Elucidation of Pathogenesis of Skeleton Deformities at Genetic Skeletal Disorders through Functional Adaptation of Bones

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Functional adaptation of bones

- is a process where influence of function leads to optimal development of bone shapes and structure of skeleton
- Genetically anchored programmes for development of expedient shapes and structures during ontogenesis assert primary oneself in embryonal period without influence of special mechanic forces, muscle activity and impact of gravity of Earth - arise basic shapes.
- Mechanisms of functional adaptation, i.e. a way how tissues respond to external epigenetic impacts, are also hereditary anchored.

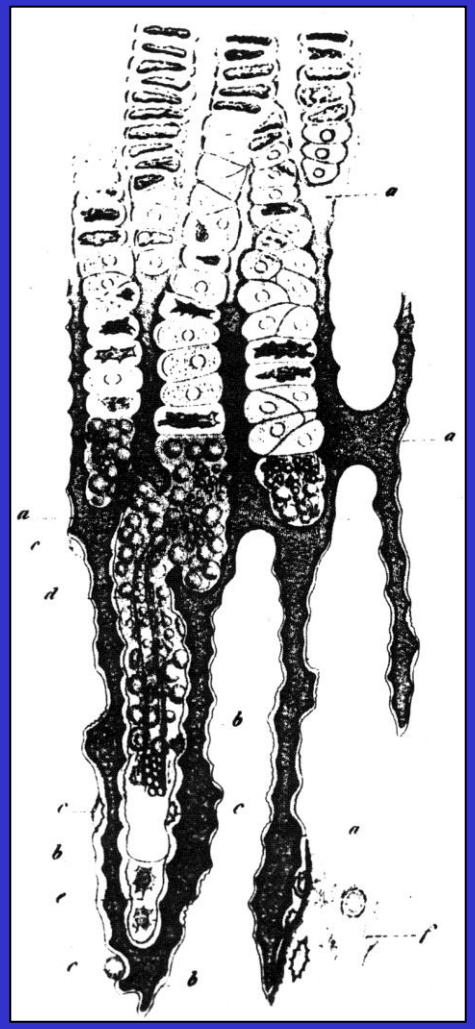
  Both genetic and epigenetic processes head towards the same goal.
- The muscle movement has morphogenetic function as early as foetal period. Muscles take the specific forming function only postnatally. It means that genetic influence assert oneself even in postnatal period when typical symptomatology of bone dysplasias (osteochondrodysplasias) develops.

Functional adaptation of bones

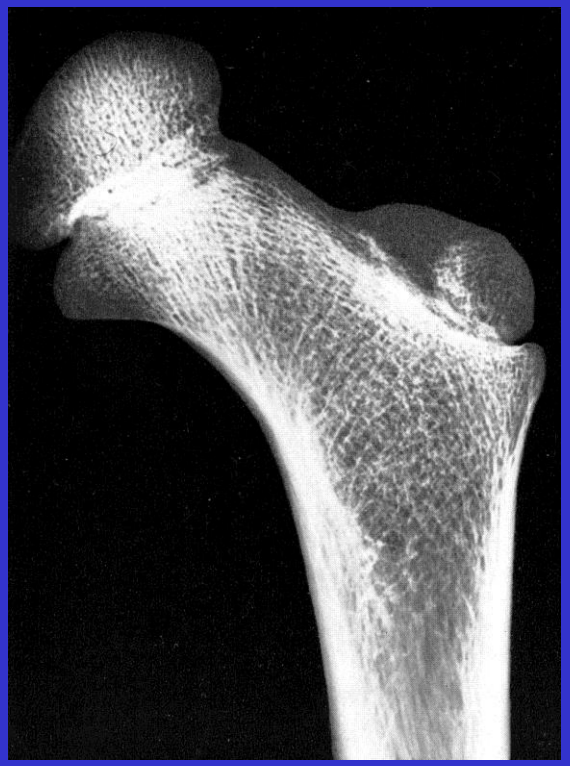
Important universal opinions in 2nd half of the 19th century:

- 1862 Carl **Hüter**: development and growth are dominated by mechanical factors.
- 1869 Richard **von Volkmann** : changes of bone shape go on under influence of mechanical forces, gravitation, pulling of muscles and he explained the change of bone shape by apposition, resorption and also deformation.
- 1866 Karl **Culmann**, mathematics calculated course of the main force trajectories in the trabecular structure of proximal end of femur
- 1892 Julius **Wolff**, the German anatomist and surgeon accepted this “trajectory” theory and generalized it for whole skeleton as natural process.

