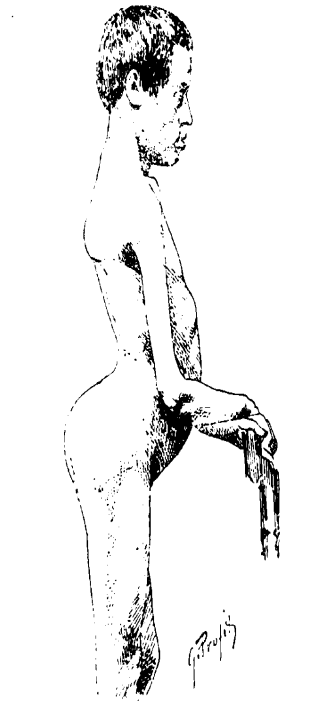
FSHD patients Meeting, Boston, August 15-17 2014



FSHD & NUTRITION

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Neuro**M**uscular **D**isease **S**pecialized **C**enter

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French National FSHD database (www.fshd.fr)

Patients included are:

FSHD1 Patients	FSHD2 / FSHD Like Patients
= Patients genetically confirmed: typical D4Z4 contraction (< 11 Repeats)	= Patients presenting with FSHD phenotype* without the typical D4Z4 contraction (≥ 11 Repeats)

* Typical FSHD Phenotype:

- ✓ Facial weakness
- ✓ Scapular girdle involvement
- ✓ Muscles of anterior leg involvement
- ✓ Asymmetry

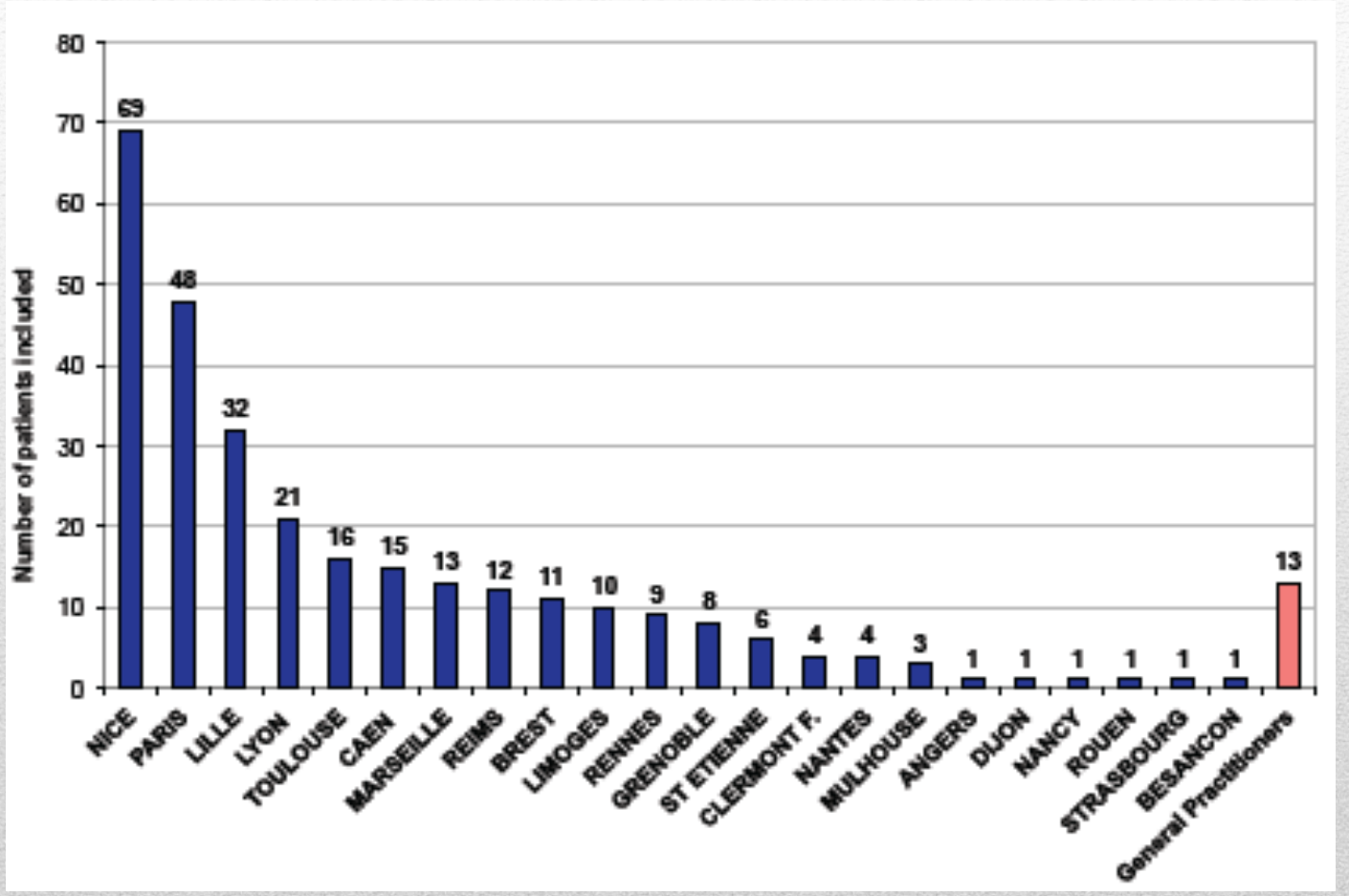
1. All patients must sign an informed consent form.
2. Two options of enrolment:

