

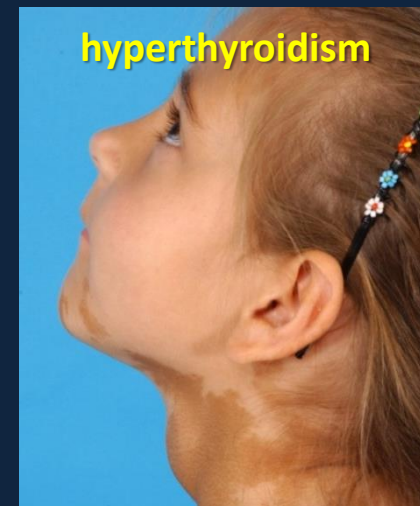


Management of Pediatric Fibrous Dysplasia/McCune-Albright Syndrome

Alison Boyce, MD

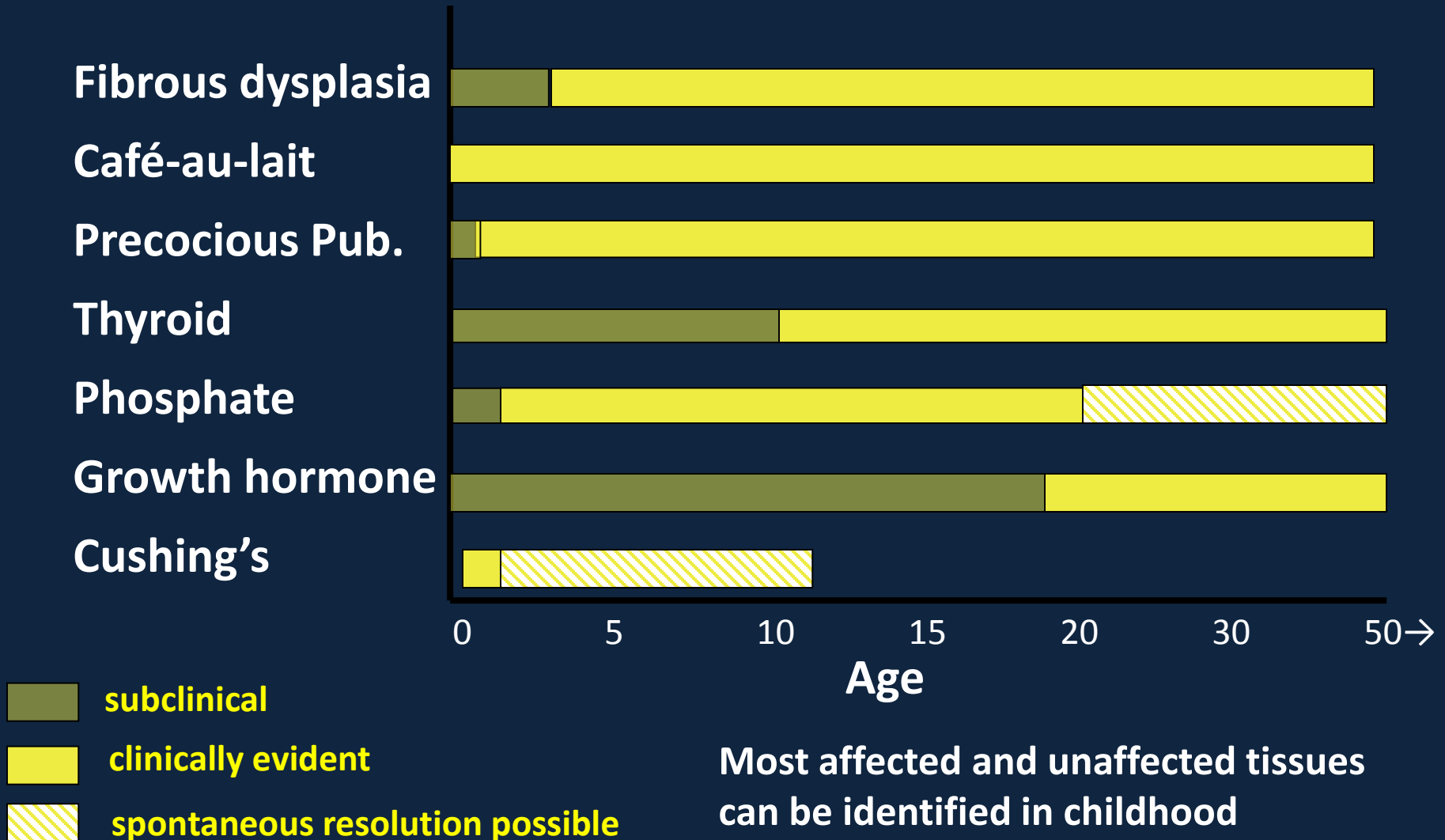
3rd Meeting of the FD/MAS International Consortium
Leiden University Medical Center, Leiden, The
Netherlands