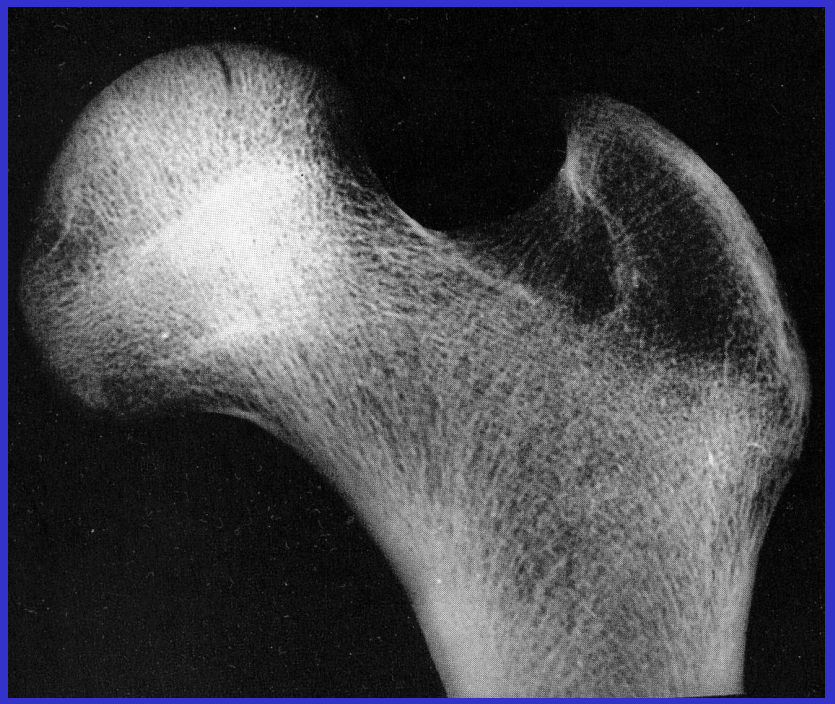
Wolff˜s transformation law



1858 Mueller



5 years



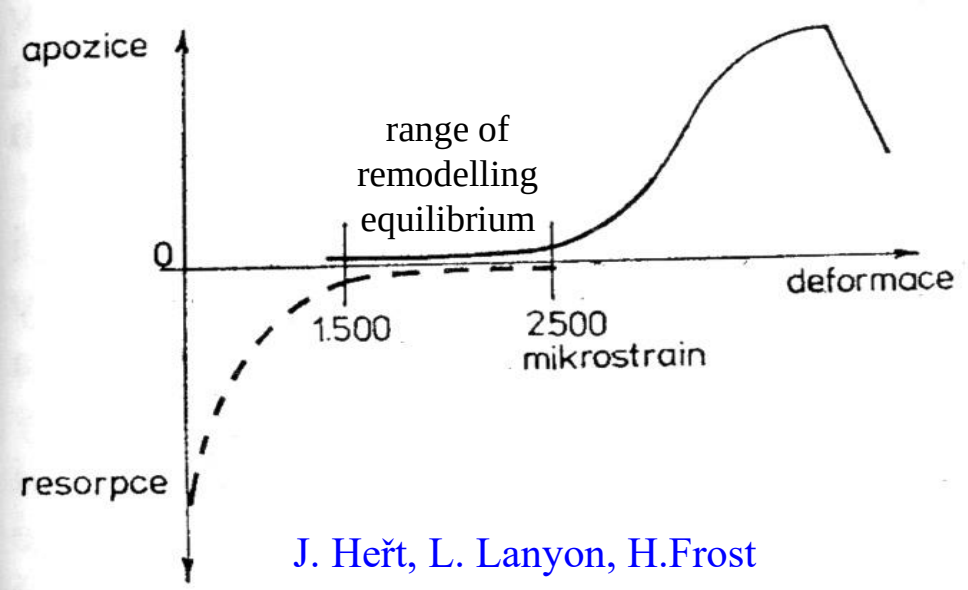
20 years

Culmanns´ “trajectory” theory (1866). Main directions of stress (tension) are perpendicular each to other (valid only for isotropic and homogenous material).

Wolff´s transformation law (1892)

- *"by consequence of changes of functional requirements comes up in bone by mathematic laws to conversion of internal architecture and only just so to secondary changes of external shape of bone".*
- Wolff did not know the nature of these processes and he incorrectly presumed that the bone grows interstitially
- Wolff˜s transformation law and remodelling has been verified in the experimental way and defined with more precision up to 70th years 20th century when 3 fundamental mechanisms (laws) of functional adaptation of connective tissues were explained - mainly growth of long bones, apposition and resorption.

Wolff´s transformation law -functional adaptation of bones



J. Heřt, L. Lanyon, H.Frost

Fig. Relation between deformation and reaction of bone tissue**.**

In range of remodelling equilibrium 1500 – 2500 microstrains, the bone does not respond to stress

>2500 ustrains- osteocytes – glucoso-6-phosphate dehydrogenase

1st mechanism of functional adaptation of bones depends on intensity of changing - cycling straining (internal stress in bone), velocity of alteration of deformation, number of cycles, etc. - strictly speaking on activity of osteoblasts (osteocytes) and osteoclasts that are influenced – activated by supraliminal deformation. Supraliminal values of changing - cycling straining cause **apposition**, subliminal bone **resorption**.

Wolff´s transformation law

- **2nd mechanism** of bone adaptation is caused by **periosteum**. The push of periosteum (and also endosteum) against the bone surface causes the resorption of bone tissue, whereas its take up is a cause of apposition. The convex surface of the long bone (diaphysis) inclines to resorption and the concave one to apposition.
- **3rd mechanism** is a regulation of long bone growth by epiphyseal plate (so-called physis) and is possible only in growing period. According to Hüter and Volkmann law, physis creates a new bone tissue into axial pressure direction (central line). The increase of stress causes restriction of growth, on the other hand unloading of physis accelerate growth. In situation of oblique loading, the epiphyseal plate regulates the growth of long bone into the direction of the pressure resultant (central line).

Osteopathological findings in adults - insufficient lateral drift

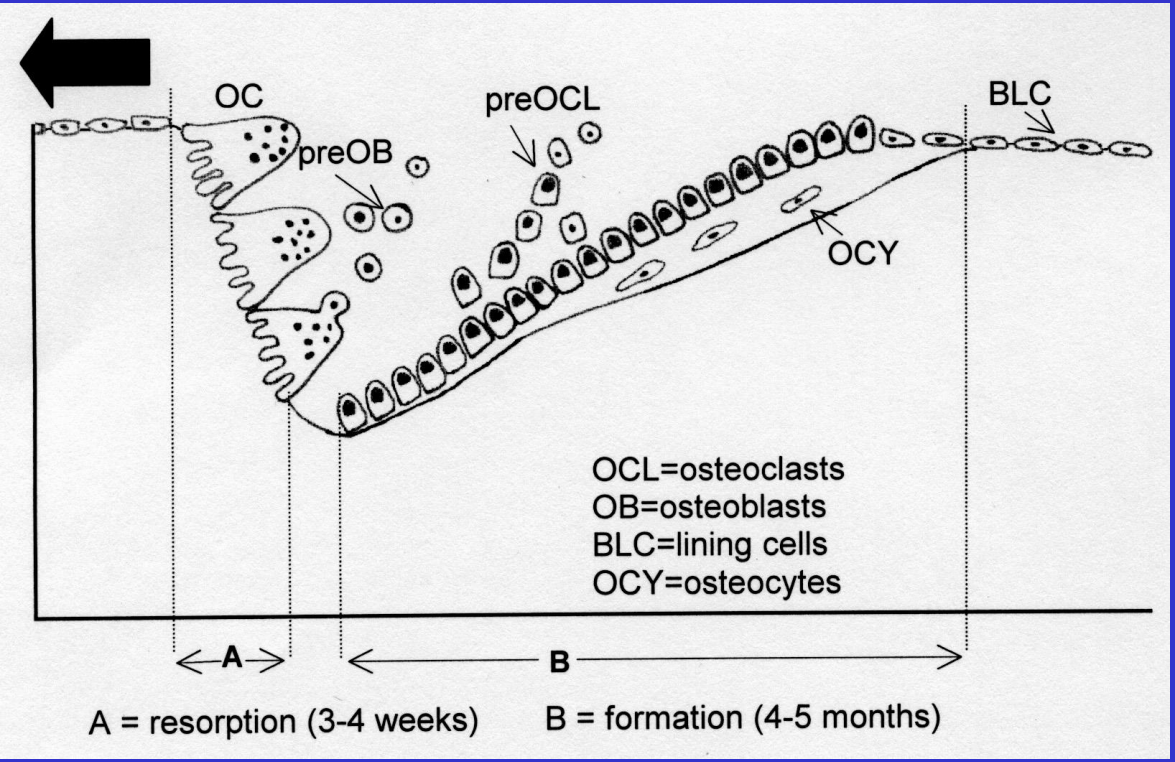
Healed fracture of the distal third of the right femur with a callus and dislocation of the dorsal fragment by about width of the shaft dorsally and a shortening by about 70 mm.

Fig. right femur, anterior view – left, posterior view – right.

Functional adaptation of bones

- ***Harold Frost, Lanyon et al.,***
- ***Jiri Heřt,***
- ***Gaston Marotti,*** *etc.*

- H. **Frost** : The **modelling** is a planar apposition and/or resorption process which changes the shape of bone.



The **remodelling** of skeleton runs variously intensively for whole life in Hoffship´s lacunae (so-called basic multicellular units) on surface of bone trabeculae, subperiostally, on cortico-endostal surface and Haversian system of osteons.

Functional adaptation of bones

Sobotka and Mařík (Pohybové ústrojí 2, 1995, No.1, p. 15-24) arrived at

Deformational-rheological theory of bone remodelling

- There exist instantaneous **elastic** deformation changes arising immediately with changes of loading and furthermore the time-dependent **viscoelastic** deformation changes occurring at constant load or after unloading.