	FSHD1 patients	FSHD2 / FSHD Like patients
Self-Reported Form *filled by the patient*	YES	NO
Clinical Evaluation Form *filled by the NMD specialized physician*	YES	YES

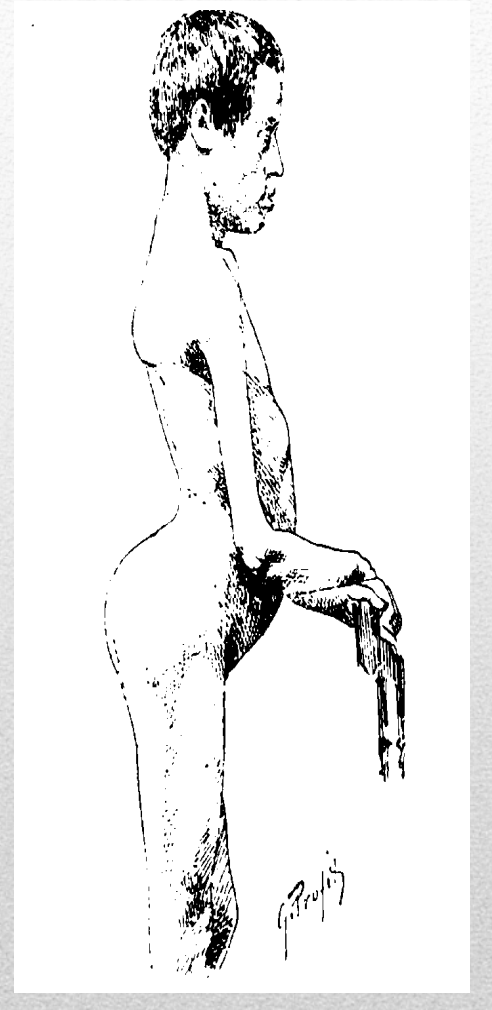
3. Data are entered and validated by clinical and molecular curators.
4. A unique patient identification number (PIN) is generated.
5. Patient and referring physician access to the data thanks to the PIN via the website.

Data content is related to: **genetic diagnosis**, **muscular** and **extra-muscular involvement**, **pain** and **patient care**. A Manual Muscular Testing (MMT) is collected in the Clinical Evaluation Form.

French National FSHD database (www.fshd.fr)



300 patients: 143 women, 157 men, age from 11 to 89, mean age 54.2
95,9% are FSHD1 (1-11 D4Z4 RU); 4,1% are FSHD2/FSHDlike



