### Genetic Diseases in Dogs and Humans

**Duchenne Muscular Dystrophy, Copper Toxicosis, and Narcolepsy**

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### Duchenne Muscular Dystrophy

**Background:** Golden Retriever Muscular Dystrophy (GRMD) in dogs and Duchenne Muscular Dystrophy in humans are characterized by on-going muscle fiber necrosis and regeneration.

**Causes:** X-linked recessive mutation / deletion in DMD gene that encodes for dystrophin, a vital protein for supporting muscle fiber strength and preventing muscle fiber injury.

**Dogs:** RNA processing error from single point mutation → early termination of translation and truncated dystrophin.

**Symptoms:** elevated creatine kinase (CK) levels at birth (indicating abnormal muscle degradation), progressive deterioration of muscles.

**Dogs:** gait abnormalities (*“bunny” shuffle*), muscle atrophy, fibrosis, contractures, cardiomyopathy.

**Humans:** mutations or deletions in DMD gene.

### Copper Toxicosis

**Causes:** X-linked recessive mutation / deletion in copper metabolism genes COMMD1 or ATP7B.

**Dogs:** loss of function mutation in COMMD1.

**Symptoms:** liver inflammation → necrosis → cirrhosis.

**Dogs:** liver most affected. Often no signs initially; differences in severity depending on breed; lethargy, vomiting, icterus, hepatic encephalopathy.

**Humans:** liver, brain, and cornea affected. Kasyer-Fleischer rings in eyes; neurological issues (anxiety, schizophrenia, depression); abnormal serum ceruloplamin concentrations.

**Humans:** muscle fatigue, learning difficulties, loss of mobility, breathing difficulties and heart disease by 20.

### Narcolepsy

**Causes:** Deficit in the hypocretin signaling pathway causing abnormal hypothalamic function.

**Dogs:** Mutation/deletion in Hcrt2 (hypocretin receptor 2) → loss of protein function.

**Humans:** No mutation in gene noted; most likely acquired by destruction of hypocretin synthesizing cells.

**Symptoms:** cataplexy following emotional stimuli, excessive daytime sleepiness, disrupted REM sleep.

**Dogs:** develops between 4 weeks and 6 months.

**Humans:** develops between age of 7-25.

### Treatment

**Dogs:** methoxamine and zinc compounds to inhibit GI absorption of copper, especially for presymptomatic or pregnant patients.

**Humans:** sodium oxybate; tricyclic antidepressants for cataplexy; daytime naps.


**Cell-Based Therapy:** transplant stem cells

**Humans:** physical therapy, insulin-like growth factor, cardiac drugs, corticosteroids, aminoglycoside antibiotics.

**References:**

6. Andrographoliode (AG) in a rat model, copper is stained red (Roy 2011).

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**A** Affected Golden Retriever at (A) 3 months and (B) 6 months (NCIDMD 2014)

**B** Necrotic muscle cells replaced by fibrous and fatty tissue (Pestronk 2013)

**C** Affected child using hands to push body up due to lower limb weakness (Gower’s Sign).

**D** Necrotic muscle cells filled by fibrous and fatty tissue (Pestronk 2013)

**E** Reddish-brown Kayser-Fleischer ring in the right eye (Sullivan 2002)

**F** Catalepsy in a Doberman (Nishino 2007)

**G** Loss of hypocretin cells in humans (Thamnickal 2000)