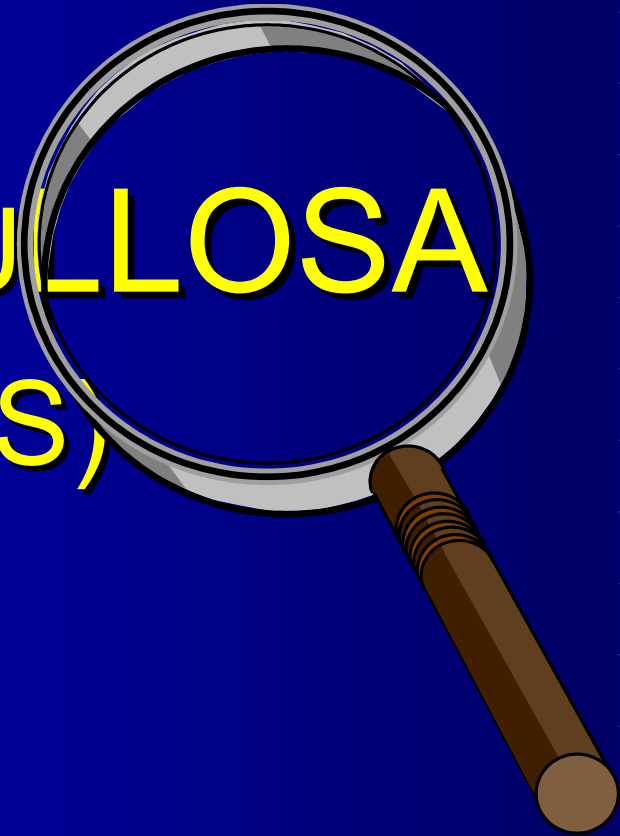
- The analysis of the mode of inheritance of EBH cases showed 35 patients (59%) with AD mode of inheritance and recurrence risk of 50 %, 9 patients (15%) with AR mode of inheritance and recurrence risk 25%, and 15 patients (26%) were classified as sporadic cases without clear pedigree criteria for a single gene (Mendelian) mode of inheritance.
- The application of the genealogical method was mandatory in the assessment of the recurrence risk of the appropriate family members.