- ✓ **DYSPHAGIA**

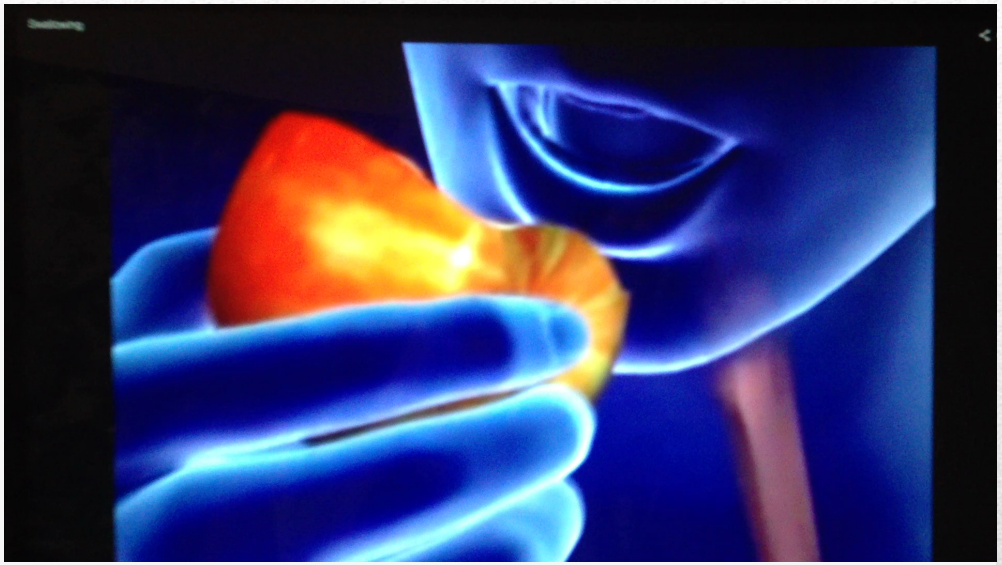
  sensation suggesting difficulty [illegible]assage of solids or liquids from the mouth to the stomach.

- ✓ **WEIGHT**
- ✓ **OSTEOPOROSIS**
- ✓ **DIETARY SUPPLEMENTS**

DYSPHAGIA

Physiology of swallowing

1) Oropharyngeal Phase:



Buccal Phase
Food bolus is **voluntary**
pressed by the tongue up
against the roof of the month
and backwards towards the pharynx

Pharyngeal Phase
Swallowing center
in the medulla initiate
reflexes that prevent food
entry in respiratory pathways.

- **Uvula contraction** closes the nasal passages
- **Laryngeal muscles contraction** closes the glottis on the top of trachea and epiglottis covers closed glottis. The respiration is temporalely inhibited.
- The **Upper Esophageal Sphinter** relaxes and pharyngeal contraction drives the bolus into esophagus

2) Esophageal Phase:

- **Primary ways of perilstalsis** initiated by swallowing center pushes the bolus throught the oesophagus.
- The **Lower Esophageal Sphyncter** relaxes allowing entering of the food into the stomach

DYSPHAGIA

Introduction and classification

Dysphagia : sensation suggesting difficulty in the passage of solids or liquids from the mouth to the stomach.

Dysphagia is classified into **three major types**:

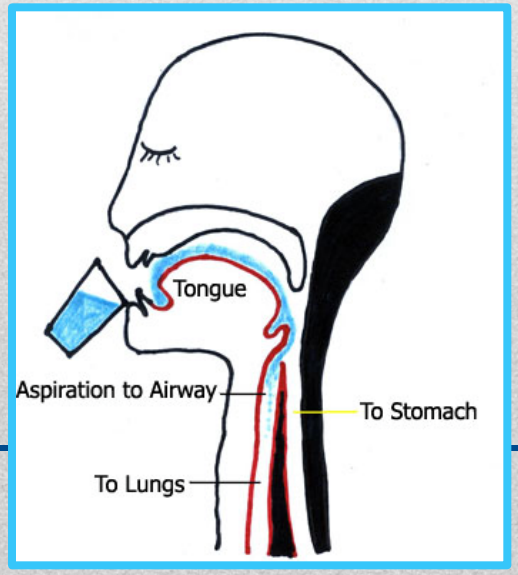
- **Oropharyngeal dysphagia**
  - ✓ inability to control food or saliva in the mouth,
  - ✓ difficulty initiating a swallow,
  - ✓ gurgly or wet voice after swallowing, nasal regurgitation,
  - ✓ coughing, choking, frequent pneumonia, unexplained weight loss.
- **Esophageal dysphagia**
  - ✓ inability to swallow **solid food**, which the patient will describe as 'becoming stuck' or 'held up' before it passes into the stomach;
  - ✓ **Achalasia**: difficulty in **swallowing fluids** due to peristaltic failure throughout esophagus length.
- **Functional dysphagia**