Fibrous Dysplasia/McCune-Albright syndrome: A complex bone and endocrine disorder



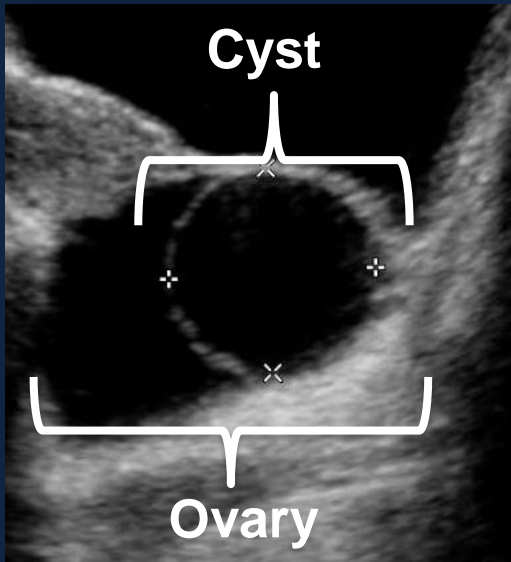
Bone, pituitary, gonads, thyroid, adrenal, other

Onset of manifestations of affected tissues



Most affected and unaffected tissues can be identified in childhood

Precocious Puberty in MAS



ovarian cysts



- Recurrent ovarian cysts
- Breast development, growth acceleration
- Vaginal bleeding when cysts resolve

Precocious Puberty in MAS



Estrogen causes early closure of growth plates

Treatment is needed to:

- Prevent disabling short stature in adulthood
- Prevent psychosocial consequences of early sexual maturation

AVOID SURGERY

Current Treatment Options

Tamoxifen (Eugster et al, 2003)

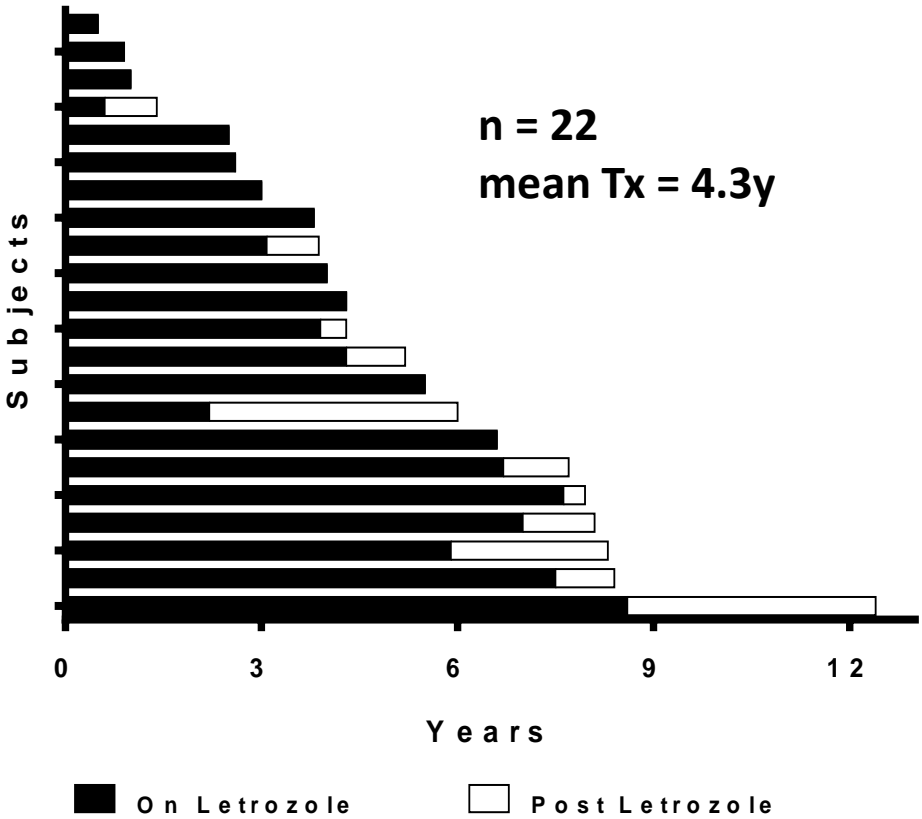
- Alters estrogen receptor activity
- 12 month prospective trial, 25 girls with MAS
 - Decreased: linear growth, bone age advancement and vaginal bleeding
 - increased: uterine volume