Type of inheritance of EBH in Bulgaria

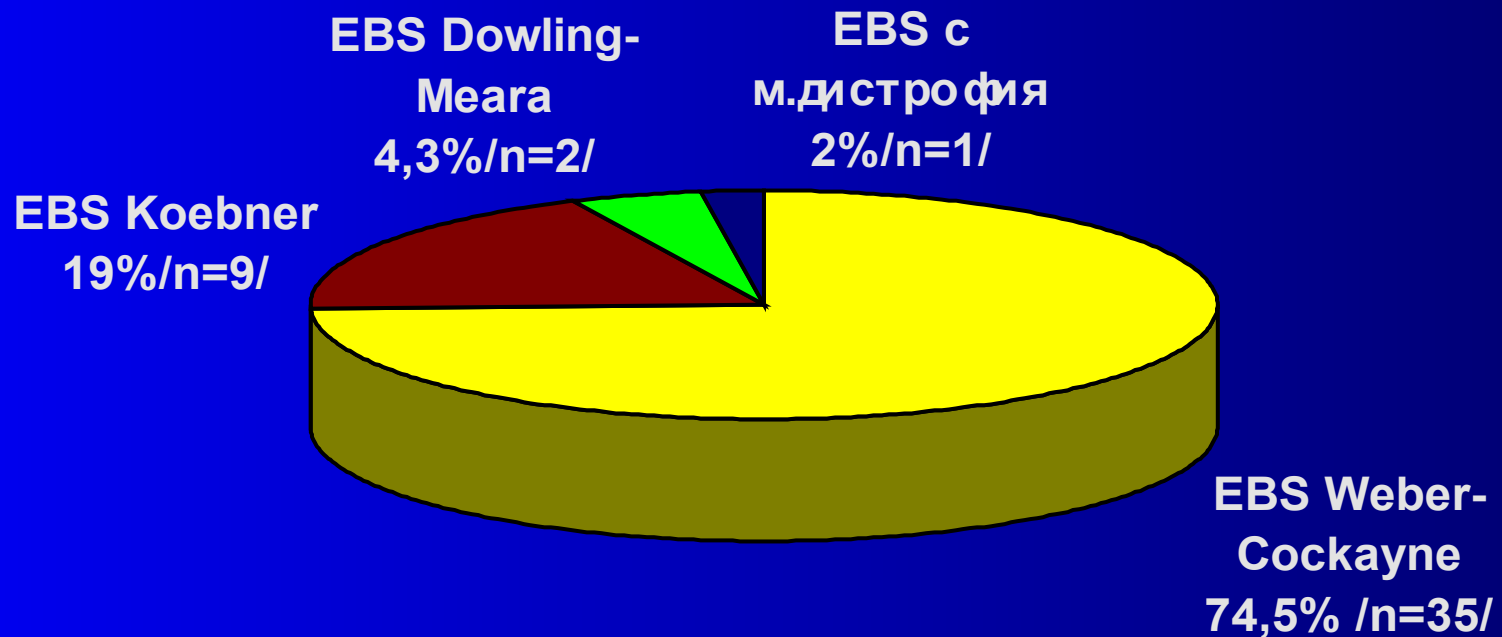


EPIDERMOLYSIS BULLOSA SIMPLEX (EBS), n=48

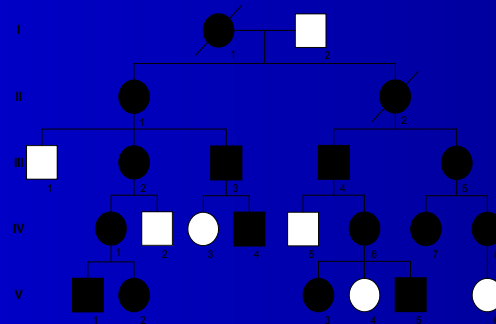
male - 26
female - 22
12 families



Distribution of the patients with EBS by subtypes



EBS subtype Weber-Cockayne (n=33)



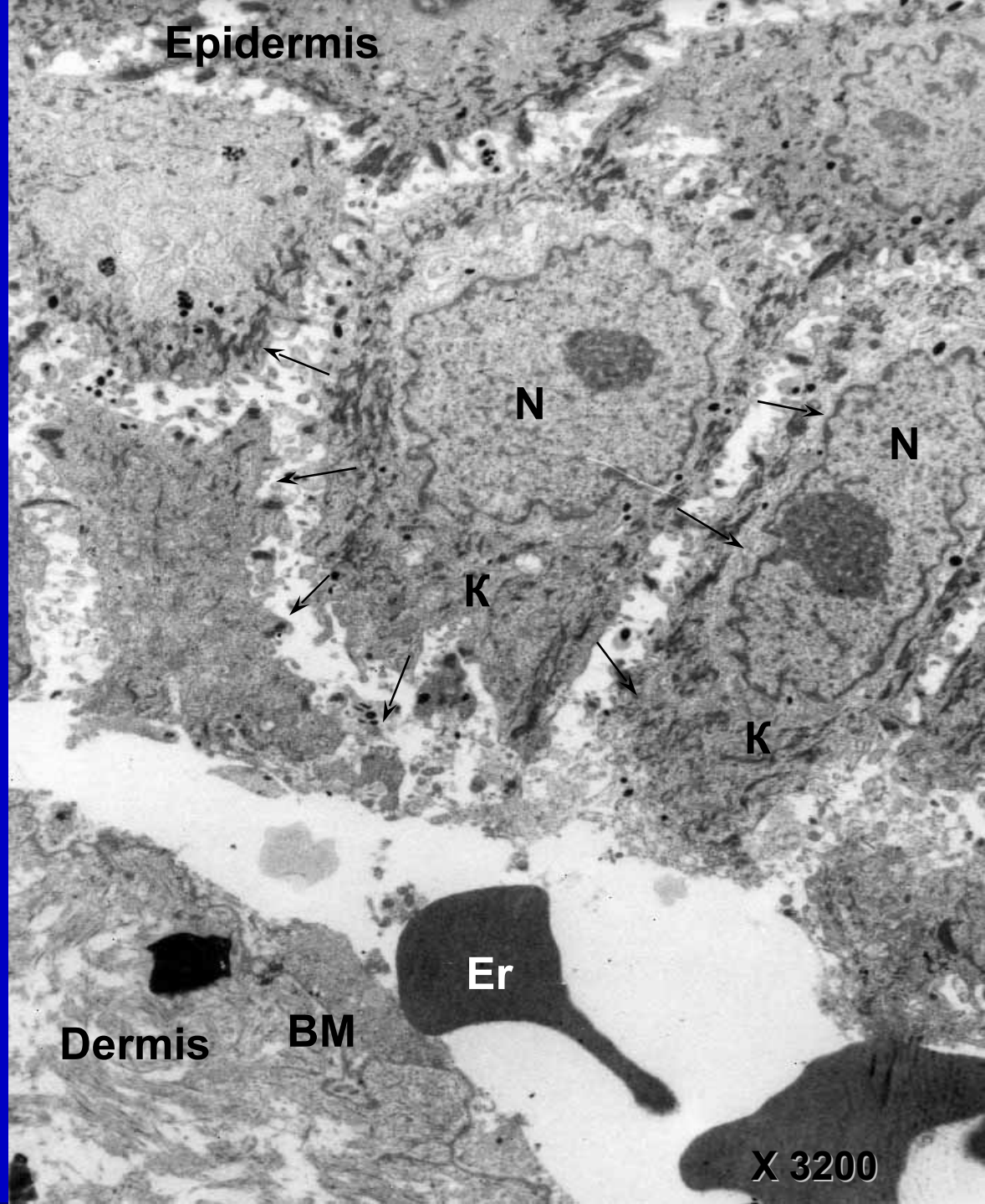
EBS subtype Koebner (n=8)