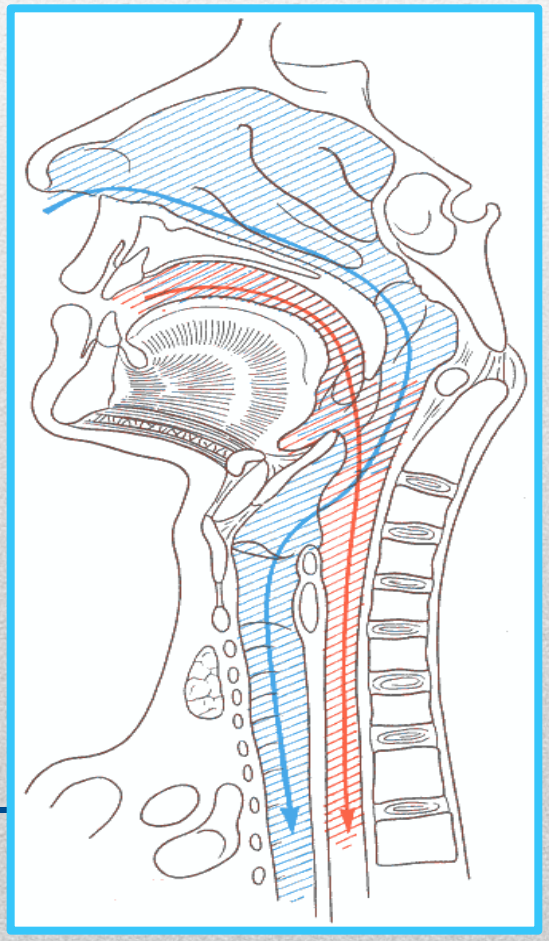
✓ No organic cause found, paraclinical examination normal.

Consequences of dysphagia

Crossing of respiratory and digestive pathways:
risk of food being ingested into the bronchial system (pulmonary aspiration):

- **choking**
- **aspiration pneumonia**
- **dehydration, malnutrition**





DYSPHAGIA and FSHD

***Table 2** Results of videofluoroscopic evaluation, DOSS score, and MRI of the tongue*

Pt	Problems with oral transit	Pharyngeal delay	Laryngeal penetration/ aspiration	Problems with pharyngeal transport and compensations*	Pharyngeal residue	DOSS score	Tongue volume, cm^3†
1	No	No	Once/aspiration, with cough	Reduced tongue base retraction, Extended pharyngeal transit/laryngeal elevation *(m), Multiple swallows to clear the pharynx*	Yes (sc)	4	131.3
2	Piecemeal deglutition	Yes‡	No	Reduced tongue base retraction, Multiple swallows to clear pharyngeal residue*	Yes (sc)	5	117.8
3	Piecemeal deglutition	No	No	Slight struggle with pharyngeal transit	No	5	66.2
4	Piecemeal deglutition	Yes‡	No	Reduced tongue base retraction, Slight struggle with pharyngeal transit	Yes (sc)	5	103.5
5	Piecemeal deglutition	Yes‡	No	Moving head backward to facilitate bolus transit through the pharynx*	No	5	63.2
6	Piecemeal deglutition	No	No	Extended laryngeal elevation to facilitate pharyngeal transit *(m)	No	5	106.8
7	No	No	No	Impaired esophageal transit	No	7	Na
8	Piecemeal deglutition	Yes‡	Once aspiration, with cough	Reduced tongue base retraction	No	5	89.8

Wohlgemuth, Neurology 2006

DYSPHAGIA and FSHD

20 FSHD1 patients genetically confirmed
12M, 8W, mean age 38.1, mean disease duration 16.7
8 patients (**40%**) complain of dysphagia: 5 oropharyngeal, 3 esophageal

Patient	Age (years)	Sex	Disease duration (years)	AMS (/10)	Dysphagia	CXR	Radiology	Manometry
1	19	M	5	8.5				
2	22	M	4	8.7		+		
3	26	F	7	9.1	+	+	+	
4	27	M	5	8.3				+
5	29	F	10	7.9		+		
6	29	F	7	7.7	+		+	
7	31	M	6	8.4				
8	34	M	14	7.1		+		
9	35	M	9	8.6				
10	38	F	17	8.3	+		+	
11	39	M	20	7.7	+			+
12	39	M	14	7.5				
13	42	F	25	6.9	+	+	+	
14	43	F	18	7.5				
15	45	M	22	8.1				
16	45	F	26	7.0	+			
17	47	M	20	7.4		+	+	
18	53	M	34	6.7	+			+
19	57	M	31	7.1				
20	61	F	39	6.2	+	+	+	

- 2 patients with **ineffectual pharyngeal contraction**
- 2 patients with **cricopharyngeal and upper esophageal relaxation**
- **2 patients with pharyngeal (Zenker's) diverticula**
- 1 patient with difficulty in **primary perilstalsis**

Dysphagia in FSHD1 may be due to **heterogeneous causes**

Stubgen, Dysphagia 2008

DYSPHAGIA and FSHD

French National FSHD database (www.fshd.fr)