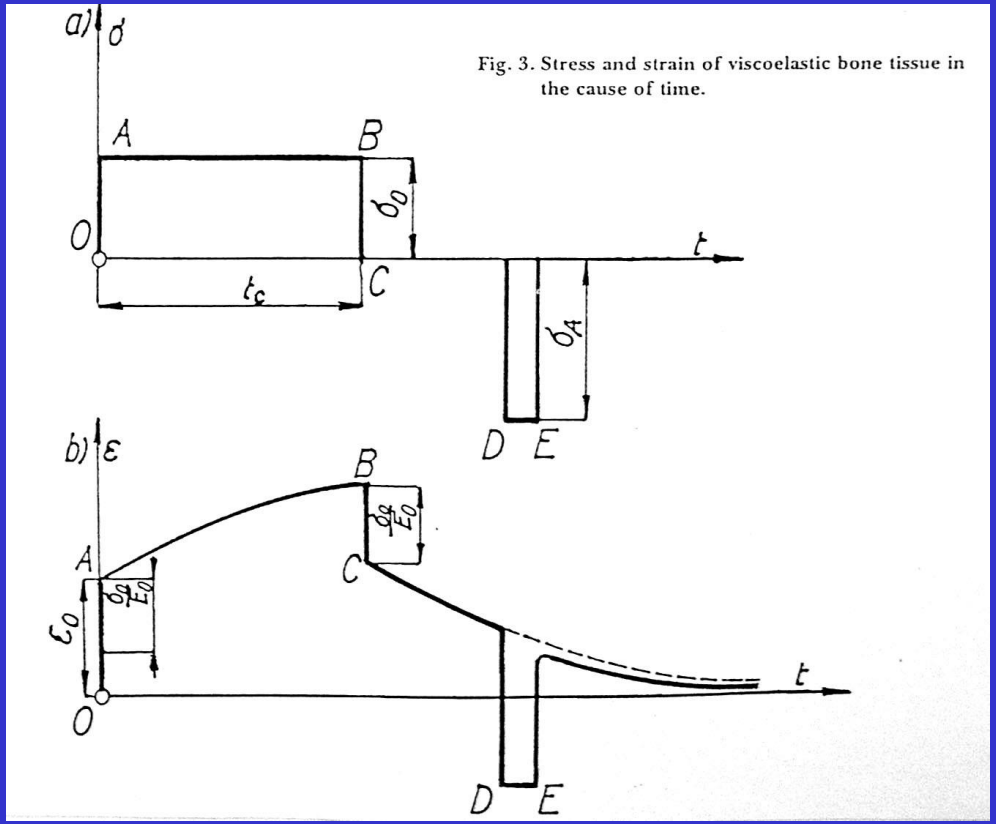


Fig. 3. Stress and strain of viscoelastic bone tissue in the cause of time.

Functional adaptation of bones

Sobotka and Mařík (Pohybové ústrojí 2, 1995, No.1, p. 15-24)

Deformational-rheological theory of bone remodelling.

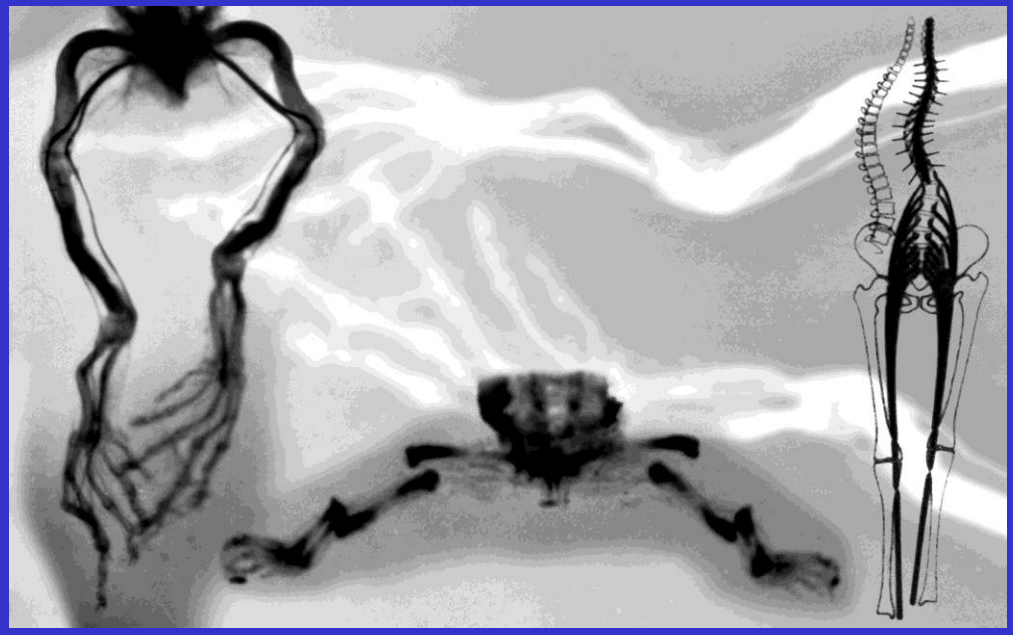
- According to this theory, the remodelling of bone tissue depends on its time-varying straining represented by extensions and shortenings. Because of the viscoelastic properties of bones (bone tissue contains collagen fibres, proteoglycans and fluids in skeleton), the strains vary not only at varying loading but the **strain changes continue and fade** as elastic after-effects at constant loads and after unloading – in rest, in sleep. The intensity of remodelling then depends on the amount, changes and duration of straining.
- By this theory we can explain and understand efficiency of **orthotic treatment** in the night regime or effectiveness of **physiotherapy** on remodelling of locomotion system.

Functional adaptation of bones by Assoc. Professor Milan Roth, MD, DSc

Left. Neuroadaptive-dysplastic experimental-teratogenic deformities of the hindlimbs in a frog tadpole that was kept in water with alcohol (0.5 per cent alcohol solution). Growing bones had to adapt to too short, straight coursing sciatic nerves. (1, 3).

Middle. Dislocation at the knee and at the cruro-tarsal joints in an osteolathyric frog tadpole. A tadpole specimen, magnification about 6–8x, staining with Sudan black (4, 5).

Right. The scheme of idiopathic scoliosis as a consequence of “neuroadaptive“ response of vertebral envelope to exaggerated slowness of spinal neural growth. Idiopathic scoliosis involve the lower thoracic spine because Th5-10 spinal cord segments are by far the longest so that their growth is more energy-consuming and more vulnerable. Growth slowness becomes manifest in neuroadaptive deformity of the growing vertebral envelope (2).



Functional adaptation of bones

Patients and Methods

During more than 30 years a group of more than **700 children** suffering with **g**enetic **s**keletal **d**isorders (GSD, bone dysplasias, metabolic bone diseases, genetic syndromes, etc.) has been investigated from the point of the fundamental laws of bone remodelling described above. We diagnosed around **120 GSD**.

X-ray documentation of children with **GSD** was studied,

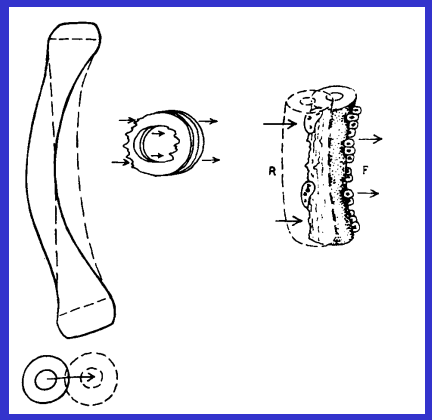
per-operative observation of long bones was used and results of orthotic and surgical treatment were documented by photos and X-rays and evaluated.