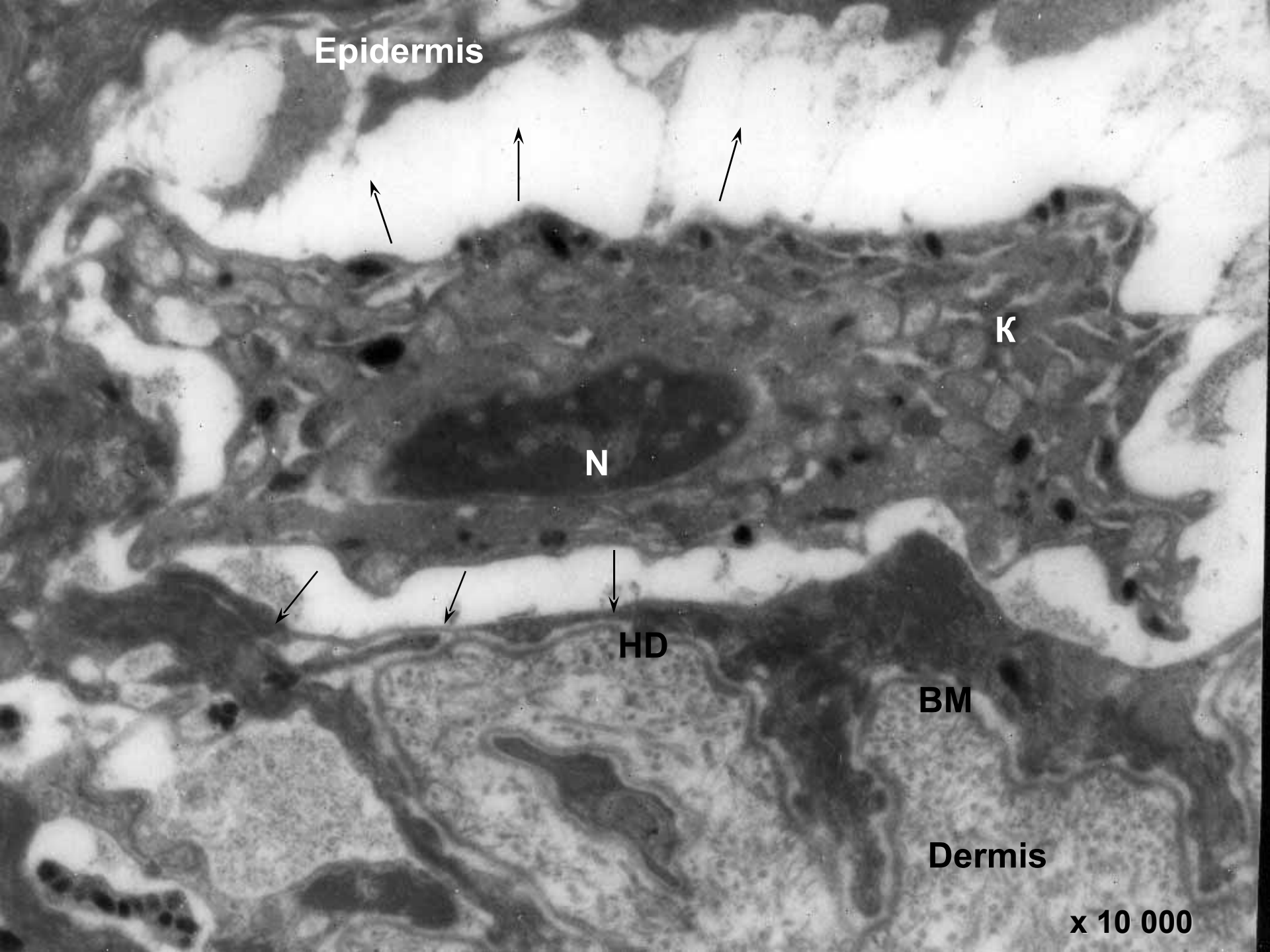


EBS subtype Dowling-Meara (n=2)