- **Most of the** patients with dysphagia have **facial weakness** (*orbicularis oculi and orbicularis oris*)
- **Some of them also** have **dysarthria**
- **Few of them** have **tongue atrophy**

Complications:

- **Weight loss: frequent**
- **Aspiration pneumonia: less frequent**
- **Chocking to death: rare** but dangerous

INFANTILE FORM of FSHD

Multisystemic involvement, early onset, rapid progression

- Early onset < 10 Y
- Symmetric muscular weakness and atrophy
- **Loss of ambulation**
- Marked hyperlordosis,
- *pectus excavatum*
- **Swallowing problems**
- **Tongue atrophy**
- **Weight loss**
- Restrictive respiratory insufficiency

Chen et al, 2014

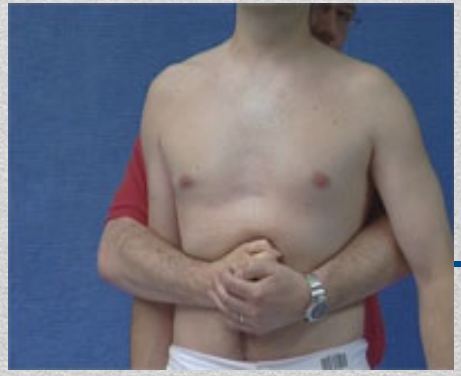
Speech Therapy and Diet

Swallowing therapy:

- ✓ **Swallowing exercises**
- ✓ Support during meals and first aid for choking

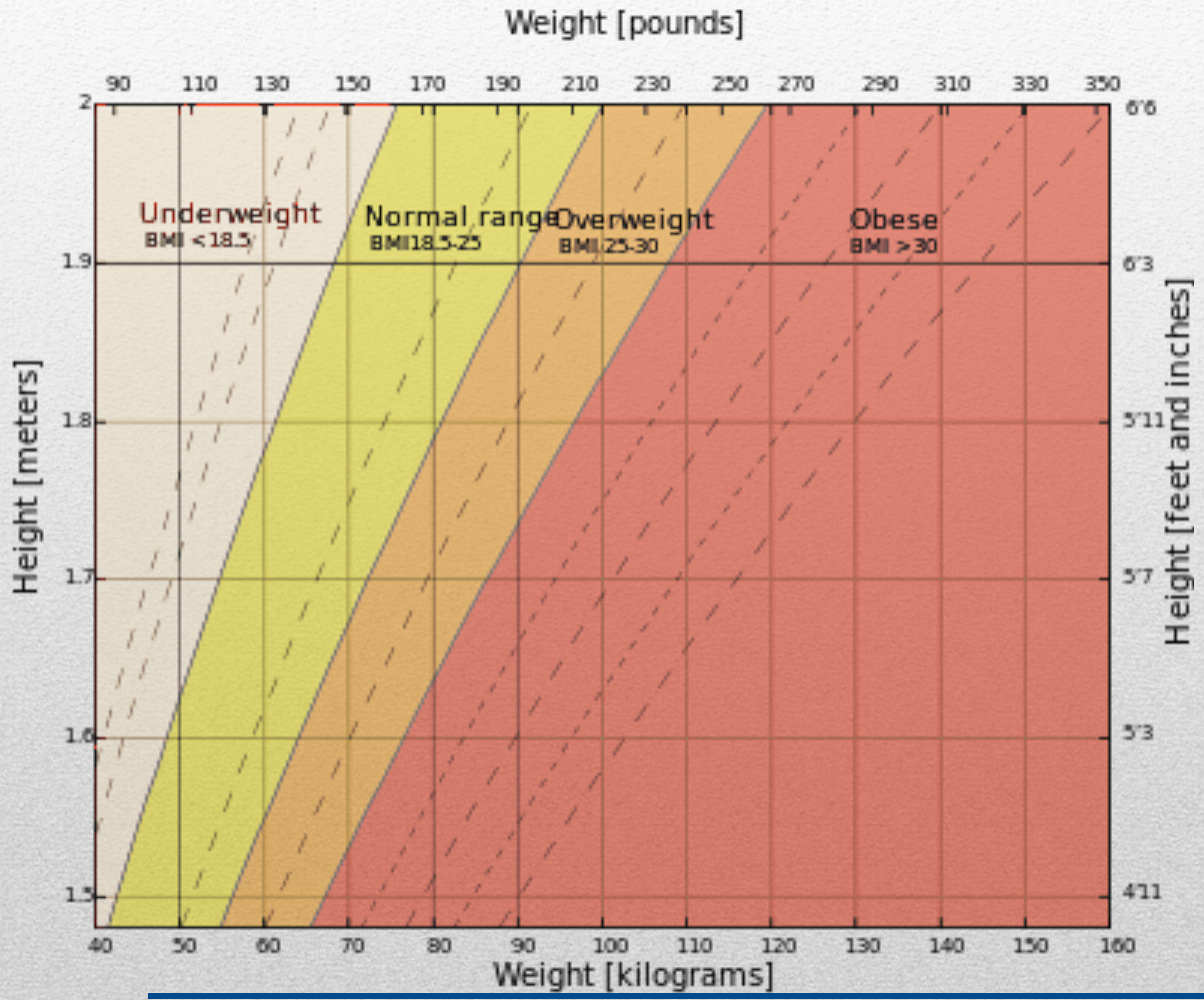
Dietary changes: insure correct caloric intake and hydration, have a balanced diet and respect patient quality of life and safety