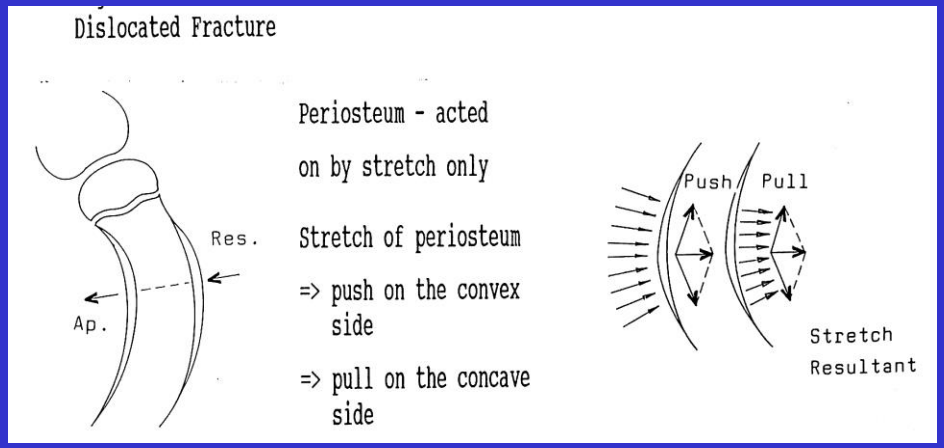
Last years we also evaluate bone density at some **GSD** by

densitometric examination (DEXA) with use of children software.

Functional adaptation of bones
Results

- The complex loading of bones involves **compression, tension, bending, shear** and **torsion . There is** so-called **lateral drift** that enable compensation of the shape and structure of growing skeleton.
- **1) incomplete correction of long bone curvature** by **lateral drift** (e.g. **rickets, genetic rickets,** hypophosphatasia, hyperfosphatasia, osteogenesis imperfecta, fibrous dysplasia, enchondromatosis etc.).

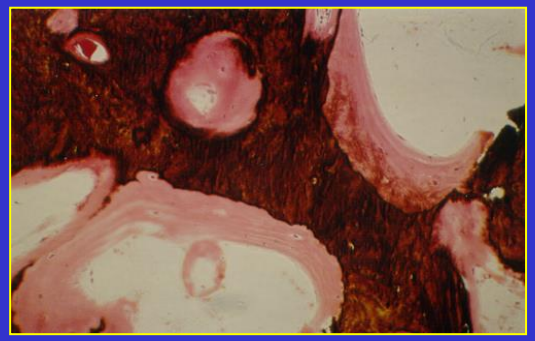




- The decrease in the resistance to deformation is often compensated by apposition of bone tissue on the external bone surface (e.g. in children with different forms of **rickets**). This increases the resistance of long bones to torsion and bending (Sobotka, Mařík 1994).

Functional adaptation of bones

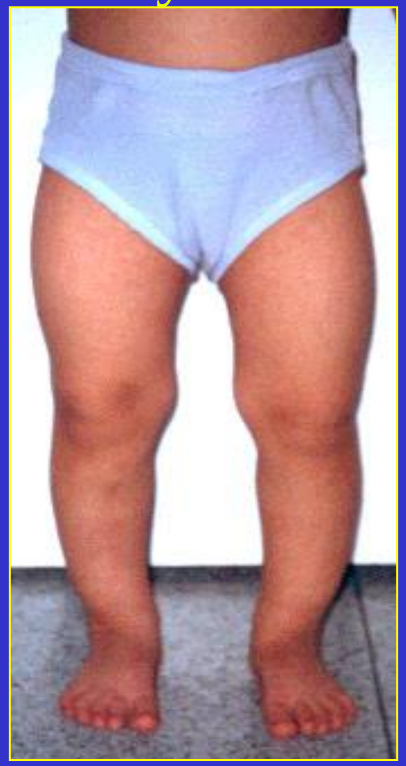
Results

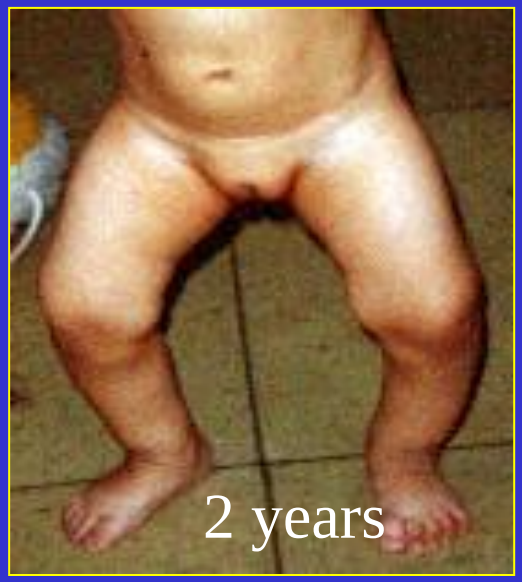


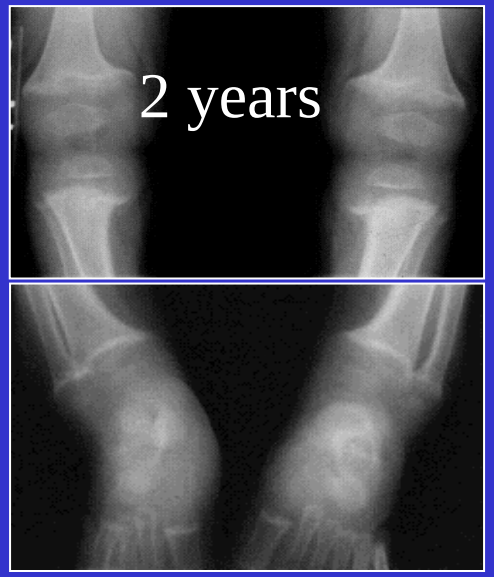
❖ **1. incomplete correction of long bone curvature** by **lateral drift: rickets -** the lack of mineral components in the bone tissue leads to osteomalatia and typical subsequent deformities .

- ➢Deformities at the ends of rachtic bones
- ➢The zone of preparatory calcification is not limited
- ➢Widening of unossified osteoid seams at the trabecules (Hematox.- Eosin)

4 years





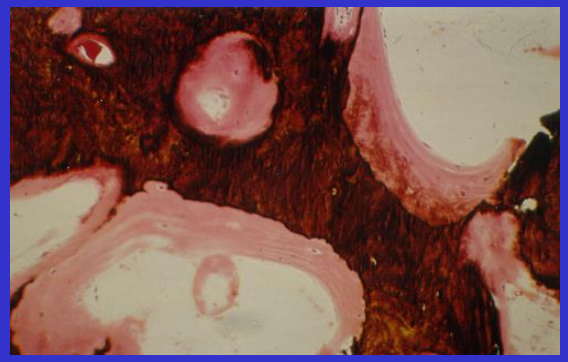


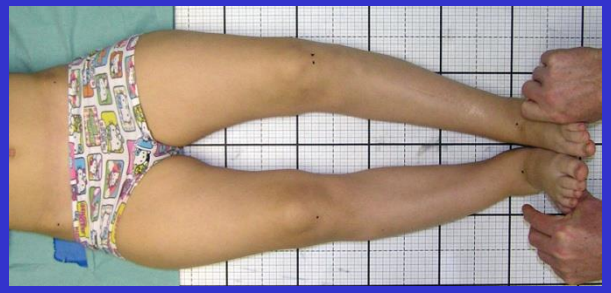
Functional adaptation of bones

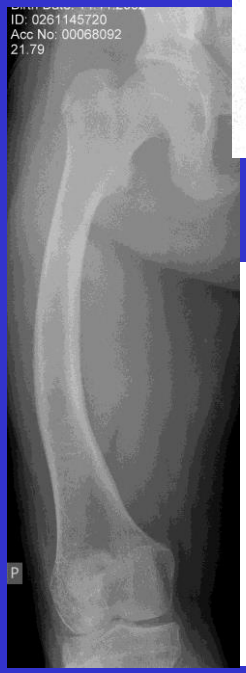
Results

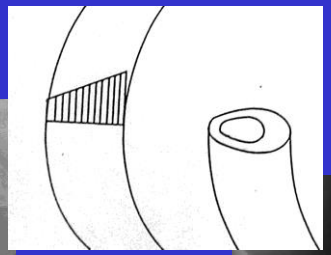
❖ **1. incomplete correction of long bone curvature** by **lateral drift: Hypophosphatemic rickets**