Ultrastructural
examination
in EBS





Epidermis

K

N

HD

BM

Dermis

x 10 000

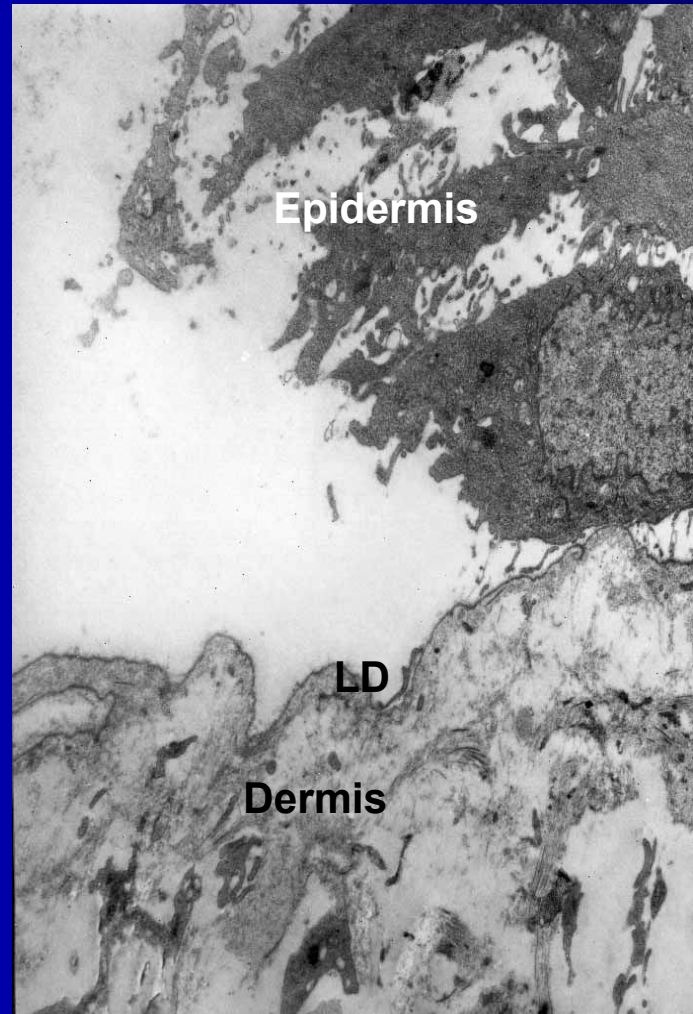
EPIDERMOLYSIS BULLOSA JUNCTIONALIS (n=5)

EBJ Herlitz - 4
EBJ non Herlitz - 1

EBJ Herlitz (letalis)
(all the 4 patients died
before they were 1)



