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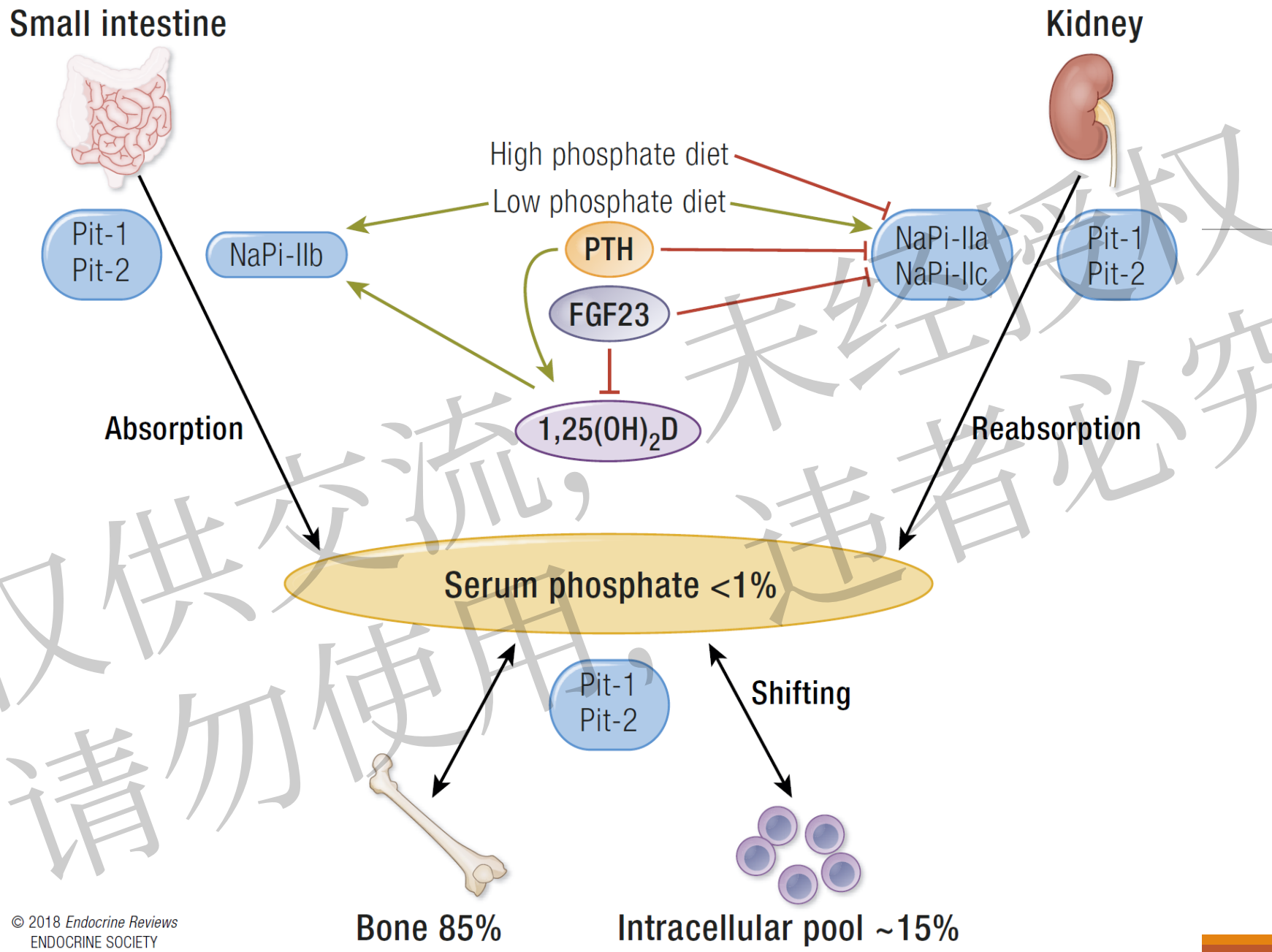
遗传性低磷性佝偻病的展望

Functions of Phosphate in the Human Body

Component	Compound	Function
Bone, tooth	Hydroxyapatite	Tissue structure
Cell membrane	Phospholipids	Cell structure
		Cellular signaling
Nucleus	Nucleic acids (DNA, RNA)	Molecular structure
		Genetic information
Intracellular space	High-energy phosphate compounds (*e.g.*, ATP, ADP)	Metabolism
	Coenzymes	Cellular signaling
	Substrate for kinase and phosphatase	Cellular signaling
Extracellular fluid	Phosphate ion (*e.g.*, HPO_4^{2-}, $H_2PO_4^-$)	Buffer
		Regulation of calcification



磷酸盐吸收是通过血清磷，PTH和1,25-维生素D之间的相互作用来控制

磷酸盐摄入量约为20毫克/千克/天，但磷的净吸收量低于总摄入量的64%

通过扩散和活性，肠道磷酸盐吸收是被动的

- 在高磷酸盐摄入期间，被动吸收是普遍的
- 在低磷酸盐摄入期间，吸收主要是主动发生的

1,25-维生素D通过调节肠细胞腔膜中Na-P转运蛋白的数量来调节磷酸盐吸收，主要是在近端空肠中

维生素D的活化受两者的调节

- 甲状旁腺激素（PTH）和
- 血清磷

Major Causes of Chronic Hypophosphatemia

- Decreased Intestinal Phosphate Absorption
  - Malnourishment
  - Gastrointestinal diseases (e.g., short bowel syndrome)
- Increased Renal Phosphate Loss
  - FGF23-related hypophosphatemic diseases
  - Hypophosphatemic rickets with hypercalciuria caused by mutations in the SLC34A3 gene

Major Causes of Chronic Hypophosphatemia

- Proximal renal tubular dysfunction
  - Congenital diseases with various responsible genes
    - Lowe syndrome caused by mutations in the OCRL gene
    - Dent disease 1 caused by mutations in the CLCN5 gene
    - Dent disease 2 caused by mutations in the OCRL gene
  - Acquired renal tubular dysfunction
    - Drug toxicity (e.g., anticancer agents, antivirals, and aminoglycoside antibiotics)
    - Multiple myeloma
    - Amyloidosis
    - Heavy metals