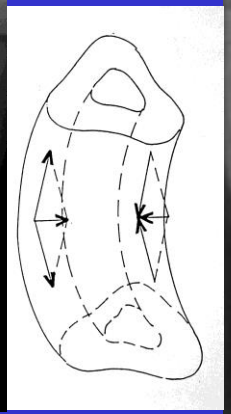
❖ **2. abnormal changes of cross-sectional areas** of long bones by subperiosteal apposition and resorption at the internal circumference causing **tubular shape of long bones**

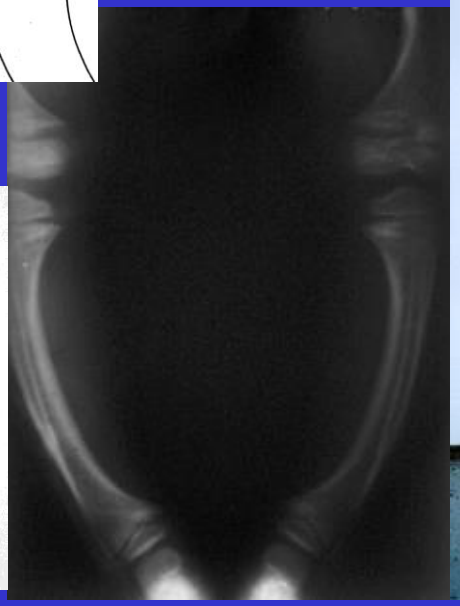


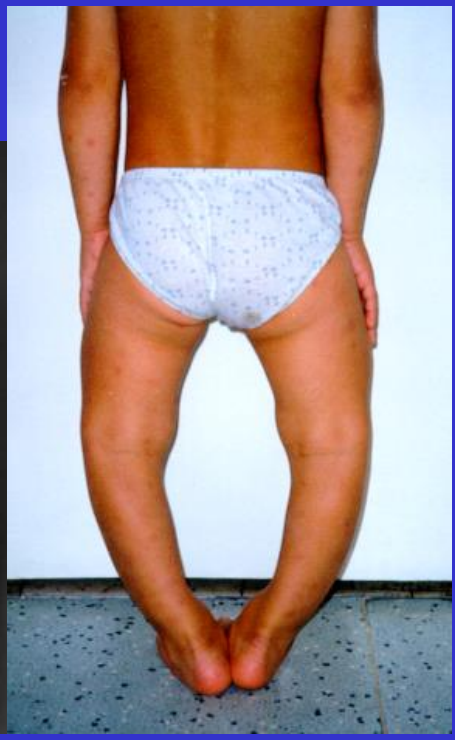








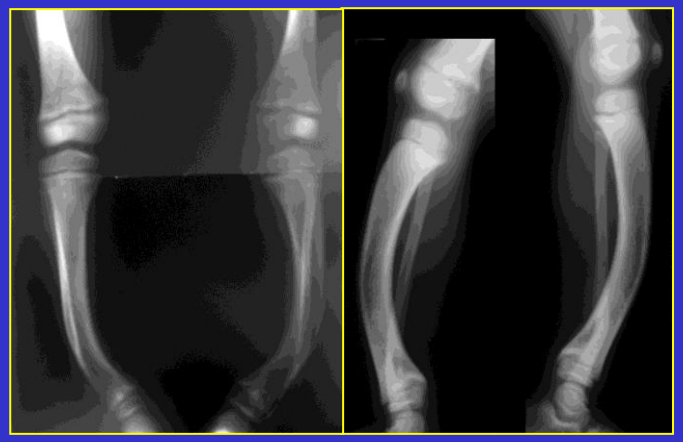


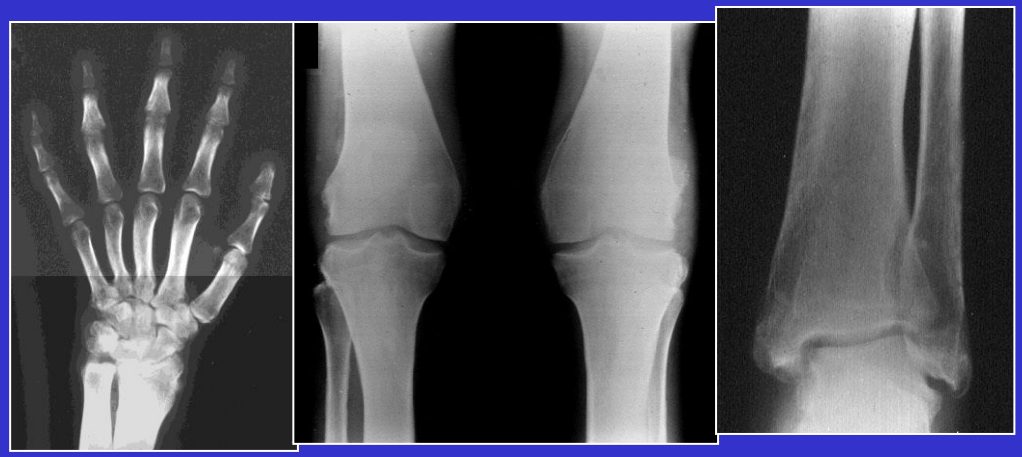


Functional adaptation of bones

Results

- **2. abnormal changes of cross-sectional areas** of long bones by subperiosteal apposition of new bone tissue at the external circumference and resorption at the internal circumference causing **tubular shape of long bones** (e.g. rickets, genetic rickets especially **hypophosphatemic rickets, pachydermoperiostosis**, severe types of osteogenesis imperfecta).





- The decrease in the resistance to deformation is often compensated by apposition of bone tissue on the external bone surface (e.g. in children with different forms of **rickets**). This increases the resistance of long bones to torsion and bending (Sobotka, Mařík 1994).

Functional adaptation of bones

Results

- **3. narrowing, displacement and vanishing of medullary canal** of patients with **osteogenesis imperfecta** that enable compensation by **lateral drift** of lower quality to resist loading and deformation. This phenomenon and so-called shepherd´s crook and sabre-like deformities were observed in severe - deforming types of osteogenesis imperfecta.