Letrozole (Feuillan et al, 2007)

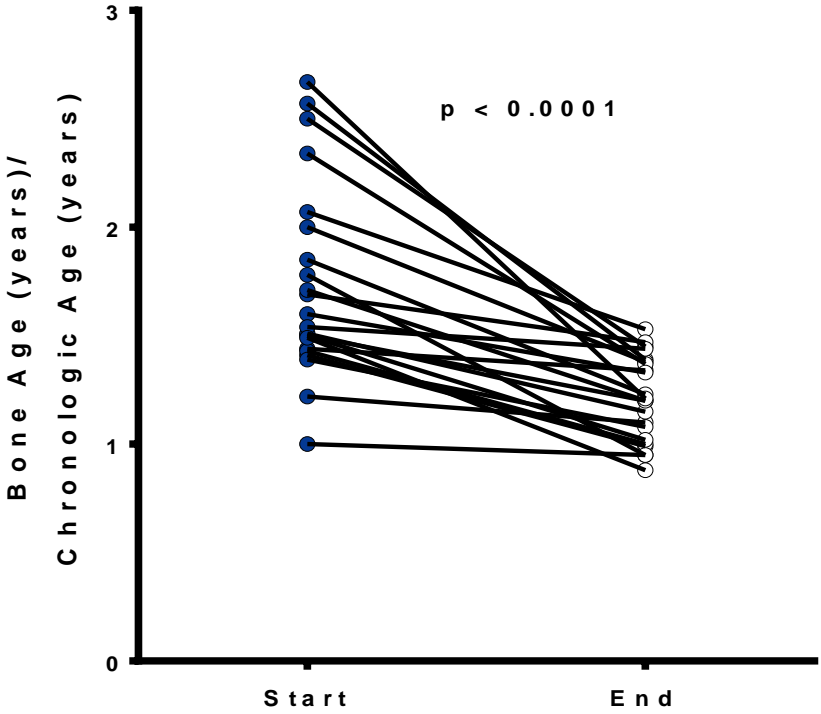
- Prevent estrogen production
- 36 month pilot study, 9 girls with MAS
 - decrease: growth rate, bone age advancement and vaginal bleeding
 - one case of ovarian torsion