Feeding tubes: percutaneous endoscopic gastrostomy only in case of severe malnutrition



FSHD and weight

Body Mass Index (weight in kilograms divided by height squared in meters)



BMI Limits:

- Underestimate fat in older patients and in patients having muscle atrophy
- Different values for children

FSHD and weight

French National FSHD database (www.fshd.fr)

N patients available= 284

Underweight seems to be more frequent in infantile onset patients, while classical and late onset are more in overweight

Low and high BMIs seem to be detrimental for patients

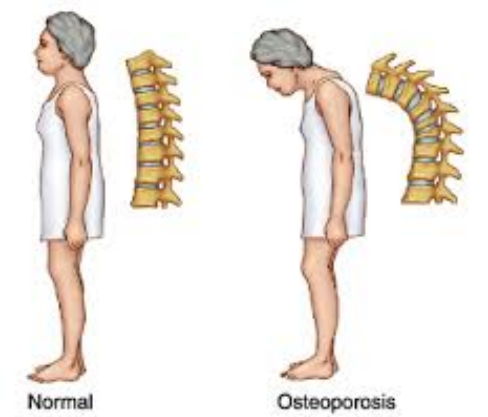
Statin may increase muscle pain and CK values in FSHD patients

Wheelchair bounded patients seem to have higher risk of osteoporosis/ osteopenia

FSHD and Osteoporosis

Risk factors that **we found statistically associated to osteoporosis/osteopenia development are**:

- Loss and reduced ambulation
- Low Vitamin D3 level
- Post menopause
- Low BMI (<18)



RECCOMANDATIONS from ESCEO:

- **Adequate dietary protein**
  (1.0-1.2g/kg body weight/d, 20-25g of high quality protein each meal)
- **Adequate vitamin D intake at 800IU/d**
  (serum 25-hydroxyvitamin D levels >50nmol/L)
- **Adequate calcium intake of 1000mg/d**
- **Regular physical activity/aerobic exercise** when possible
- **Hormone replacement therapy** when appropriate

Rizzoli et al, Maturitas 2014

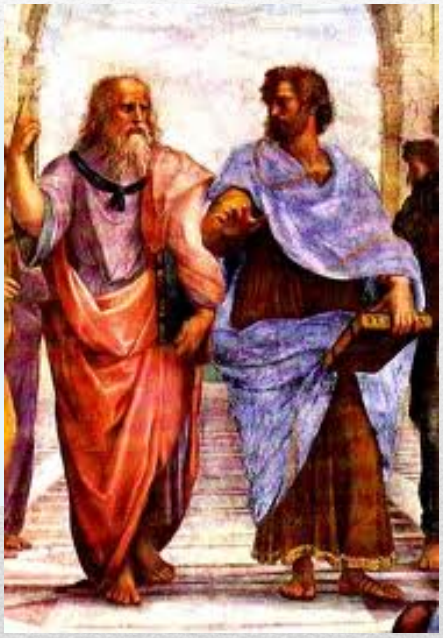
FSHD and dietary supplements

In a survey conducted in our center on 72 FSHD patients **32 patients commonly use auto-prescribed dietary supplements** including: vitamin E, vitamin B6 and B12, vitamin C, folate, green tea extract, coenzyme Q10, zinc, melatonin, and creatine, among many others.

Be cautious about taking dietary supplements or giving them to a child. They may have side effects or interfere with others therapies!!!

In medio stat virtus

Aristoteles, Nicomachean Ethics



Inserm

AFM
Association Française contre les Myopathies

cnrs
dépasser les frontières

IRCAN

Thank you for your attention !!