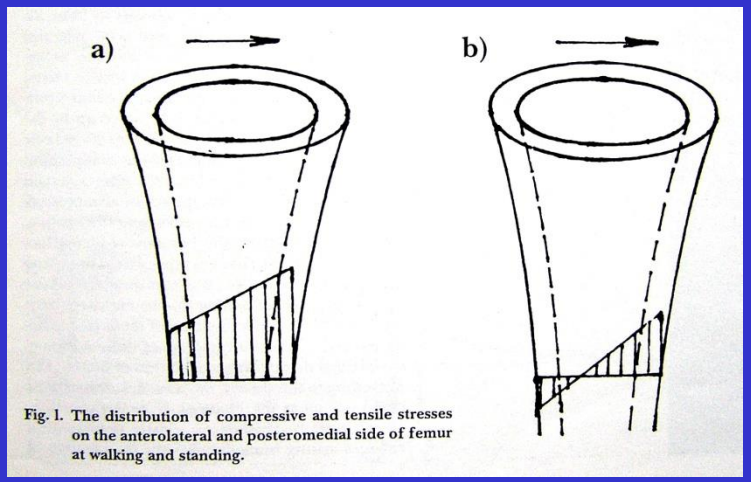
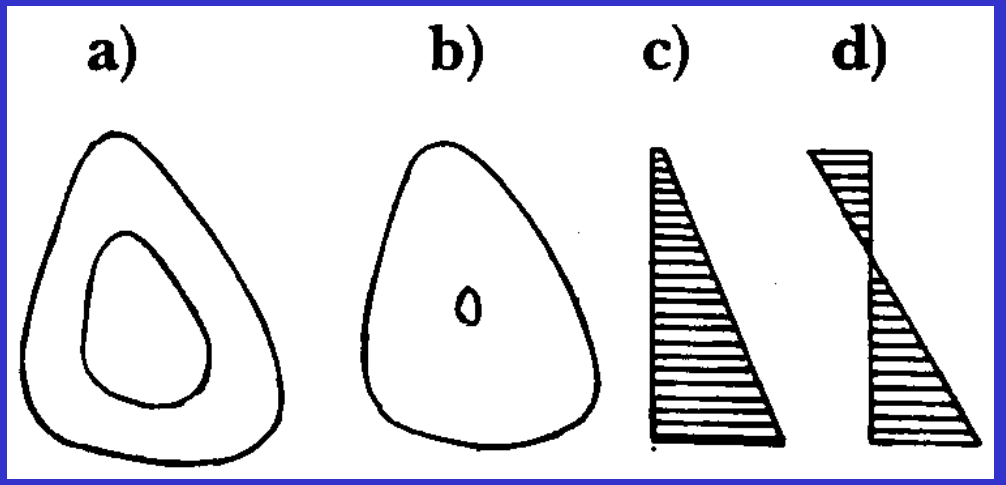


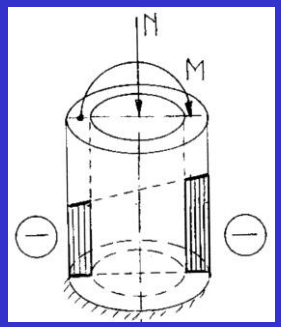
Fig. 1. The distribution of compressive and tensile stresses on the anterolateral and posteromedial side of femur at walking and standing.

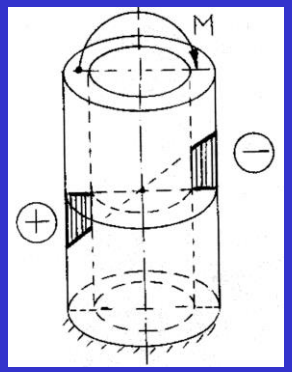


Functional adaptation of bones

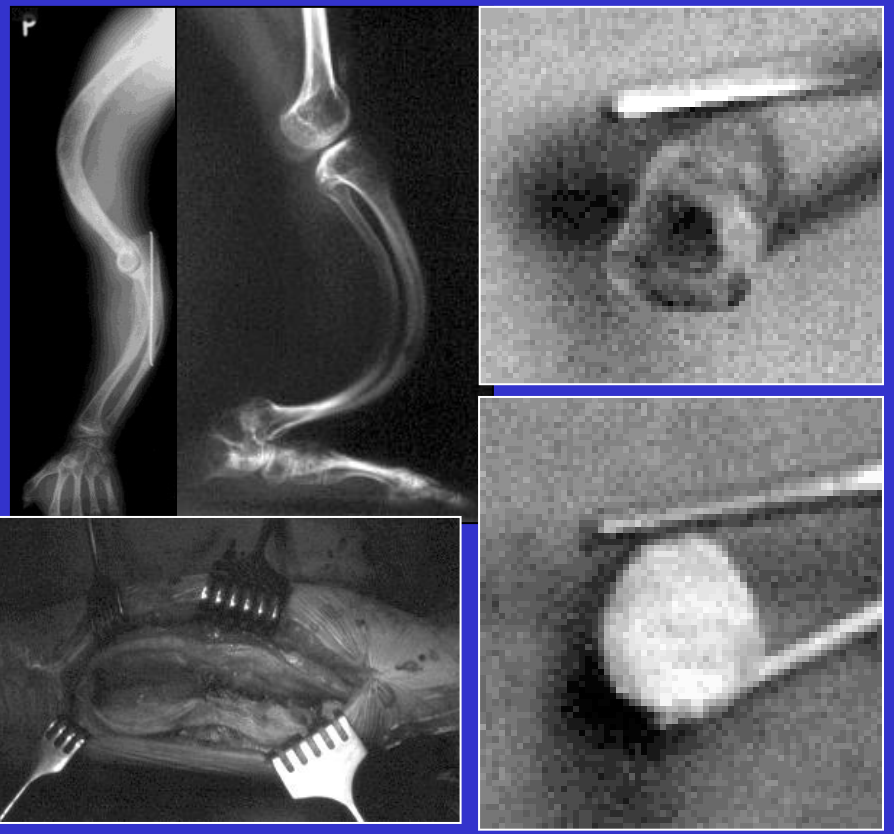
Results

❖ **3. the phenomena of narrowing, vanishing and disappearing of medullary canal** of the long bones of children with different types of **osteogenesis imperfecta ,** i.e. **collagenopathy, type I** cause typical **shepherd´s crook** and **sabre-like deformities**





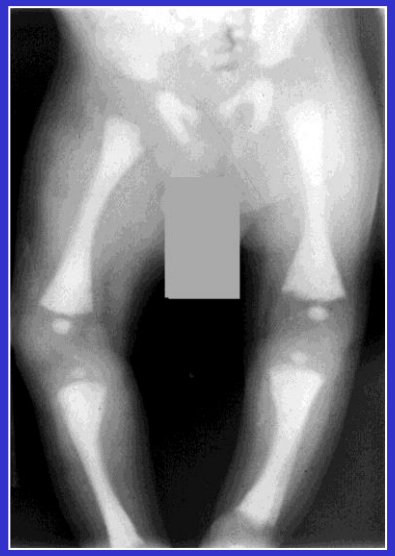
❖ distribution of compressive and tensile stresses on **anterolateral** (left) and **posteromedial** (right) side of femur at **walking** (on top) and **standing** (at the bottom)