Extended efficacy of letrozole in NIH cohort

length of treatment



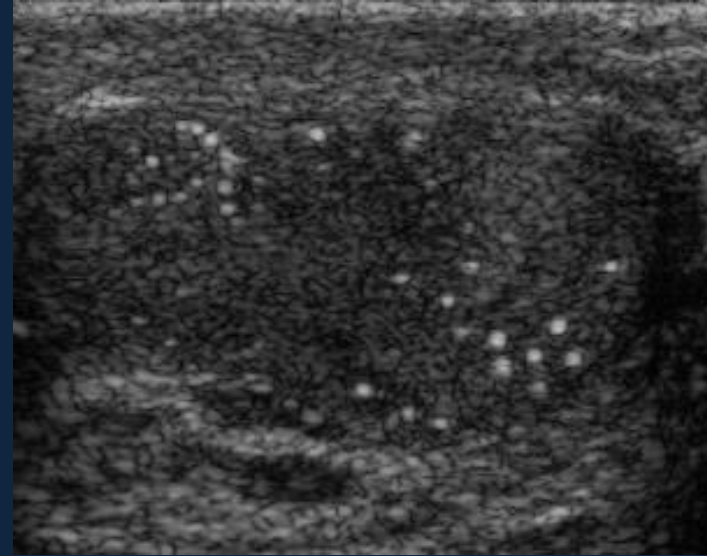
bone age advancement



MAS Testicular Disease



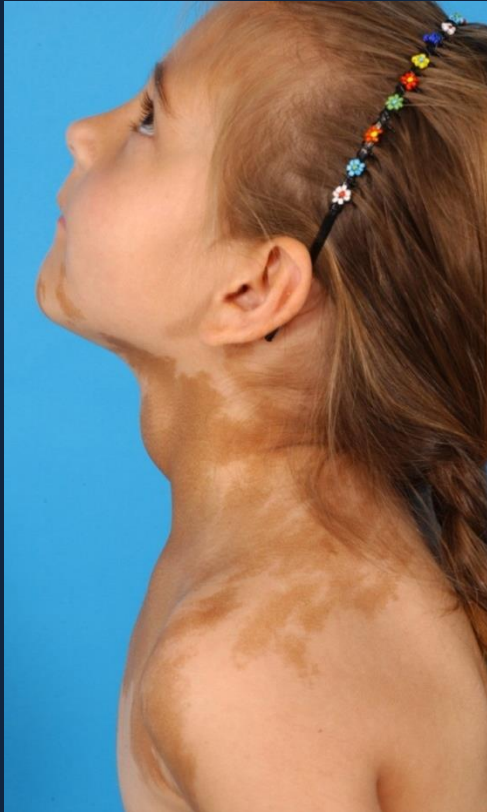
Leydig cell hyperplasia



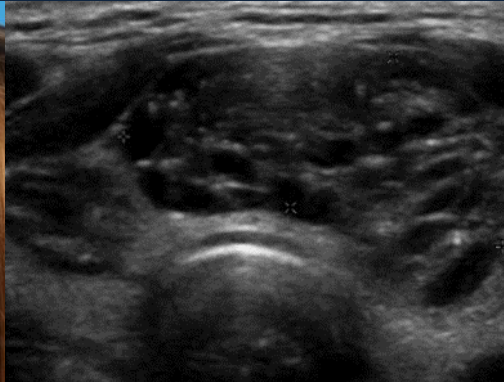
Leydig cell hyperplasia with Sertoli component

- Testicular lesions in ~85%
- Precocious puberty in ~15%
- Treatment: Spironolactone + letrozole
 - NO SURGERY!
- Cancer has been rarely reported
 - Ongoing monitoring

Thyroid Disease in MAS



goiter



characteristic ultrasound

- US abnormalities in ~66%; hyperthyroidism in ~30%
- T3 overproduction; increased T3/T4 ratio (>20)
- Kids with US abnormalities may develop hyperthyroidism later

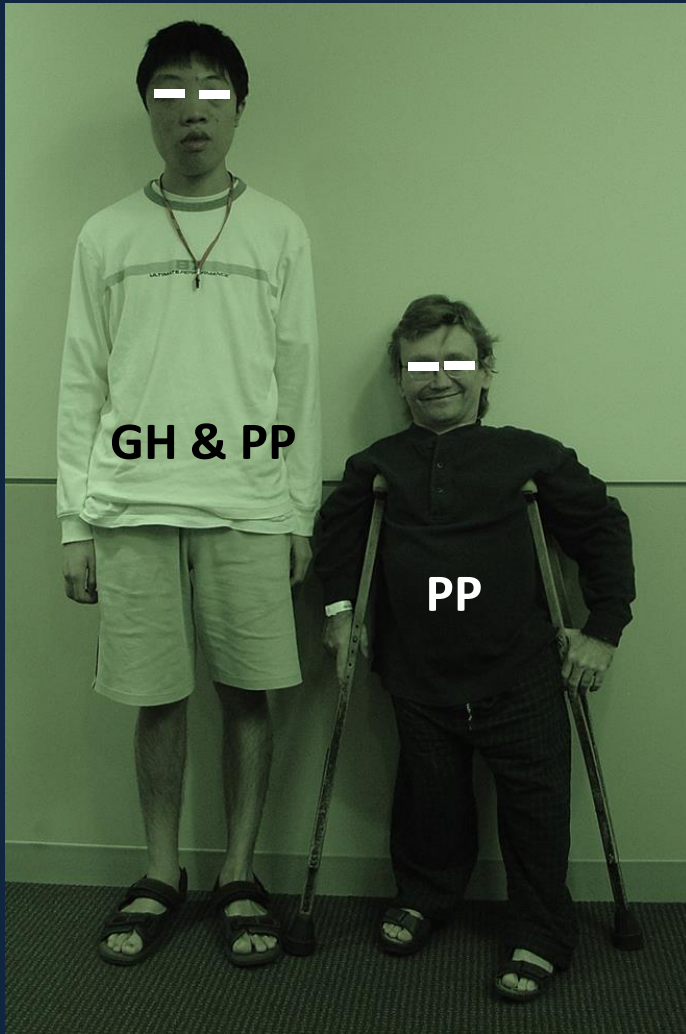
Thyroid Disease in MAS

Management

- Short-term: methimazole
- Long-term:
 - Surgery
 - prefer high-volume center
 - May regrow
 - Radioactive iodine
 - cancer reported

