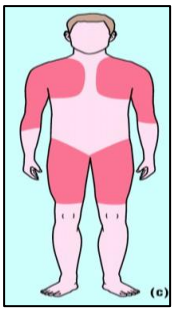
Unit VII – Problem 1 – Biochemistry: The Muscular Dystrophies

- **Definition**: heterogeneous group of genetically determined, primary degenerative myopathy (muscle disease). They are characterized by variable degree of muscle weakness.
- **Classification of muscular dystrophies:**

X-linked recessive	**Example**: Duchenne and Becker
Autosomal dominant	**Examples**: facioscapulohumeral and scapuloperoneal
Autosomal recessive	**Examples**: limb girdle (scapulohumeral) and congenital muscular dystrophy

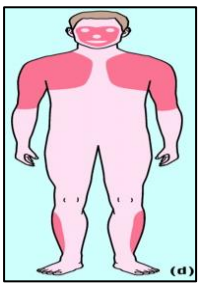
- **Limb-Girdle Muscular Dystrophy (LGMD):**

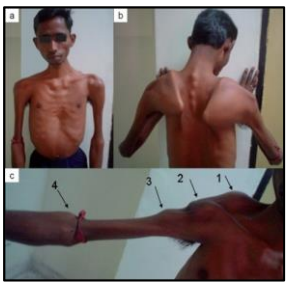


  - It includes at least 10 different inherited disorders.
  - Occurs equally in both sexes (males=females).
  - Initially affects the muscles around the shoulder region and hips **(see the figure)**. Later it may involve other muscles in the body as it is progressive and becoming worse with time. One of the observations is enlargement of calf muscles (although they are not included in the shoulder or hip regions).
  - **It is genetically heterogeneous with both dominant and recessive forms:**
    - ✓ *Autosomal dominant LGMD:*
      - ❖ Shows adult onset.
      - ❖ In addition to muscle weakness, creatine kinase (CK) values are elevated by 4-10 times.
        - Creatine kinase test measures blood levels of certain muscle and brain enzyme proteins. There are 3 isoforms of creatine kinase:

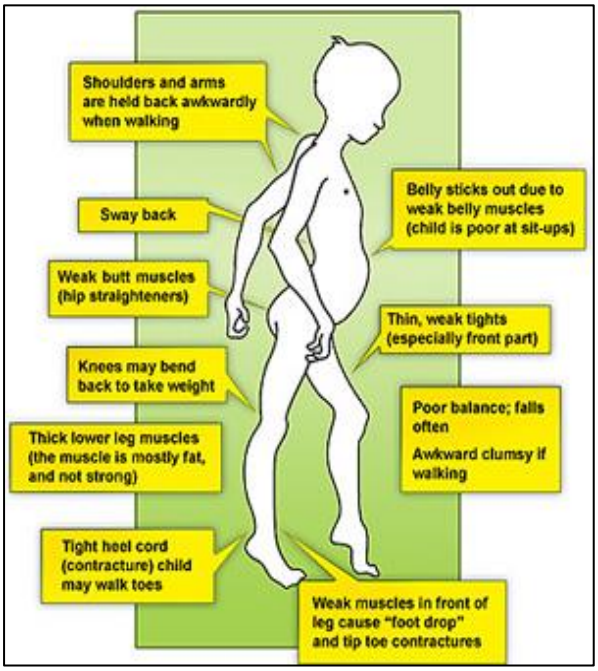
CK-I or BB	In brain & smooth muscles
CK-II or MB	In heart muscle
CK-III or MM	In skeletal muscles

      - ❖ There is no pre-natal or pre-symptomatic testing.
      - ❖ There are different mutation sites on chromosomes: 1,3,5,6 and 7
      - ❖ There are different types of autosomal dominant LGMD: 1A, 1B, 1C and 1D
      - ❖ In addition, there is different age of onset and clinical presentation.
    - ✓ *Autosomal recessive LGMD (more frequent):*
      - ❖ Shows childhood or teen-age onset.
      - ❖ Genes for at least 9 different forms are identified.
      - ❖ Types: 2B, 2C, 2D, 2E and 2F
      - ❖ There are variations according to ethnicity, systemic involvement and rate of progression.
      - ❖ Beta-sarcoglycan complex provides integrity of the muscle. This complex is deficient in autosomal recessive LGMD.
- **Facioscapulohumeral (see the figure)**:





  - It is an autosomal dominant disease in which there is a gene mutation in chromosome 4.
  - It occurs equally in both sexes (males=females) and all age groups.
  - It can be diagnosed by: enzymes – EMG or muscle biopsy.
  - PCR (RFLP) is used for pre-natal and pre-symptomatic diagnosis.
- **Duchenne muscular dystrophy**:
  - Progressive muscle wasting disorder.
  - X-linked recessive (Xp21). The gene size is 2300 kb. The protein product is dystrophine (which is absent in these patients).
  - Clinical features **(figure)**
- **Becker muscular dystrophy**:
  - It is a milder form of Duchenne.



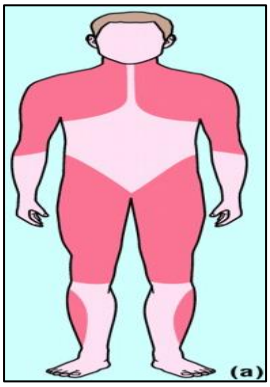


Figure: distribution of muscle weakness in both Duchenne and Becker