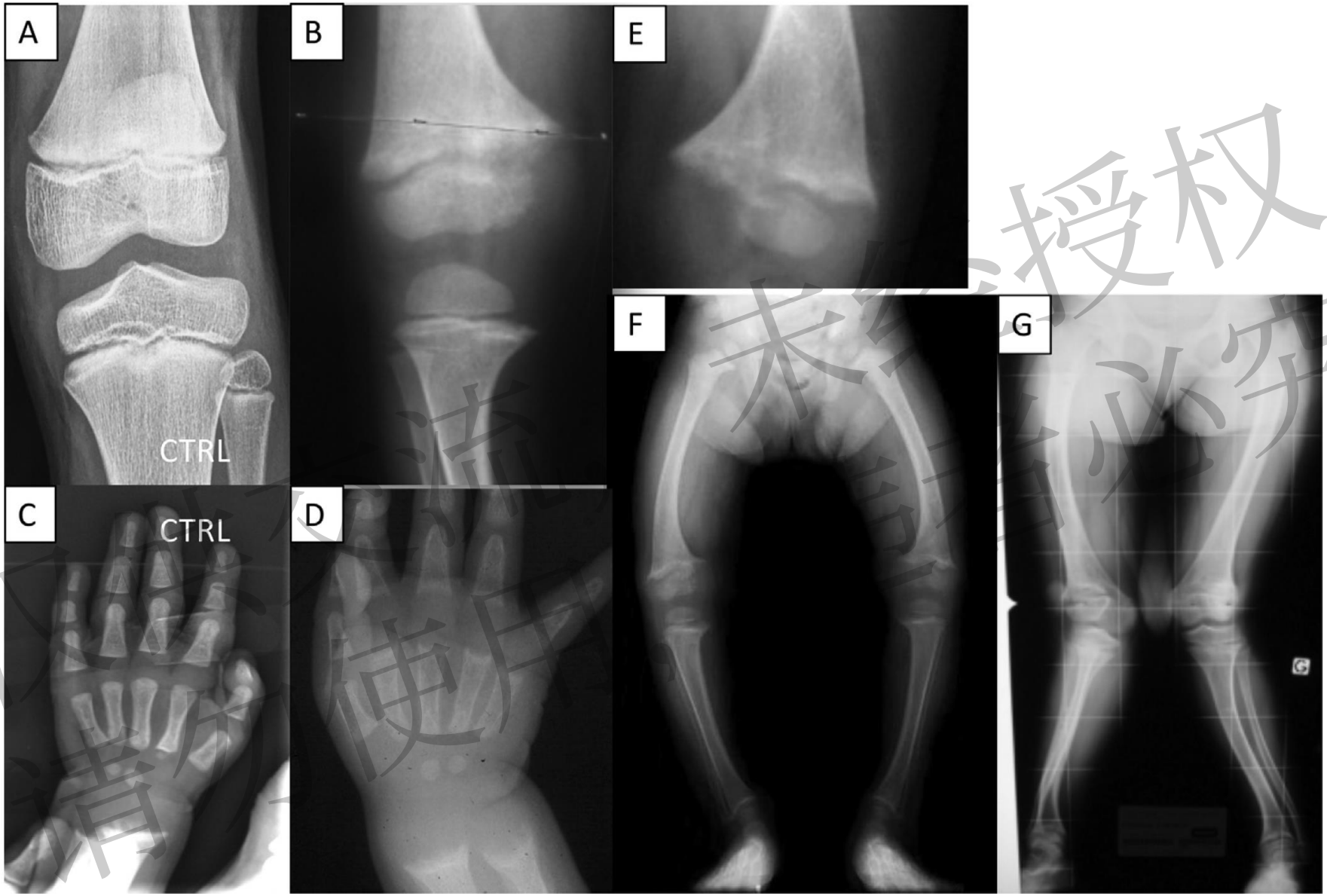
X連鎖低磷血症 - 临床表现

童年

1.腿部畸形（例如弓腿）
2.身材矮小
3.牙科疾病

成年

1.骨骼疼痛（例如下肢，下背部，臀部）
2.骨折
3.肌病
4.附著病（例如跟腱，髕腱，脊柱韌带）
5.牙科疾病
6.退行性關節病（例如膝蓋，臀部）
7.整形外科手術後的癒合延遲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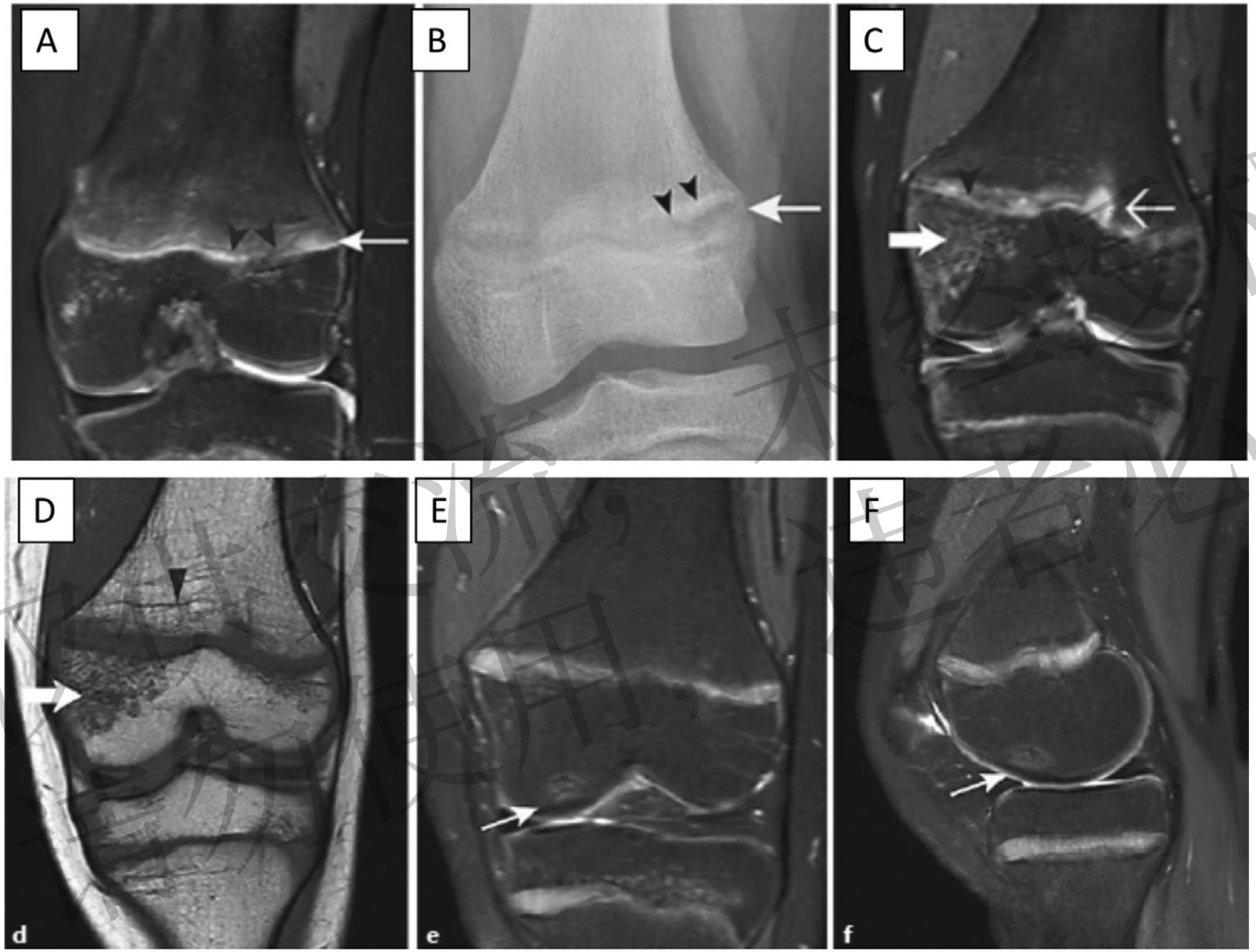
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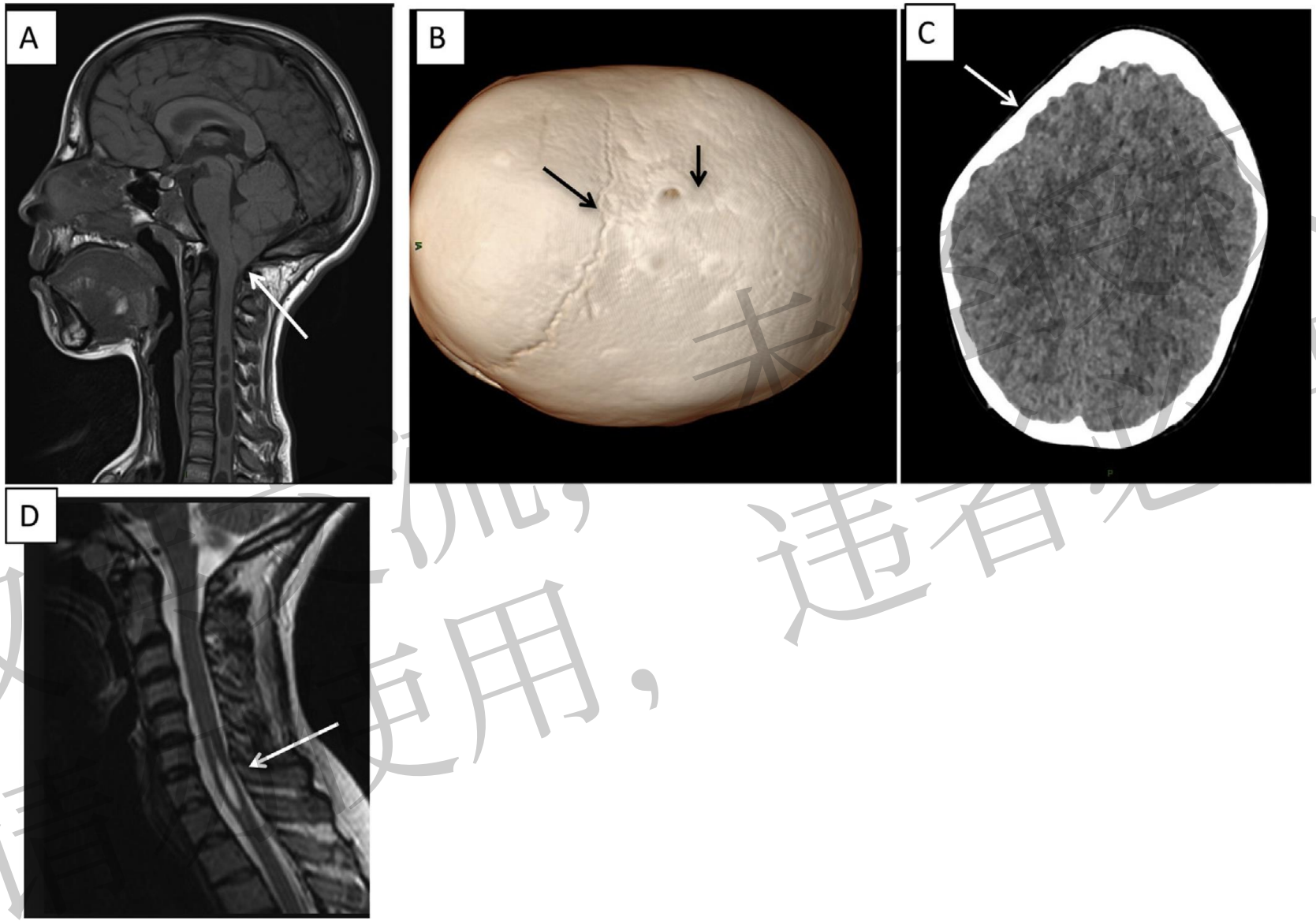
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Key biochemical assays in a child with rickets

- Blood
  - PTH
  - Calcium
  - Alkaline phosphatase
  - 25)H vitamin D
  - 1, 25 (OH)2 vitamin D
- Urine
  - Calcium
  - Phosphate