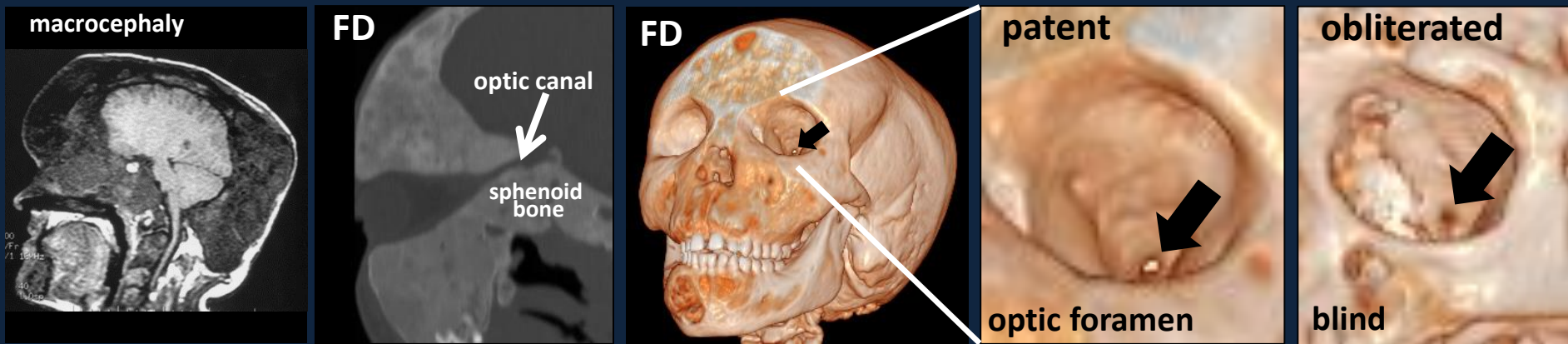


Growth Hormone Excess



- ~15% of patients
- Growth acceleration may be subtle, confounded by FD & endocrinopathies

GH excess: deformity and vision loss



Prophylactic optic nerve decompression is not indicated

Lee, NEJM, 2002 (n=38)



Watchful waiting is superior to surgery (meta-analysis)

Amit, PLoS ONE 2011



GH excess is a risk factors for vision loss

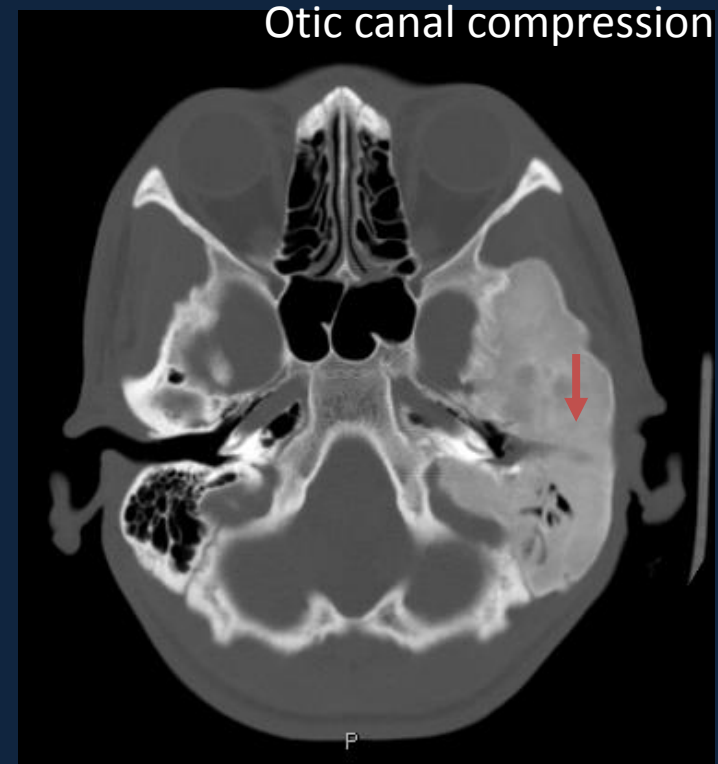
Cutler, Neurosurgery, 2006



Early GH excess treatment prevents morbidity

Boyce...Collins, JCEM 2013 (n=129)

GH excess management issues: macrocephaly, vision & hearing loss



Treatment:

- medication (octreotide, lanreotide, pegvisomant)
- surgery (hypophsectomy, always difficult)
- radiation (cancer risk)

Cushing's syndrome



- Presents age <1 year
- Early recognition is essential!
- Adrenalectomy if possible
- Caveat: spontaneous resolution in ~1/3
- Neurodevelopmental sequelae