EBJ non Herlitz



Epidermolysis bullosa dystrophica

n=32

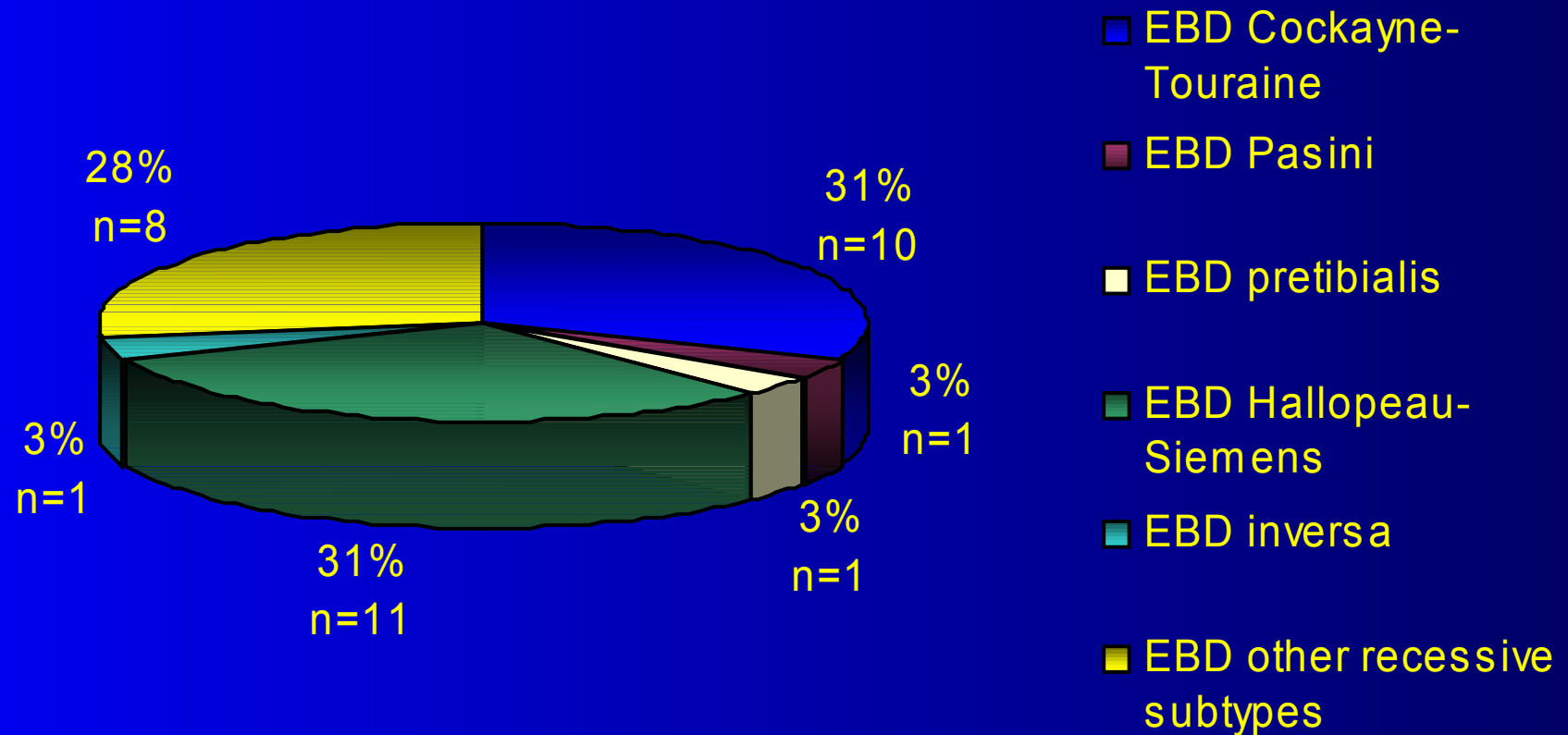
female - 20

male - 12

22 families



Distribution of the patients with EBD by subtypes



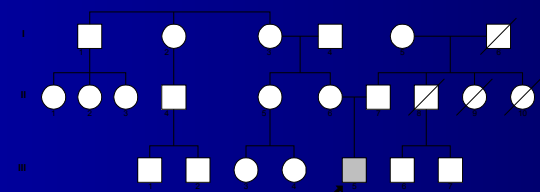


EBD inversa