肾小管磷的廓清率 TmP/GFR

磷在肾的重吸收决定血浓度

量化肾小管磷的重吸收，以肾小管磷的廓清率(TmP/GFR) 表示

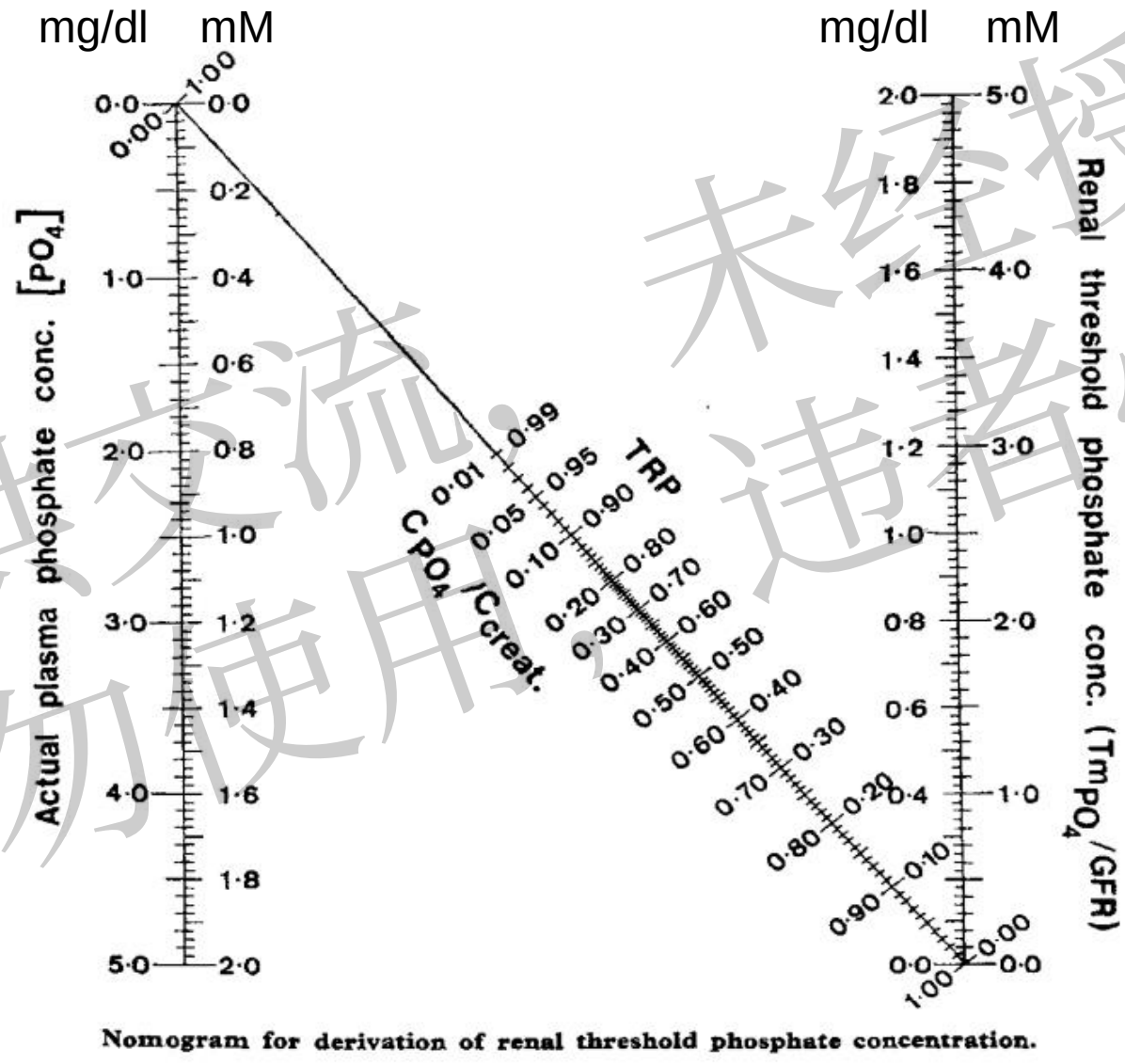
$$\%TRP = 100\,[1-(PO_{4尿}/PO_{4血})/Cr_{血}/Cr_{尿}]$$

正常 >95%，可低至 85%，与饮食中磷摄入有关

磷在肾的过度丢失的定义

- 低血磷时，TRP < 85%

Nomogram for derivation of renal threshold phosphate concentration



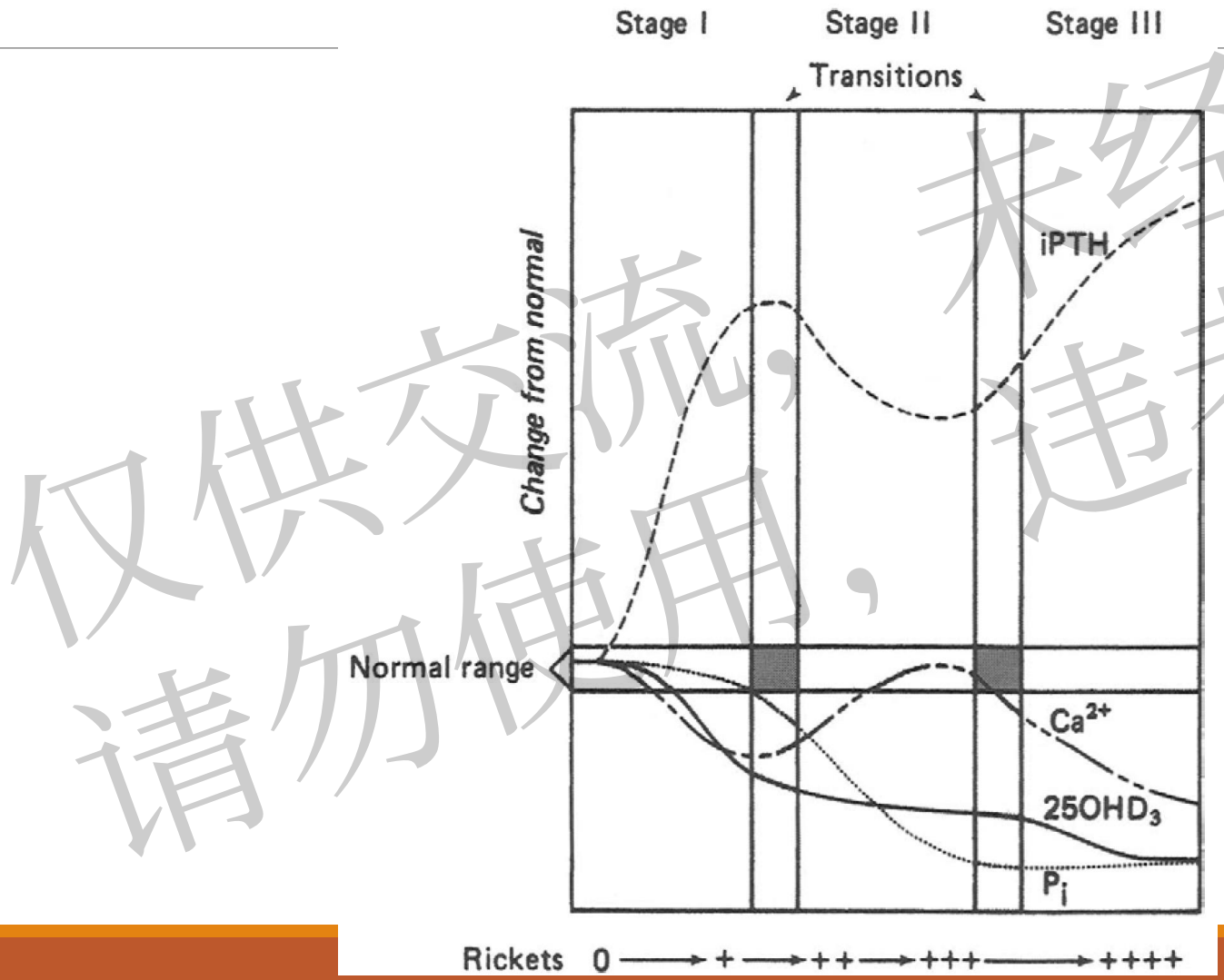
Nomogram for derivation of renal threshold phosphate concentration.

Lancet 306:309–310, 1975

Rickets	Dietary calcium deficiency	Phospho-rus Deficiency	XLH	ADHR	ARHR 1 and 2	HHRH	Vitamin D deficiency rickets	VDDR1A	VDDR1B	VDDR2	VDDR3
PTH	High	High	Nl or ULN	Nl or ULN	Nl or ULN	Nl or Low	High	Very high	Very high	Very high	High
Calcium	Nl or Low	Nl	Nl or ULN	Nl or ULN	Nl or ULN	Nl	Nl or Low	Nl or low	Nl or low	= or low	= or low
Phosphorus	Low	Low	Low	Low	Low	Nl	Low	Nl or low	Nl or low	= or low	= or low
ALP	Very High	High	High	High	High	High	Very high	Very high	Very high	Very high	Very High
25(OH)D	Nl	Nl*	Nl*	Nl*	Nl*	Nl	Very low or undetectable	Nl	Low	= *	Low
1.25$(OH)_2$D	High	Nl or High	Nl or Low	Nl or Low	Nl or Low	High	Variable	Nl or low	Nl or low	High	Low
Urinary Ca	Very Low	Variable	Low or undetec-table	Low	Variable	High	Very Low	Low or undetectable	Low or undetectable	Low or undetectable	Low or undetec-table
Urinary Ph.	variable	Low	High	High	High	High	High	High	High	High	High