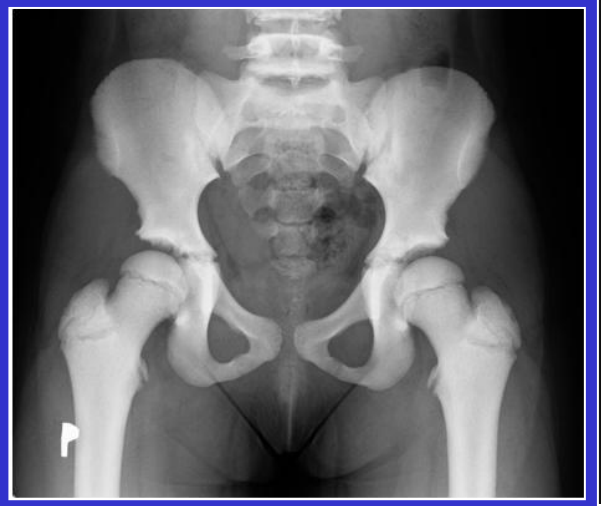
Functional adaptation of bones

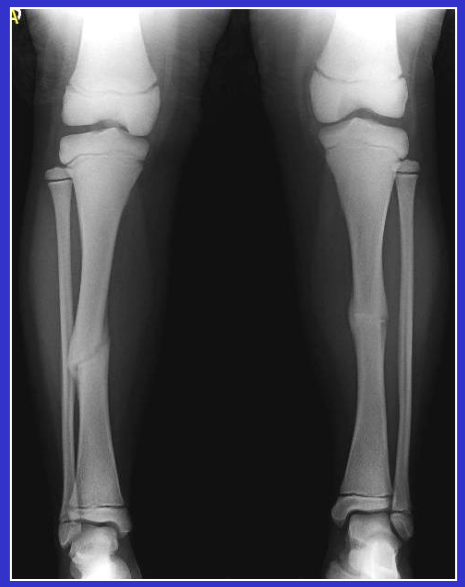
Results

- **4. abnormal modelling of metaphysis and diaphysis** (sclerosing bone dysplasias, multiple exostoses, enchondromatosis, pachydermoperiostosis, etc.)
- An excessive amount of the mineral components involves considerably hardness but also fragility of bones of children with **sclerosing bone dysplasias** (e.g. osteopetrosis) and some people at advanced age. Such bones can carry considerable static loads but they frequently fail by impact.



Infantile osteopetrosis, AR type



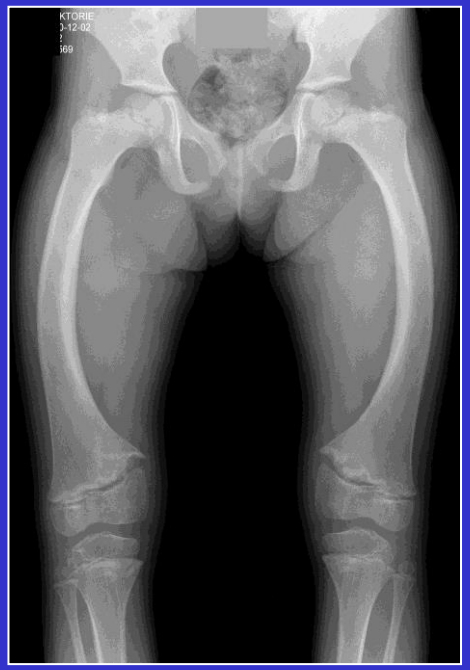


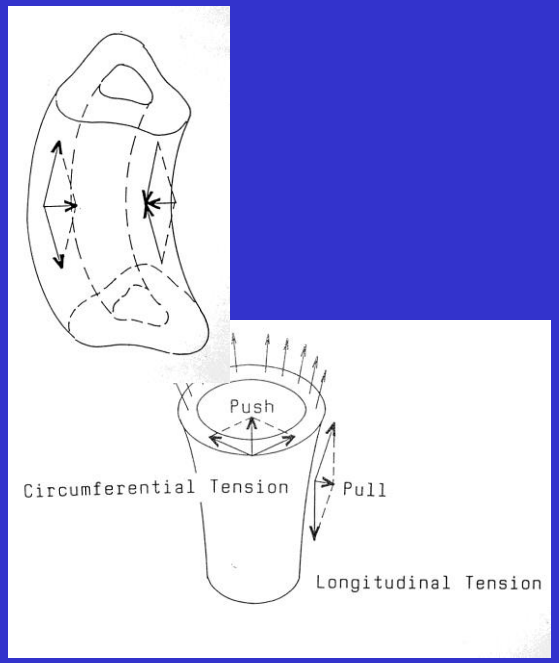
Juvenile osteopetrosis,type II

Functional adaptation of bones
Results

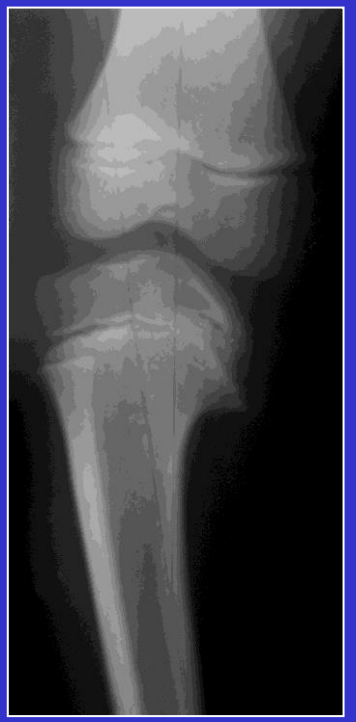
- **5. genetically predetermined oblique growth of epiphyseal plate** (e.g. **metaphyseal dysplasia**, epi-metaphyseal dysplasia,)
- **6. growth retardation localized on medial and/or lateral part of epiphyseal plate** (e.g. **morbus Blount**)

Metaphyseal dysplasia, AD: consequence is incomplete lateral drift & tubular shape of femoral diaphysis





