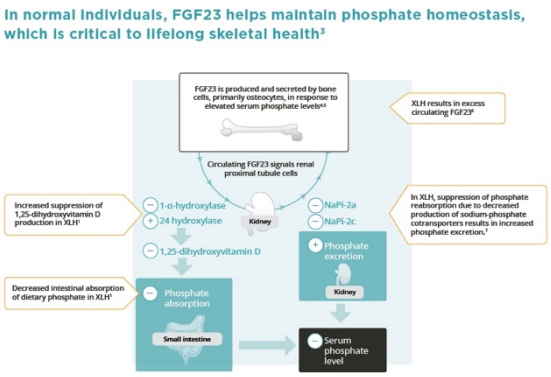
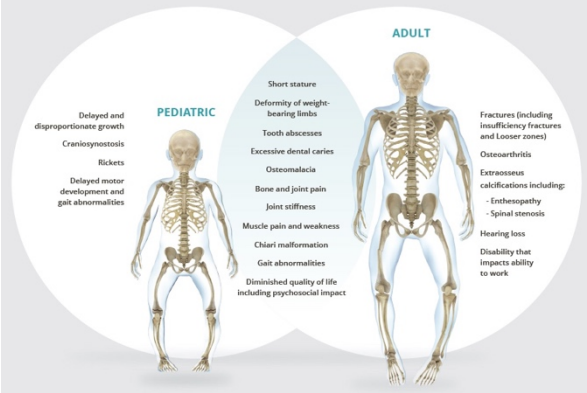
David Julian

Claim	Annotation
X-linked hypophosphatemia (XLH) is a progressive, chronic, skeletal disorder	Martin 2012_p70/para4 Martin 2012_p71/para3/ln14-18 Carpenter 2011_p1382/col2/para2
XLH is characterized by renal phosphate wasting, which is caused by excess fibroblast growth factor 23 (FGF23) production.	Martin 2012_p70/para4 Martin 2012_p71/para3/ln14-18 Carpenter 2011_p1382/col2/para2
In normal individuals, FGF23 helps maintain phosphate homeostasis, which is critical to lifelong skeletal health	Penido 2012_p2041/col1/para1 Penido 2012_p2040/col1/para1/ln2-6
 **Chart callouts:** • FGF23 is produced and secreted by bone cells, primarily osteocytes, in response to elevated serum phosphate levels • Increased suppression of 1,25-dihydroxyvitamin D production in XLH • Decreased intestinal absorption of dietary phosphate in XLH • XLH results in excess circulating FGF23 • In XLH, suppression of phosphate reabsorption due to decreased production of sodium-phosphate cotransporters, results in increased phosphate excretion	• Riminucci 2003_p687/col2/para2/ln6-10 Riminucci 2003_p688/col1/para1/ln1-6 Ferrari 2005_p1522/col2/para2/ln4-5 • Martin 2012_p78/para2/ln5-9 Martin 2012_p79/para1/ln1-4 • Martin 2012_p78/para2/ln5-9 Martin 2012_p79/para1/ln1-4 • Che Euro J Endocrin 2016_p1/col1/para1 • Gattineni 2009_pF282/col1/para1/ln4-9
In patients with XLH, excess FGF23 leads to chronic hypophosphatemia caused by • Renal phosphate wasting • Decreased intestinal absorption of phosphate	Ruppe 2017_p2/para8 Carpenter 2011_p1382/col1/para3 Carpenter 2011_p1382/col2/para2 Penido 2012_p2041/col1/para1
This leads to the skeletal manifestations of XLH	Pettifor 2008_p494/col2/para4 Pettifor 2008_p495/col1/para1/ln1-7
The consequences of XLH have a sustained impact on skeletal health	Carpenter 2014_p13/para2 Carpenter 2014_p14/para2 Carpenter 2014_p14/para3/ln8-12 Carpenter 2014_p15/para1
	MSL Deck_p17 **Specifically for "disproportionate growth"** Zivicnjak Ped Nephrol 2011/p228/col1/para1/ln3-7 **Specifically for "delayed motor development"** Che Euro J Endo 2016/p1/col2/para1/ln1-4 **Specifically for "Excessive dental carries"** CO-083266 OPTIUM Survey ADULT TABLES_01Mar2016/p5/Table4 **Specifically for Fractures (including insufficiency)** Linglart Endo Connect 2014/p10/col1/para1/ln10-11 **Specifically for Fractures and Looser zones** Pseudofractures and looser zones:

	https://radiopaedia.org/articles/looser-zones-1 **Specifically for Osteoarthritis** Che Euro J Endocrin 2016/p326/col1/para2/ Linglart Endo Connect 2014/pg9/col2/para3
Clinical manifestations in adults with XLH arise as a result of unresolved complications of XLH during childhood and/or ongoing, active disease.	Linglart_Endocr Connect_2014_pg8/col2/para1/ln7-8 Skrinar_ENDO 2015_Poster SAT-244/Conclusion