Rickets	Vitamin D deficiency rickets	VDDR1A	VDDR1B	VDDR2	VDDR3
PTH	High	Very high	Very high	Very high	High
Calcium	Nl or Low	Nl or low	Nl or low	= or low	= or low
Phosphorus	Low	Nl or low	Nl or low	= or low	= or low
ALP	Very high	Very high	Very high	Very high	Very High
25(OH)D	Very low or undetectable	Nl	Low	= *	Low
1.25$(OH)_2$D	Variable	Nl or low	Nl or low	High	Low
Urinary Ca	Very Low	Low or undetectable	Low or undetectable	Low or undetectable	Low or undetec-table
Urinary Ph.	High	High	High	High	High

Progressive depletion 25OH vit D3



Rickets	Phospho-rus Deficiency	XLH	ADHR	ARHR 1 and 2	HHRH
PTH	High	Nl or ULN	Nl or ULN	Nl or ULN	Nl or Low
Calcium	Nl	Nl or ULN	Nl or ULN	Nl or ULN	Nl
Phosphorus	Low	Low	Low	Low	Nl
ALP	High	High	High	High	High
25(OH)D	Nl*	Nl*	Nl*	Nl*	Nl
$1.25(OH)_2D$	Nl or High	Nl or Low	Nl or Low	Nl or Low	High
Urinary Ca	Variable	Low or undetec-table	Low	Variable	High
Urinary Ph.	Low	High	High	High	High

生化异常作为XLH鉴别诊断的线索

- 禁食血清、尿磷酸盐和肌酐可以确认低磷酸血症和测定TmP/GFR
- 成人血清磷酸盐标准使用不当导致儿童XLH的漏诊。在未经治疗的儿童和一些患有XLH的成年人中，碱性磷酸酶活性一般随着年龄的增长而增加。
- 25-羟基维生素D的检测可以检测维生素D的缺乏，而XLH中的1,25(OH)2D不恰当地低或正常。
- PTH，如果被测试，在诊断时经常轻度升高，并且很可能继发于FGF23对1，25（OH）2D的影响。

- 同样，应检查血清和尿钙以确认正常水平；
- 异常的血清和尿钙应引起不同疾病的怀疑。
- 低钙血症伴低磷酸血症可能提示维生素D缺乏性佝偻病，或很少由于1α-羟化酶或维生素D受体基因突变导致维生素D代谢缺陷
- 低磷酸盐血症时高钙尿症提示FANCONI综合征或HHRH。
- 同样，葡萄糖尿、蛋白尿或氨基酸尿应引起对许多范可尼综合征之一的怀疑。

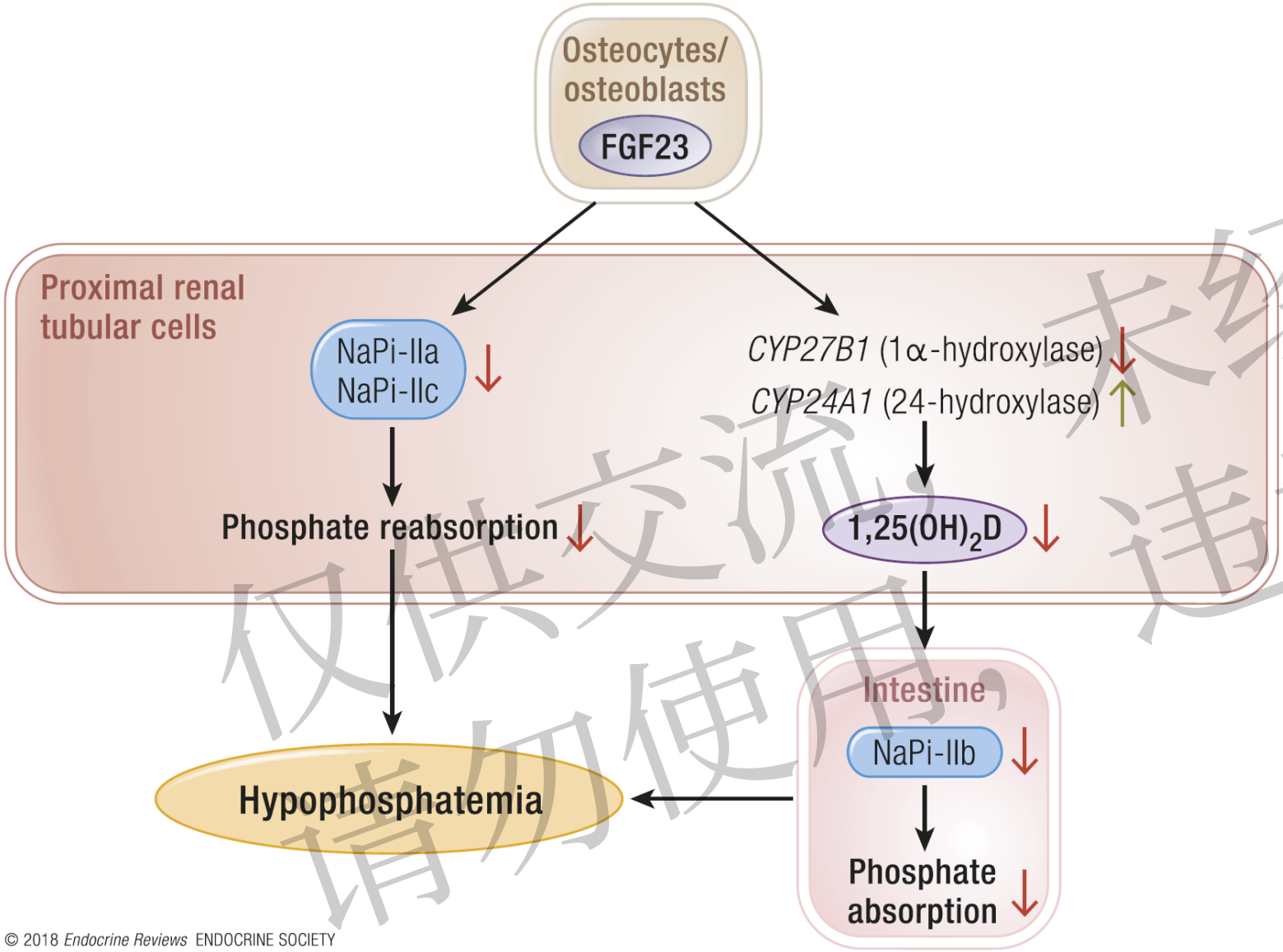
FGF23浓度升高对XLH没有特异性，即使在低磷血症的情况下，也有类似DDx的情况