EBD recesiva
Gastrostomy



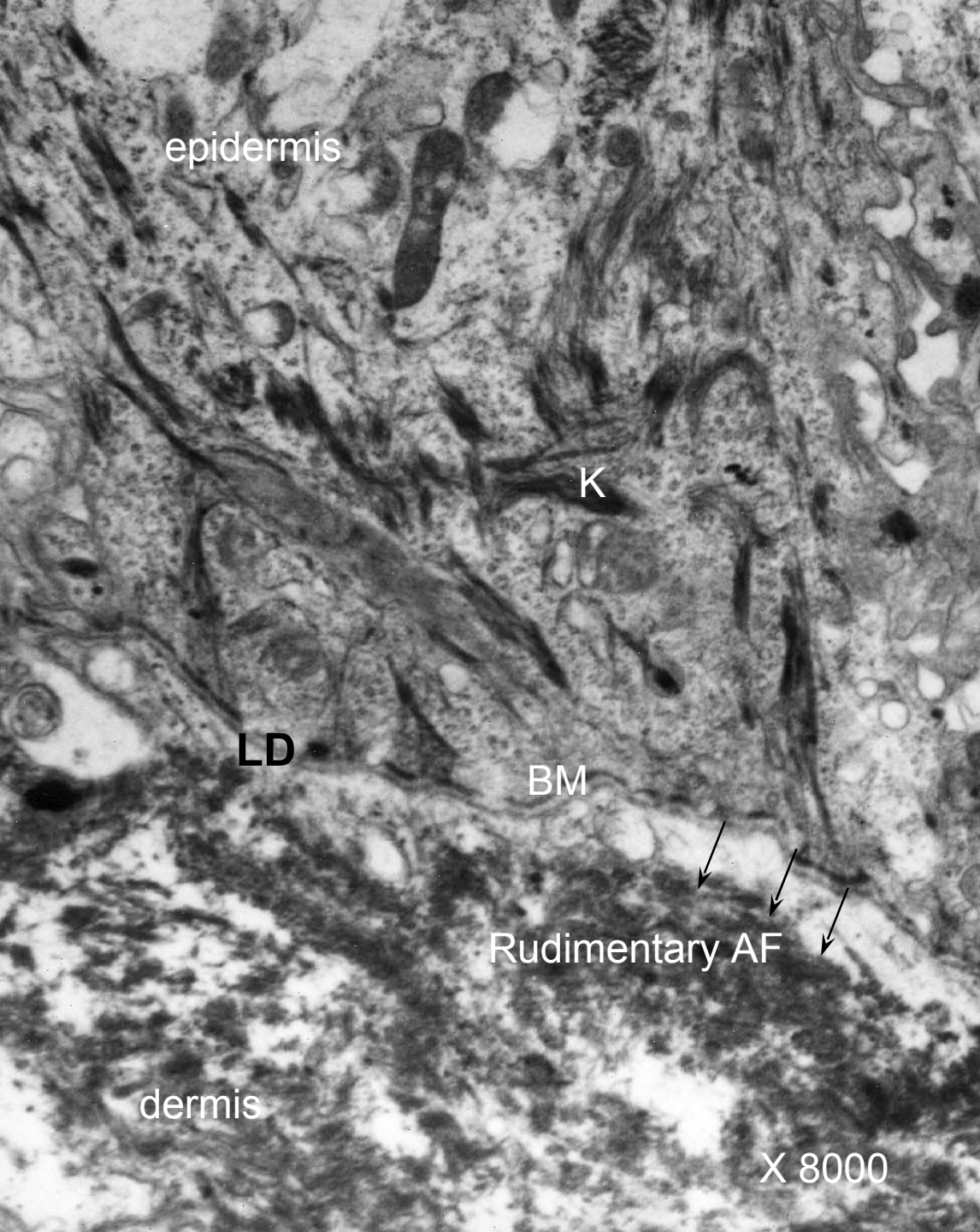
EBD Hallopeau-Siemens

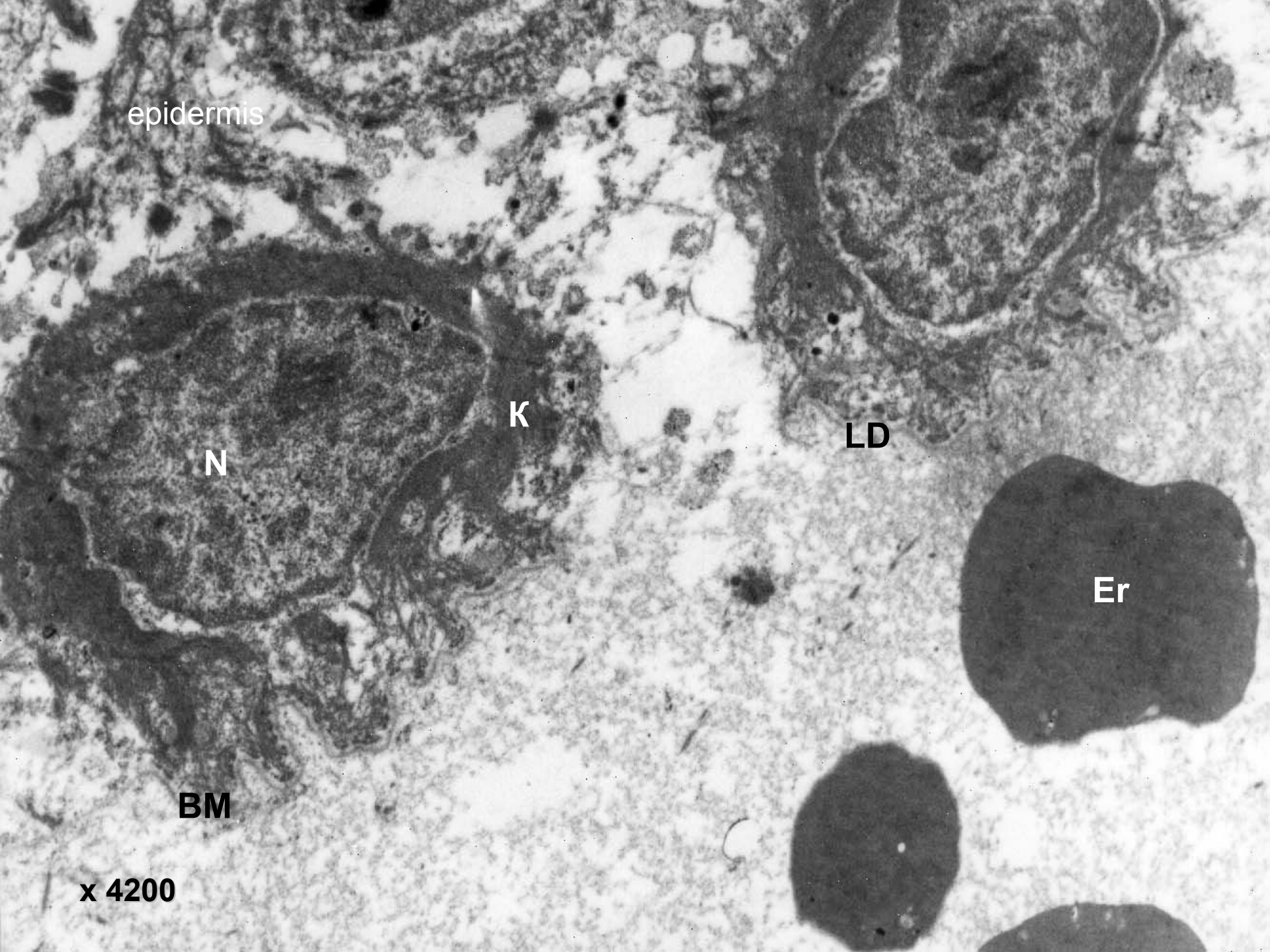


EBD Hallopeau-Siemens
Ca spinocellulare



Ultrastructural examinations in EBD





epidermis

N

K