Phosphate Wasting in FD

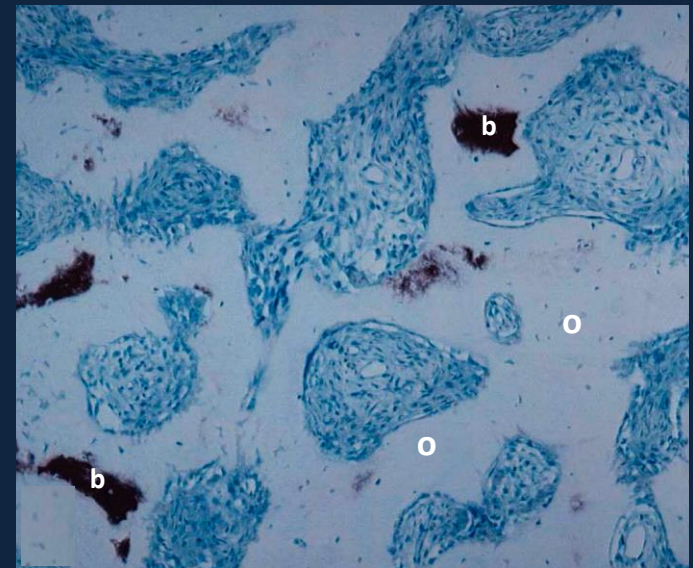
Low Blood Phosphorus



FD + rickets



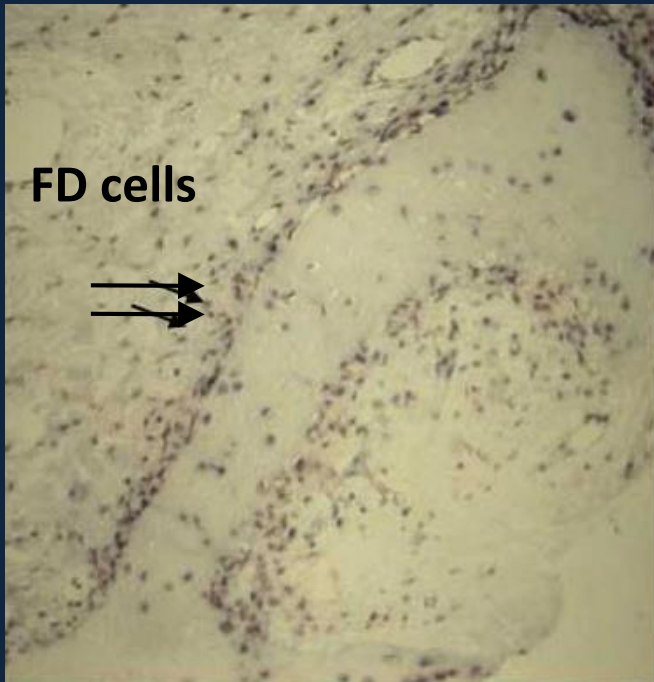
Osteomalacia, Bone Pain



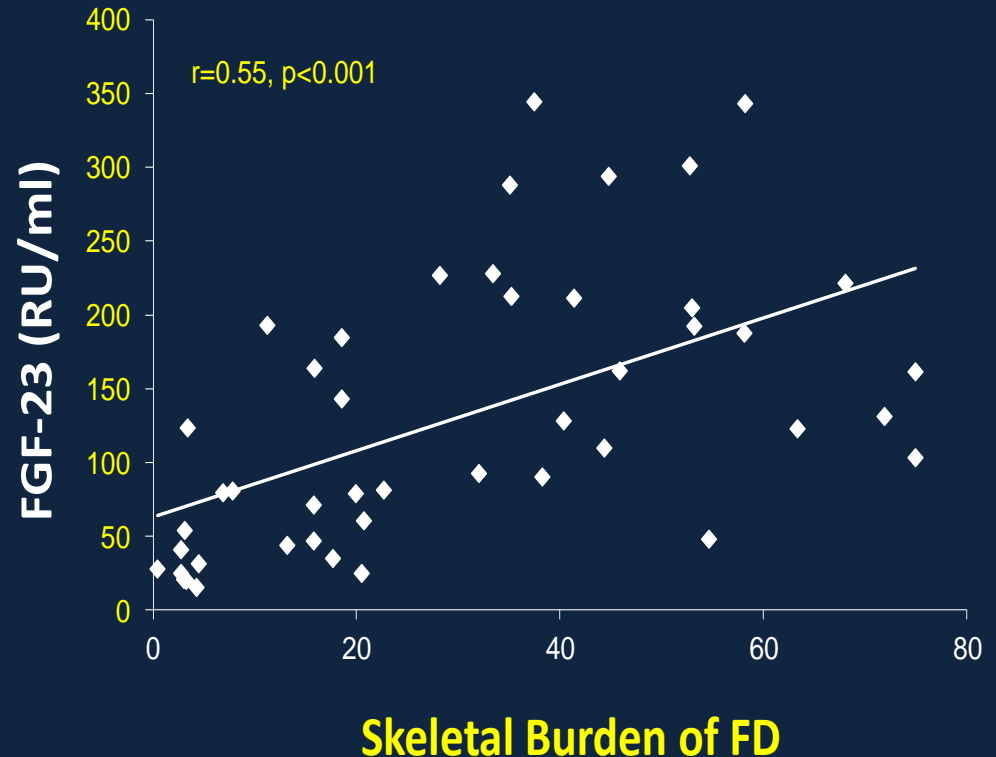
o = osteoid b = bone