- ADHR
- ARHR
- TIO and
- TiO和
- 纤维发育不良

低磷酸盐血症时FGF23浓度低提示不同的原因，例如

- 范科尼综合征
- 膳食磷酸盐缺乏症
- 吸收不良

FGF-23水平升高的病理生理学作用

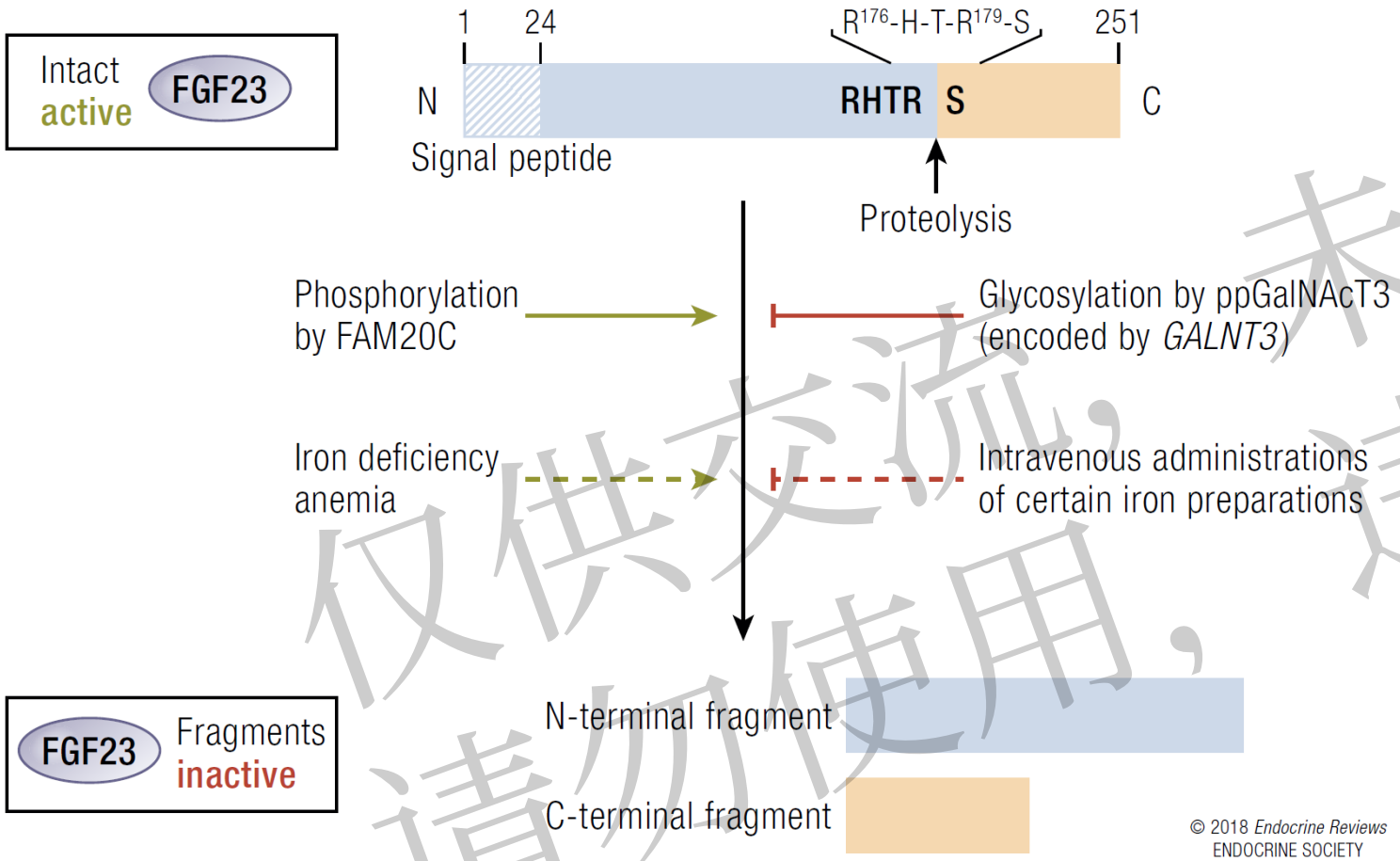


- 引起维生素D轴的异常调节（合成减少和分解代谢增加）

和

- 减少钠-磷酸盐共转运转运蛋白在近端肾小管细胞顶端表面的表达

FGF-23的调节(翻译后修饰)



Mice models of XLH: understanding the basic pathophysiological mechanisms

	Serum Biochemistry				Skeletal Phenotype	FGF23 Regulation			
Genotype	Ca	P	$1,25(OH)_2D$	PTH	Rickets/ Osteomalacia	Serum Total FGF23	Serum Intact FGF23	Bone FGF23 mRNA	Remarks
Hyp	→	↓	↓	↑	Yes	N.E.	↑	N.E.	Superimposing FGF23 deficiency onto *Hyp* mice corrected the abnormalities in serum phosphate and $1,25(OH)_2D$ levels.
Hyp/*Fgf23*$^{+/-}$	→	↓	→	↑	Yes	N.E.	↑, but less than *Hyp*	N.E.	
Hyp/*Fgf23*$^{-/-}$	↑	↑	↑	↓	No, but BMD is low	N.E.	Undetectable	N.E.	
Hyp	→	↓	→	↑	Yes	N.E.	↑	↑	Compound *Phex* and *Dmp1* mutant mice did not display worsening of serum FGF23 elevations, hypophosphatemia, and severity of rickets.
Dmp1$^{-/-}$	→	↓	→	↑	Yes	N.E.	↑	↑	
Hyp/*Dmp1*$^{-/-}$	→	↓	→	↑	Yes	N.E.	↑	↑	
Phex mutant (K496X)	↓	↓	→		Yes	↑	↑↑	↑	In double-mutant mice, significantly upregulated bone *FGF23* mRNA with increased proteolytic cleavage of FGF23 protein was observed.
Galnt3$^{-/-}$	→	↑	→		No	↑	↓	↑	
Phex/*Galnt3*$^{-/-}$ double mutant	↓	↓	→		Yes, but less severe	↑↑	↑	↑↑	

FGF-23相關的低磷血症

	相關基因	突變
X連鎖低磷血症性佝僂病：XLH	PHEX	滅活
常染色體顯性遺傳性低磷血症性佝僂病: ADHR	FGF23	激活
常染色體隱性低磷血症性佝僂病1: ARHR1	DMP1	滅活
常染色體隱性低磷血症性佝僂病2: ARHR2	ENPP1	滅活
骨質疏鬆症發育不良	FGFR1	激活
Jansen 型乾骺端軟骨發育不良	PTH1R	激活
低磷血症與牙齒異常和異位鈣化	FAM20C	滅活
McCune-Albright 綜合症	GNAS1	激活
表皮痣綜合徵: ENS	HRAS, KRAS, NRAS	激活
腫瘤誘發的骨軟化症: TIO	FN-FGF1, FN-FGFR1	激活

Disorder (abbreviation)	OMIM	Gene/ location	Urinary Calcium	FGF23	PTH	$1,25(OH)_2D$
Rickets/osteomalacia with renal tubular phosphate wasting due to elevated FGF23 levels/signaling						
X-linked hypophosphatemia (XLH)	#307800	*PHEX*/ Xp22.1	Low Undetectable	Normal or moderately elevated	Normal or moderately elevated	Within normal range but decreased relative to the phosphate concentration
Autosomal dominant hypophosphatemic rickets (ADHR)	#193100)	*FGF23*/ 12p13.3	Low Undetectable	Elevated	Normal or moderately elevated	Within normal range but decreased relative to the phosphate concentration
Autosomal recessive hypophosphatemic rickets 1 (ARHR1)	#241520	*DMP1*/ 4q22.1	Low Undetectable	Normal or moderately elevated	Normal or moderately elevated	Within normal range but decreased relative to the phosphate concentration
Autosomal recessive hypophosphatemic rickets 2 (ARHR2)	#613312	*ENPP1*/ 6q23.2	Low Undetectable	Normal or moderately elevated	Normal or moderately elevated	Within normal range but decreased relative to the phosphate concentration
Hypophosphatemic rickets and hyperparathyroidism	#612089	KLOTHO/ 13q13.1	Low	Elevated	Very elevated	Within normal range but decreased relative to the phosphate concentration
Osteoglophonic dysplasia (OD)	#166250	FGFR1/ 8p12	Low	Normal or moderately elevated	Normal or moderately elevated	Within normal range but decreased relative to the phosphate concentration
Fibrous dysplasia (FD)	#174800	*GNAS*/ 20q13.3 -	Low	Normal or moderately elevated	Normal or moderately elevated	Within normal range but decreased relative to the phosphate concentration
Tumor induced osteomalacia (TIO)	#163200	*RAS*/ 1p13.2	Undetectable			
Cutaneous skeletal hypophosphatemia sd (SFM)						
Rickets/osteomalacia due to primitive renal tubular phosphate wasting[a]						
Hereditary hypophosphatemic rickets with hypercalciuria (HHRH)	#241530	*SLC34A3*/ 9q34.3	Normal or high	Low or undetectable	Low normal or undetectable	Elevated
X-linked recessive hypophosphatemic rickets (XL-RHR)	#300554	*CLCN5*/ Xp11.23	Normal or high	Varies	Varies	Elevated
Hypophosphatemia and nephrocalcinosis (NPHLOP1)	#612286 #613388	*SLC34A1*/ 5q35.3	Elevated	Low or undetectable	Varies	Elevated
Fanconi reno-tubular sd 2 (FRTS2)						
Iatrogenic proximal tubulopathy			Varies	Low or undetectable	Varies	Elevated

Rickets/osteomalacia with renal tubular phosphate wasting due to elevated FGF23 levels/signaling						
X-linked hypophosphatemia (XLH)	#307800	*PHEX*/ Xp22.1	Low Undetectable	Normal or moderately elevated	Normal or moderately elevated	Within normal range but decreased relative to the phosphate concentration
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Autosomal recessive hypophosphatemic rickets 2 (ARHR2)	#613312	*ENPP1*/ 6q23.2	Low Undetectable	Normal or moderately elevated	Normal or moderately elevated	Within normal range but decreased relative to the phosphate concentration
Hypophosphatemic rickets and hyperparathyroidism	#612089	KLOTHO/ 13q13.1	Low	Elevated	Very elevated	Within normal range but decreased relative to the phosphate concentration
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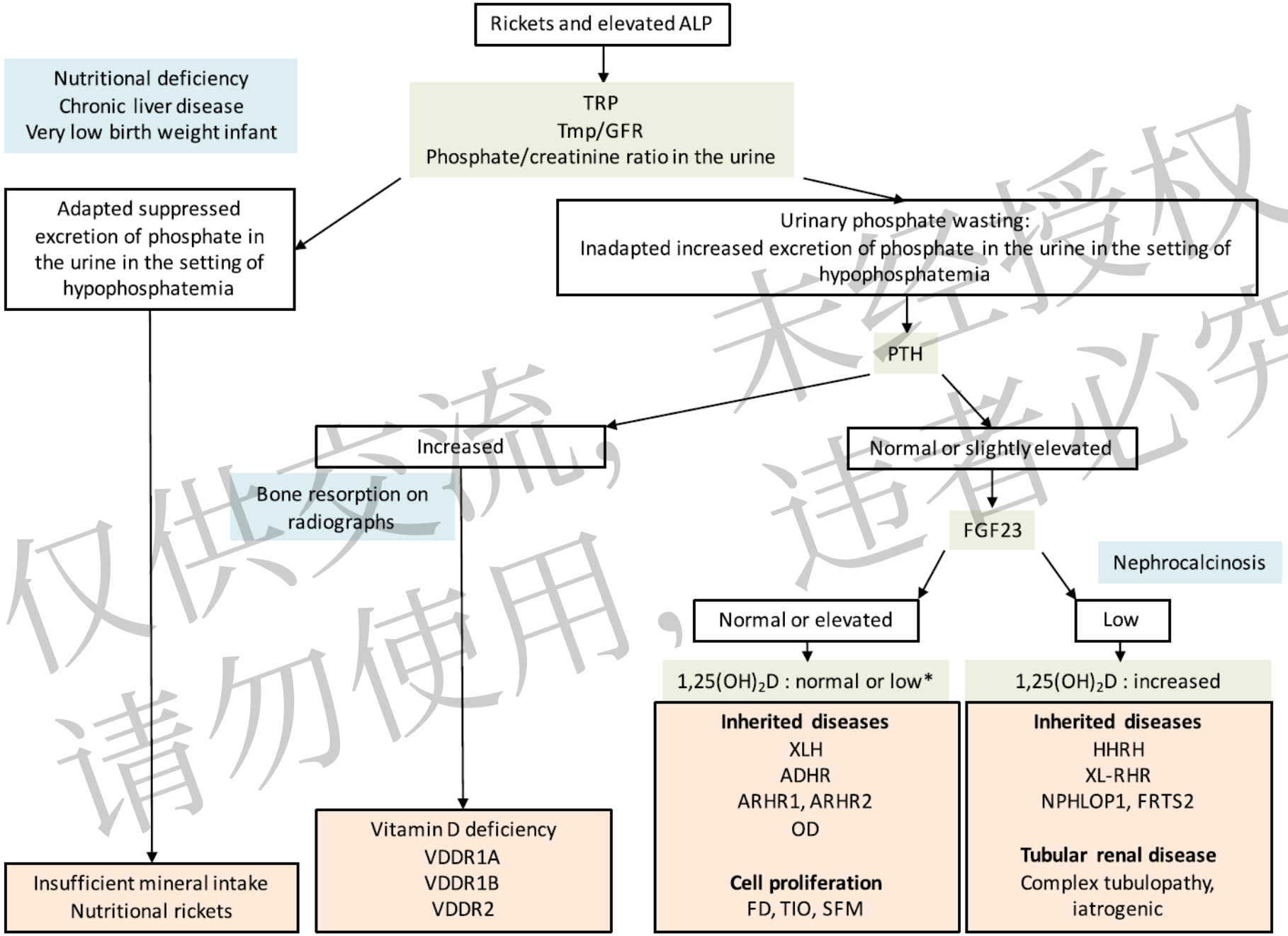
Cutaneous skeletal hypophosphatemia sd (SFM)						