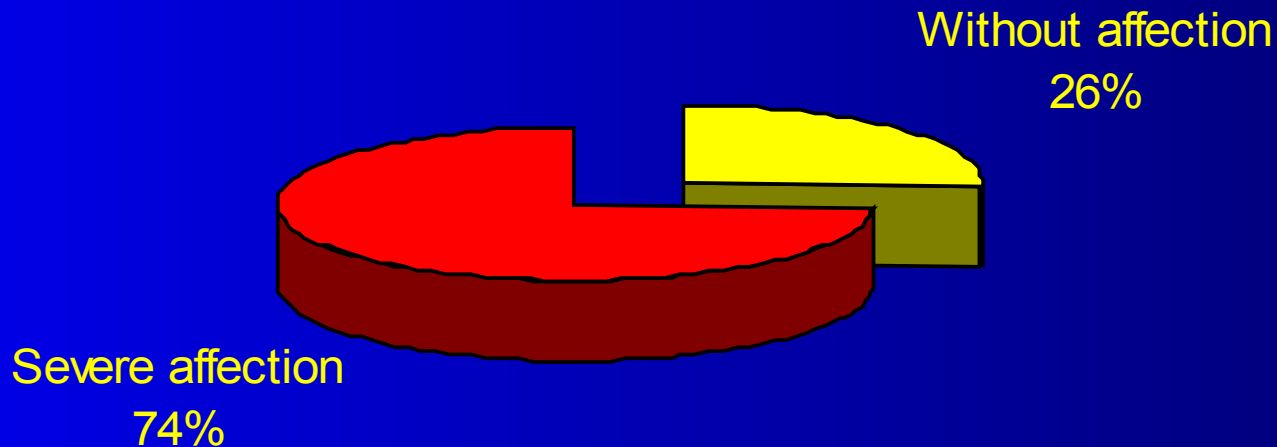
LD

Er

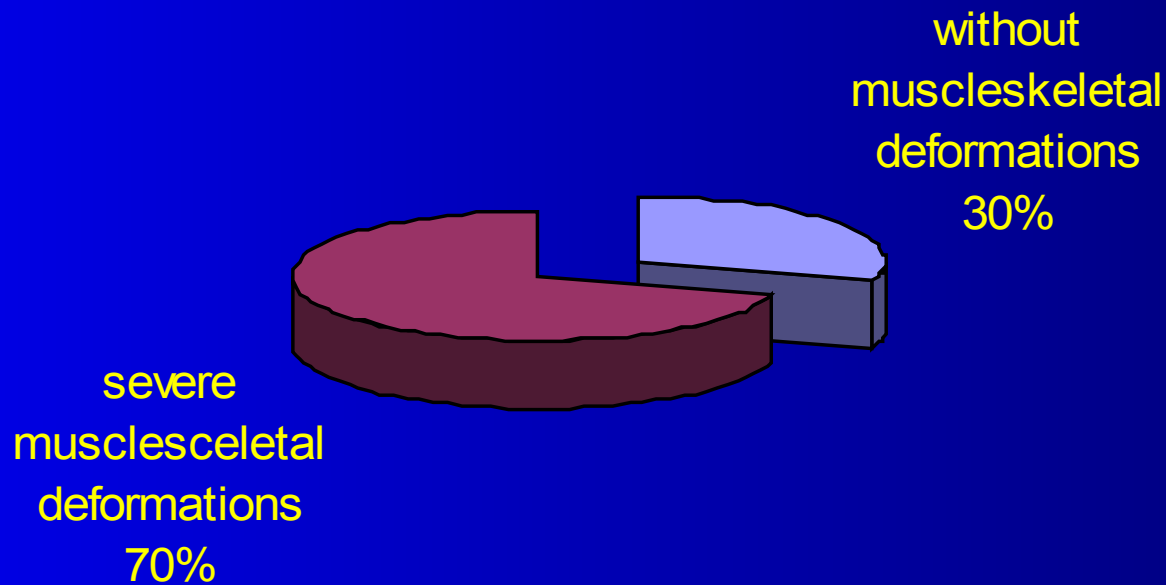
BM

x 4200

Mucous membrane affection in the patients with EBD (mouth, pharynx, esophagus)



Muscleskeletal and joint deformations in the patients with EBD (n=32)