FGF23 is a Hormone that Causes Phosphate Wasting in FD

FGF23 is made by FD cells

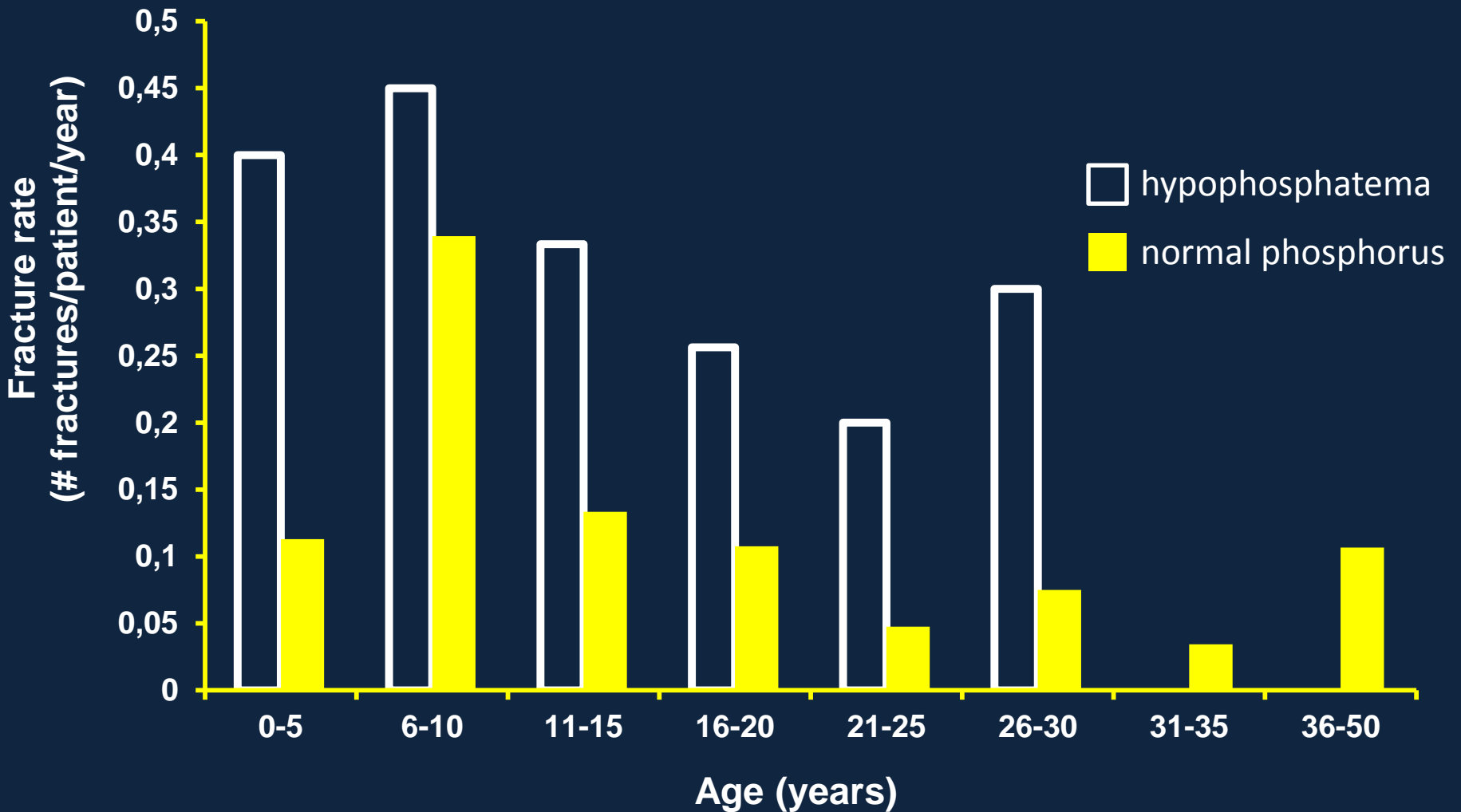


More FD = More FGF23



May show up during times of rapid growth (ex: infancy, puberty)
May resolve in adulthood