Rickets/osteomalacia due to primitive renal tubular phosphate wasting[a]						
Hereditary hypophosphatemic rickets with hypercalciuria (HHRH)	#241530	*SLC34A3*/ 9q34.3	Normal or high	Low or undetectable	Low normal or undetectable	Elevated
X-linked recessive hypophosphatemic rickets (XL-RHR)	#300554	*CLCN5*/ Xp11.23	Normal or high	Varies	Varies	Elevated
Hypophosphatemia and nephrocalcinosis (NPHLOP1)	#612286 #613388	*SLC34A1*/ 5q35.3	Elevated	Low or undetectable	Varies	Elevated
Fanconi reno-tubular sd 2 (FRTS2)						
Iatrogenic proximal tubulopathy			Varies	Low or undetectable	Varies	Elevated



XLH – 治疗 & 目标

- 磷酸盐口服剂量 (分成每天4次或5次用量)
  - 80-100 mg/kg/天
- 1,25-$(OH)_2D3$ (分成每天一次或者两次的用量)
- 根据监测的临床症状与生化指标来个体化调整剂量

- 治疗目标
  - 使得生长与X线摄影改变标准化
  - 预防变形
  - 预防肾钙质沉着症

监测XLH病人治疗效果的综合方案

- 血清电解质, 尿素, 肌酐, 钙 (参考范围, 2.25 到 2.75 mmol/L)

- 血清碱性磷酸酶是骨骼反应最有用的生物标志物
  - 通常在治疗前适度升高，并随治疗而降低
  - 在治疗开始后可观察到短暂的增加

监测XLH病人治疗效果的综合方案

- 清晨口服磷酸盐前，以及服用后1小时，2小时，3小时，4小时分别测定血清磷酸盐水平
  1. 1.6 - 2.4 mmol/L (年龄小于 6月)
  2. 1.3 - 1.9 mmol/L (6 月 -12 岁)
  3. 0.8 - 1.6 mmol/L (大于12 岁)
- 每6个月测定血清甲状旁腺激素水平 (参考范围, <0.6 µg/L).
- 24小时尿液检查
  - 钙和磷酸盐排泄水平 **[< 0.15 mmol / kg/天] 或者**
  - 收集随机尿，测定尿钙与尿肌酐比 **[<0.6 (mM/mM)]**

尿Ca/Cr比值

0 - 12月:	<2.1 mg/mg	< 5.9 mM/mM
13-24月:	<0.45 mg/mg	< 1.3 mM/mM
2 - 5 岁:	<0.35 mg/mg	< 1.0 mM/mM
6 -10 岁:	<0.3 mg/mg	< 0.8 mM/mM
11-18岁:	<0.26 mg/mg	< 0.7 mM/mM
> or =19岁:	<0.22 mg/mg	< 0.6 mM/mM

治疗XLH面临的困难

- 口服磷酸盐及维生素D可能改善生长状态，但是会有一些并发症包括：
  - 肾钙质沉着症
  - 甲状旁腺功能亢进
  - 血压升高
  - 心血管畸形
- 甲状旁腺功能亢进可能是较早发生的并发症,特别是血压升高，预防甲状旁腺功能亢进包括适当的磷酸盐及维生素D剂量补充。
- 有研究表明，钙类似物药物-西那卡塞特治疗接受血液透析的继发性甲状旁腺功能亢进症病人有效。
  - 有相关初步证据表明对XLH病人有益。

Unique Treatment of FGF23-Related Hypophosphatemic Diseases

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Burosumab Therapy in Children with X-Linked Hypophosphatemia

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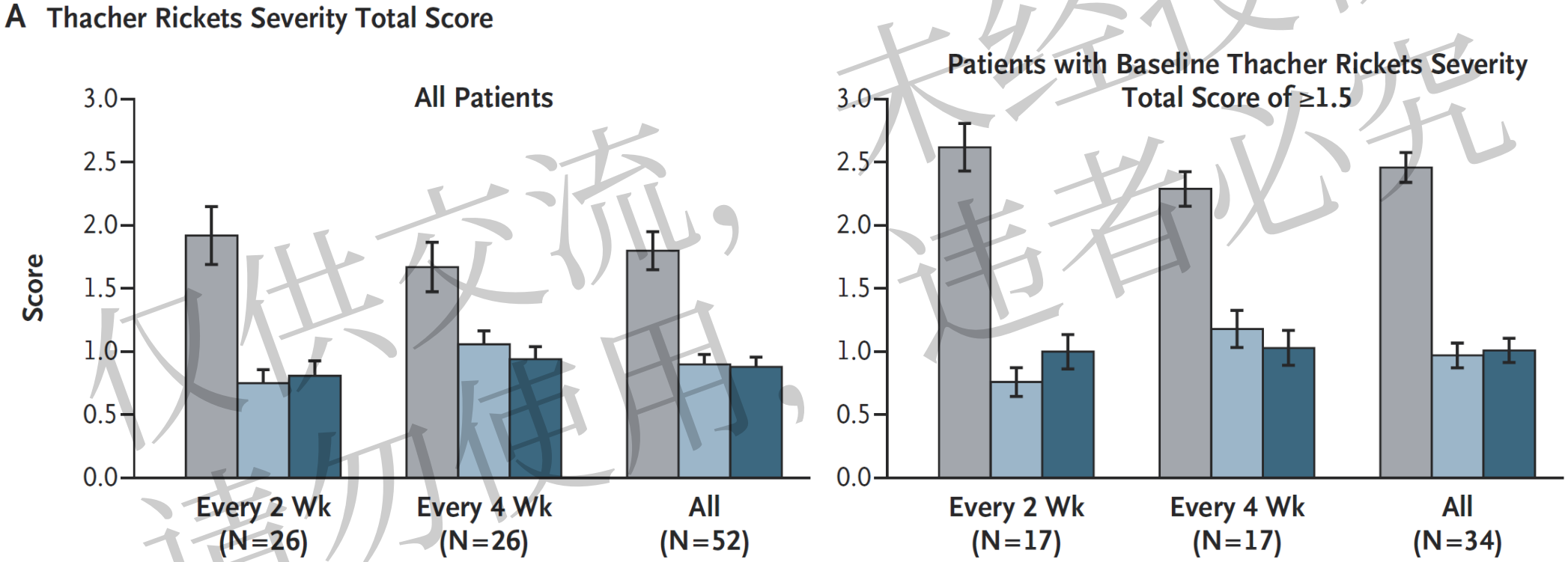