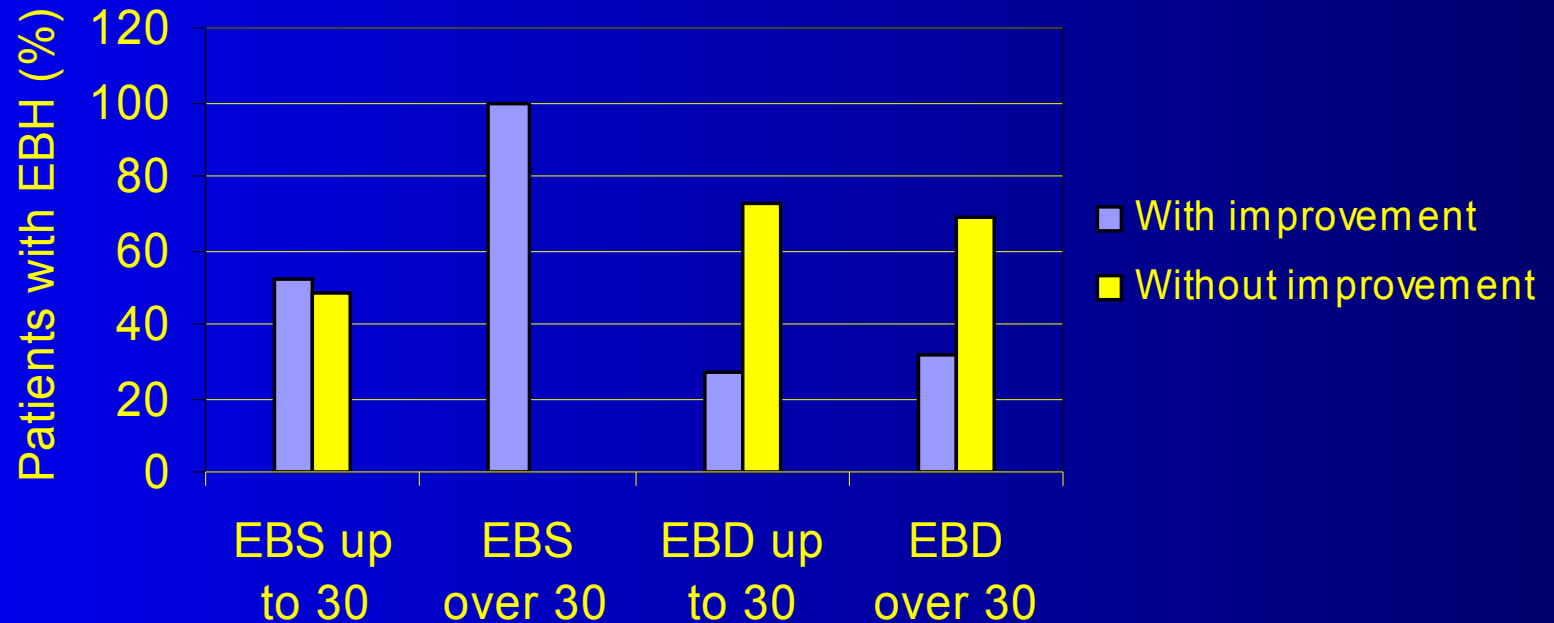
Causes for death of the patients with EBD (1970 -2007)

6 deceased patients with EBD Hallopeau-Siemens:

4 patients - Sepsis

2 patients - Ca spinocellulare

Improvement of the clinical features with age in the patients with EBS and EBD



Book

**“Medical management of the patients with Epidermolysis
bullosa hereditaria”**

(for patients with EB and General Practitioners)

Medical management and health politics; issue 3/2001 –
Medical University Sofia, Center for medical information

- Diagnosis and classification of the disease.
- Genetic consultation.
- Medical care for skin and mucous membranes.
- Nutrition in the different types EB and different ages.
- Diagnostic algorithm for EB.
- Algorithm for wound treatment.
- Prevention of the musculoskeletal and joint deformations by physiotherapy.



Founded:

February 1994,
Department of Dermatology,
Medical University, Pleven

Prof. Mariana Trashlieva

A.E.B.B. – member of a network of organizations for EB in the world
– DEBRA INTERNATIONAL

The aims of A.E.B.B.

- To create a National Register and information Bank for the patients with EB in Bulgaria;
- To support daily necessities of the patients with EB (medicines, dressings and food);
- To prepare information materials for physicians, nurses, patients with EB and their relatives;
- To establish personal contacts between the patients and consolidate the international links with the organizations of EBH individuals in Europe;
- To create favorable conditions for raising, education, professional orientation of the patients with EB.

A.E.B.B.

- <http://www.debrabg.com/>
- Workshops – 2000, 2004, 2005, 2006.
- Relations with ICRDOD – Plovdiv, Bulgaria (2005)
- Member of Alliance of the people with rare diseases – Bulgaria (2007)
- Collaboration with PD Dr. Cristina Has and Prof. Dr. Leena Bruckner-Tuderman EB Center in the Clinic of Dermatology - Freiburg, Germany – DNA mutagen analysis of Bulgarian patients with different forms of EB.

Thank you for your attention!