Hypophosphatemia Increases Fractures



(Leet ,JBMR, 2004)

Hypophosphatemia: Treatment

1. Phosphorus Supplements

- Pills, powder, or liquid
- Short-acting, must give 3-5 times a day
- Diarrhea, GI discomfort

2. Calcitriol

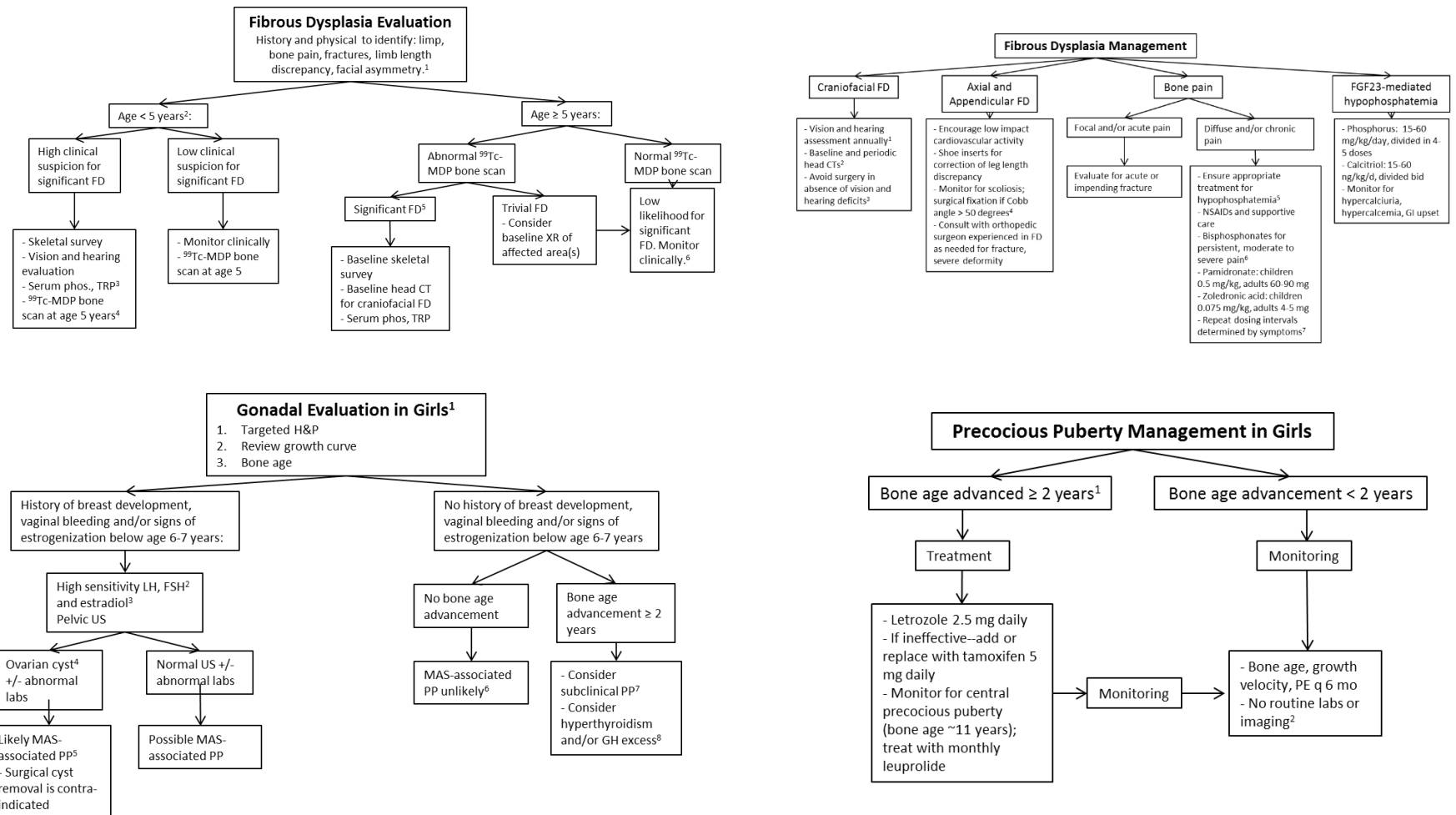
- Prevents hyperparathyroidism (major side effect of Phosphorus supplements)
- May increase urine calcium
 - Monitor urines and kidney ultrasounds



Fibrous Dysplasia/McCune-Albright Syndrome

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Questions?