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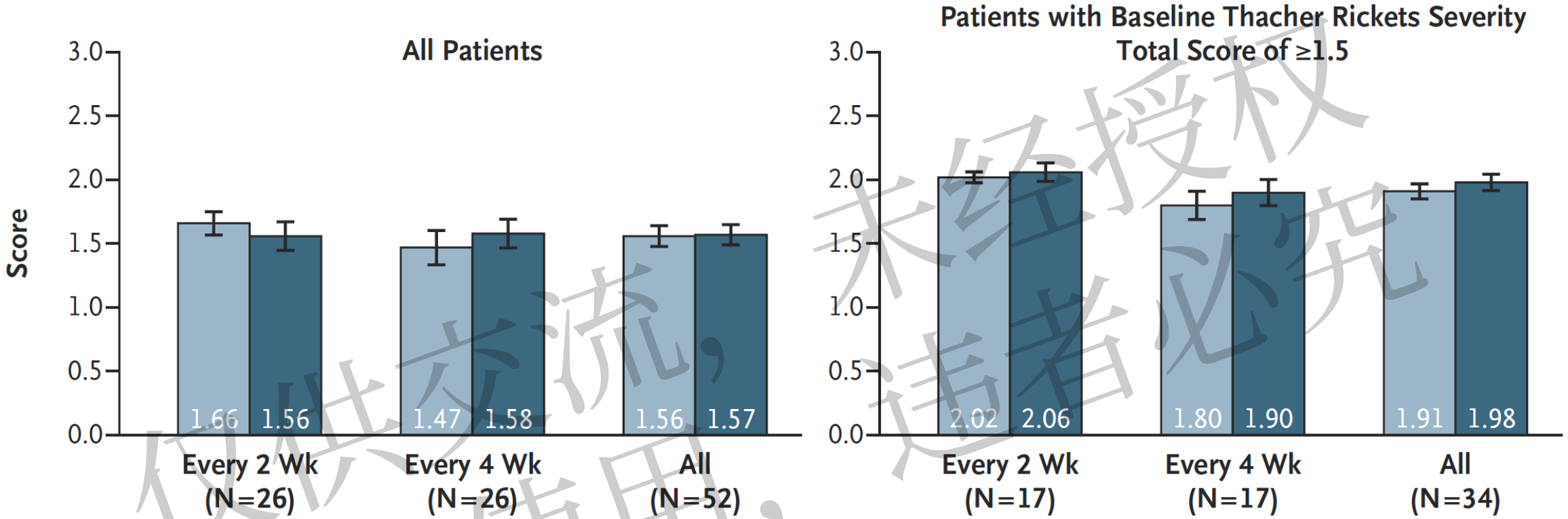
B Radiographic Global Impression of Change Score



A 7-point ordinal scale:

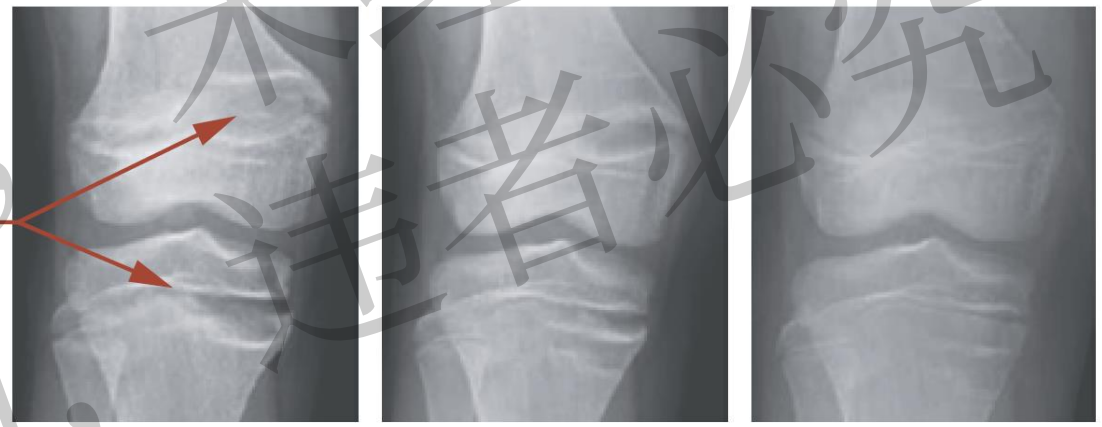
3 (complete healing) 2 (substantial healing) 1 (minimal healing)

0 (unchanged)

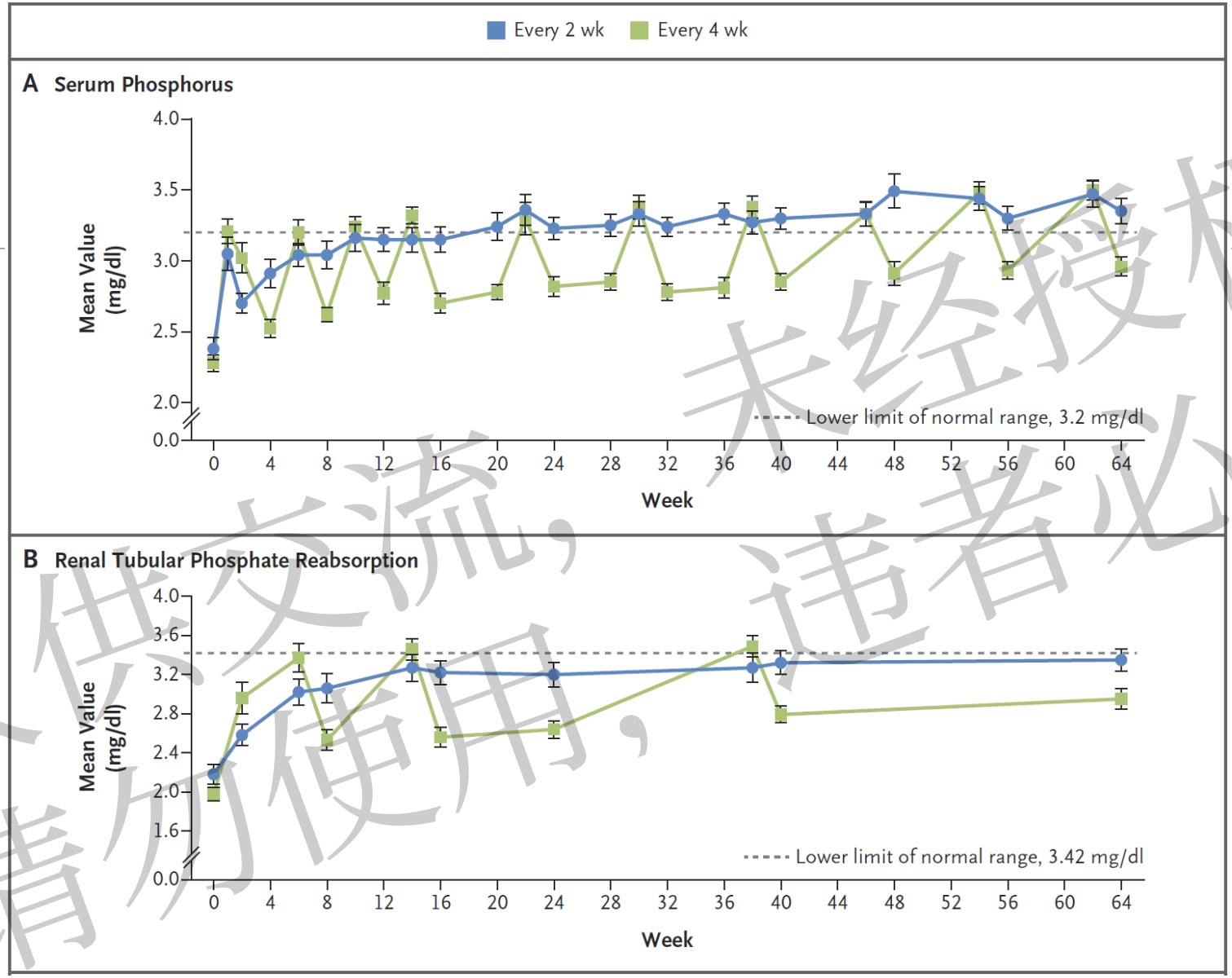
−1 (minimal worsening), −2 (moderate worsening) −3 (severe worsening)

A set of radiographs of the knee from an 11-year-old girl who had been receiving conventional therapy for 9 years before she was enrolled in the trial and was randomly assigned to receive burosumab every 2 weeks.

C Radiographs of the Knee in an 11-Year-Old Girl



	Baseline	Wk 40	Wk 64
Thacher Rickets Severity Knee Score	2.0	1.0	0.0
Radiographic Global Impression of Change Global Score		2.0	2.3



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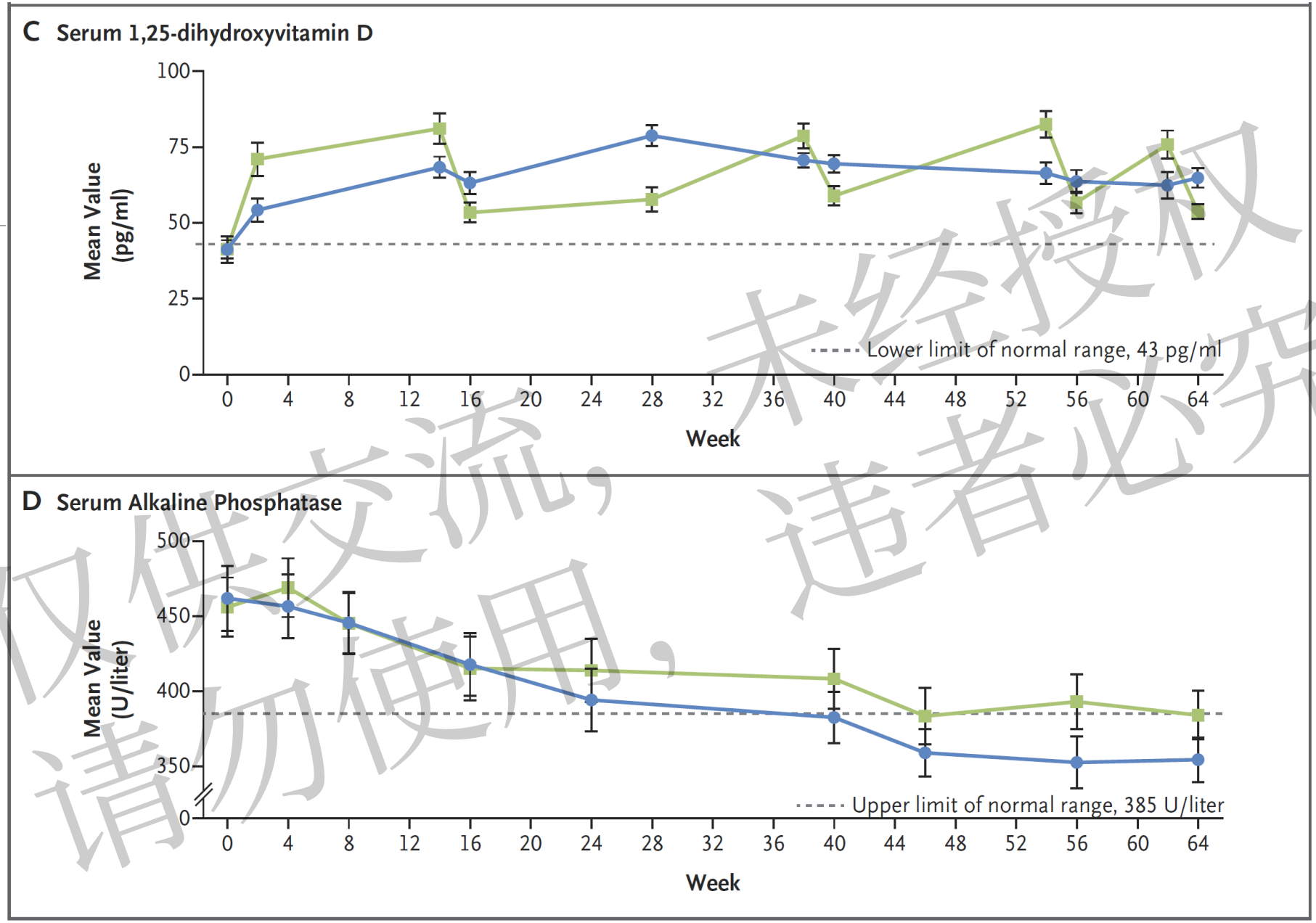

Assessment	Burosumab Every 2 Weeks (N=26)	Burosumab Every 4 Weeks (N=26)	All Patients (N=52)
Standing-height z score*			
Baseline	−1.72±1.03	−2.05±0.96	−1.89±1.00
Week 64	−1.54±1.13	−1.92±0.84	−1.73±1.00
Change from baseline	0.19±0.05	0.12±0.06	0.15±0.04
6-Minute walk test†			
Baseline			
Percentage of predicted distance	79.32±2.60	81.42±2.96	80.37±1.96
Distance (m)	479.9±16.6	486.4±21.3	483.1±13.4
Week 64			
Percentage of predicted distance	85.00±2.03	84.74±2.67	84.87±1.66
Change from baseline in percentage of predicted distance — percentage points	5.69±2.02	3.32±1.96	4.50±1.41
Distance (m)	533.85±11.51	525.85±17.56	529.85±10.41
Change from baseline in distance (m)	52.67±8.82	40.59±9.57	46.63±6.48
Sports and physical functioning, normative score*‡			
Baseline	34.6±15.7	32.2±19.3	33.4±17.4
Week 64	41.7±15.7	42.8±13.7	42.2±14.6
Change from baseline	7.7±2.6	9.8±2.5	8.8±1.8
Pain and comfort scale, normative score*‡			
Baseline	35.2±15.3	34.8±16.8	35.0±15.9
Week 64	41.0±17.0	43.0±11.5	42.0±14.5
Change from baseline	5.6±2.9	7.7±2.1	6.7±1.8
Global functioning, normative score*‡			
Baseline	37.5±14.0	35.6±17.2	36.6±15.5
Week 64	43.1±16.1	45.1±11.2	44.1±13.8
Change from baseline	6.0±2.7	8.7±2.0	7.4±1.7

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Study [ref] / ClinicalTials.gov number	Carpenter *et al.* JCI 2011 [86] NCT00830674	Imel et al. JCEM 2015 [87], Ruppe *et al.* Bone Reports 2016 [28] NCT01340482, NCT01571596	Carpenter *et al.* NEJM 2018 [29] NCT02163577	Insogna *et al.* JBMR 2018 [21] NCT02526160
Population	Adults with XLH	Adults with XLH	Children with XLH, ages 5–12 years at enrollment	Adults with XLH and Brief Pain Inventory worst pain score ≥ 4
Treatment arms	Single dose	Multidose for 16 months:	Multidose for 64 weeks, with dose titration period [c]	Multidose for 24 weeks:
	Intravenous burosumab 0.003–0.3 mg kg^{-1} (n = 17) *vs.* placebo (n = 5)	4-month dose escalation phase Every 4 weeks burosumab 0.05–0.6 mg kg^{-1} (n = 28),	Every 2 weeks burosumab (mean dose at week 40 was 0.98 mg kg^{-1}) (n = 26)	Every 4 weesk burosumab 1 mg kg^{-1} (n = 68)
	or	followed by	or	or
	Subcutaneous burosumab 0.1–1 mg kg^{-1} (n = 12) *vs.* placebo (n = 4)	12-month extension phase Every 4 weeks burosumab 0.1–1 mg kg^{-1} (n = 22) [b]	Every 4 weeks burosumab (mean dose at week 40 was 1.5 mg kg^{-1}; n = 26)	Every 4 weeks placebo (n = 66)

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Population	Adults with XLH	Adults with XLH	Children with XLH, ages 5–12 years at enrollment	Adults with XLH and Brief Pain Inventory worst pain score ≥ 4
Treatment arms	Single dose Intravenous burosumab 0.003–0.3 mg kg^{-1} (n = 17) *vs.* placebo (n = 5) or Subcutaneous burosumab 0.1–1 mg kg^{-1} (n = 12) *vs.* placebo (n = 4)	Multidose for 16 months: 4-month dose escalation phase Every 4 weeks burosumab 0.05–0.6 mg kg^{-1} (n = 28), followed by 12-month extension phase Every 4 weeks burosumab 0.1–1 mg kg^{-1} (n = 22) [b]	Multidose for 64 weeks, with dose titration period [c] Every 2 weeks burosumab (mean dose at week 40 was 0.98 mg kg^{-1}) (n = 26) or Every 4 weeks burosumab (mean dose at week 40 was 1.5 mg kg^{-1}; n = 26)	Multidose for 24 weeks: Every 4 weesk burosumab 1 mg kg^{-1} (n = 68) or Every 4 weeks placebo (n = 66)
Primary outcome	Safety and tolerability	Proportion of subjects achieving maximum fasting serum Pi in normal range	Change in RSS from baseline to week 40 and 64	Percent of subjects achieving mean serum Pi in the normal range across the midpoint of dosing intervals
Biochemical findings	Increased serum Pi, serum $1,25(OH)_2D_3$, and TmP/GFR	Increased serum Pi, serum $1,25(OH)_2D_3$, and TmP/GFR	Increased serum Pi, serum $1,25(OH)_2D_3$, and TmP/GFR; decreased serum alkaline phosphatase.	Increased serum Pi, serum $1,25(OH)_2D_3$, and TmP/GFR
Radiographic outcomes			Improved rickets by RSS and RGI-C. Greater changes seen with every 2-week dosing, and in those with higher baseline RSS	Improved healing of active fractures/pseudofractures from baseline: burosumab (43.1% of fractures healed) compared to placebo (7.7%)
Other outcomes		At baseline: Impairment of physical function Over 4 months of treatment: Improved role limitations due to physical health (SF-36v2), physical functioning and stiffness (WOMAC)	Increased standing height z-score; Among those with baseline impairments in 6MWT, the distance walked improved On PODCI, among those with impairments, burosumab improved: Sports and physical functioning domain, Pain and comfort domain, Global functioning	WOMAC: Decreased stiffness scores

Burosumab（Crysvita®; Kyowa Hakko Kirin Co.，Ltd。和Ultragenyx Pharmaceutical Inc.）是針對成纖維細胞生長因子23（FGF23）的完全人單克隆抗體。

過量的FGF23產生與各種低磷血症疾病有關。

通過burosumab抑制FGF23導致腎磷酸鹽重吸收增加，血清磷和活性維生素D水平升高。

2018年2月，EMA授予皮下burosumab條件上市許可，用於治療X連鎖低磷血症（XLH），其中1歲及以上兒童和骨骼生長的青少年患有骨病。

2018年4月，美國FDA批准使用burosumab治療成人和1歲及以上兒童的XLH。

目前，成人和兒童XLH患者正在進行burosumab的多國III期臨床試驗。

Burosumab也正在美國以及日本和韓國的成人腫瘤誘發的骨軟化和表皮痣綜合徵的II期環境中進行評估。