Morbus Blount

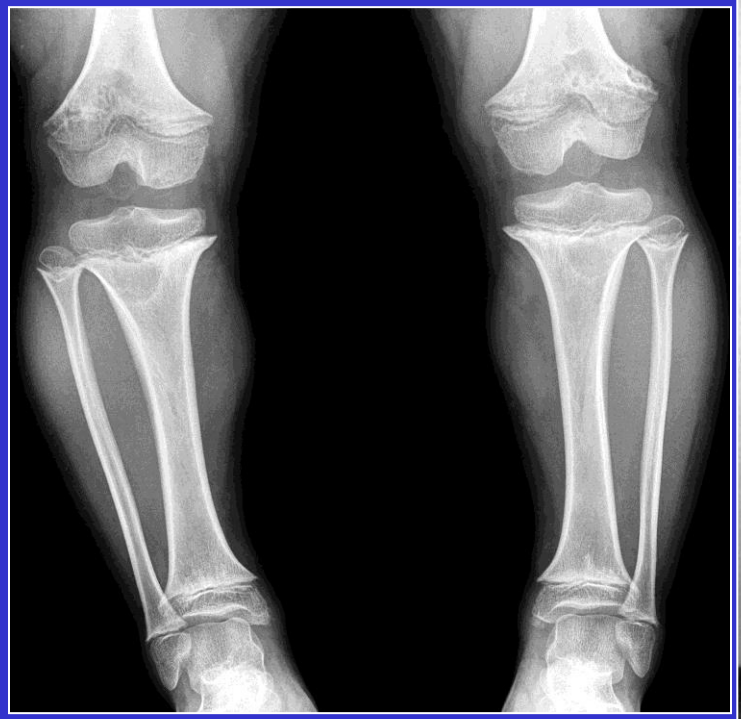


Functional adaptation of bones

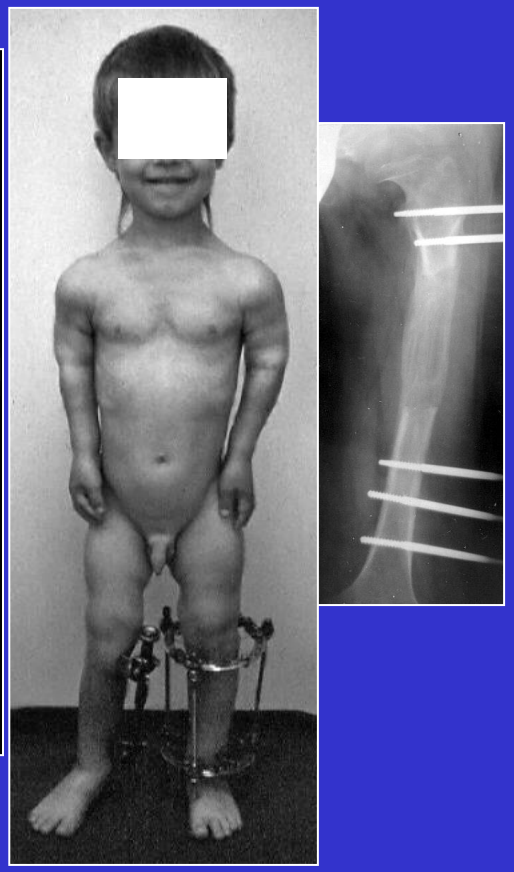
Results

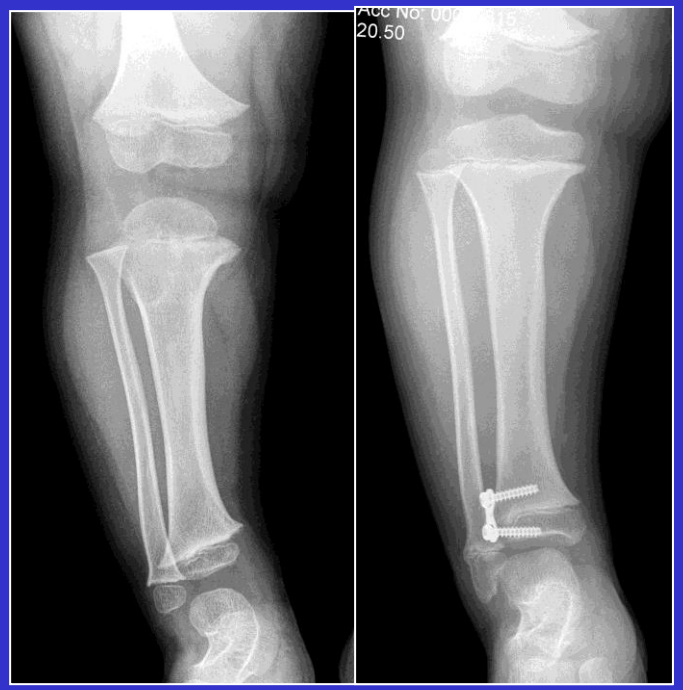
- **7. varosity of shanks due to overgrowth of fibula** (**achondroplasia**, **hypochondroplasia**, pseudoachondroplasia,, etc.)

  Consequence of fibula „overegrowth“



Achondroplasia



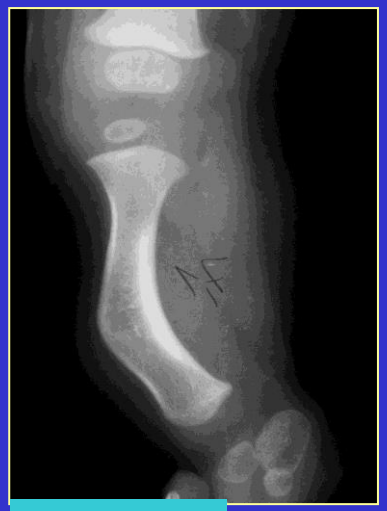


Hypochondroplasia

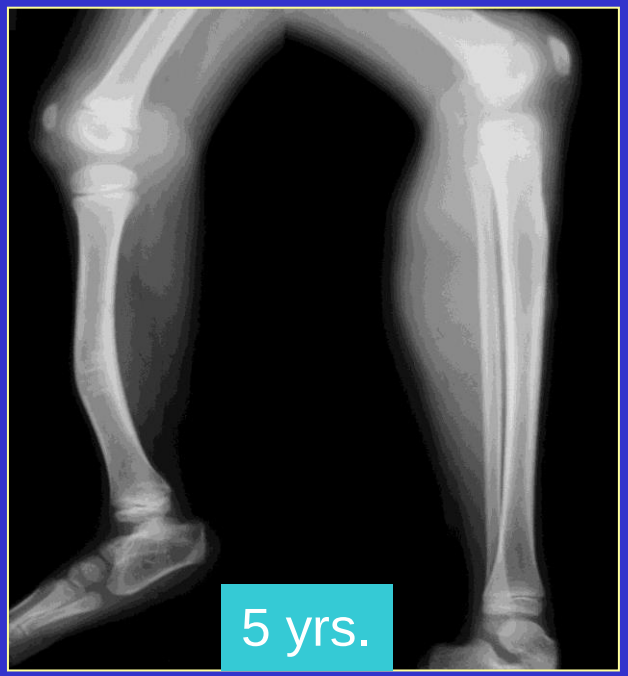
Functional adaptation of bones

Results

- **8. anteromedial angulation of tibia at fibular hemimelia**, type 2 due to fibular fibrocartilage (anlage).

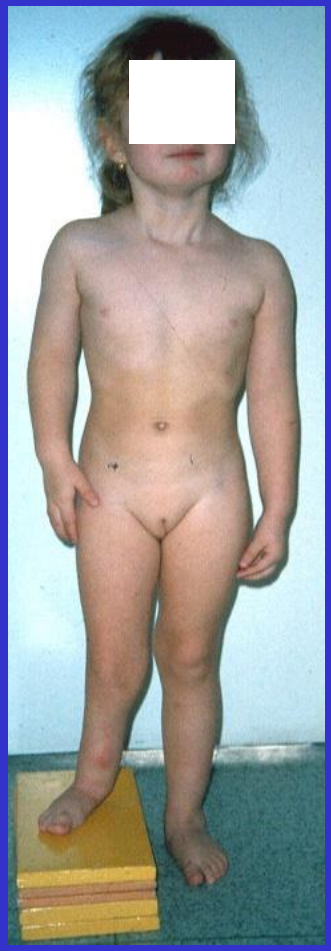


1 year



5 yrs.

Fibular hemimelia, type 2

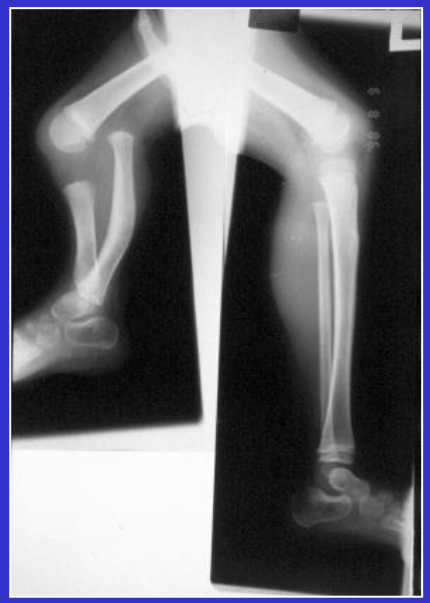


Functional adaptation of bones

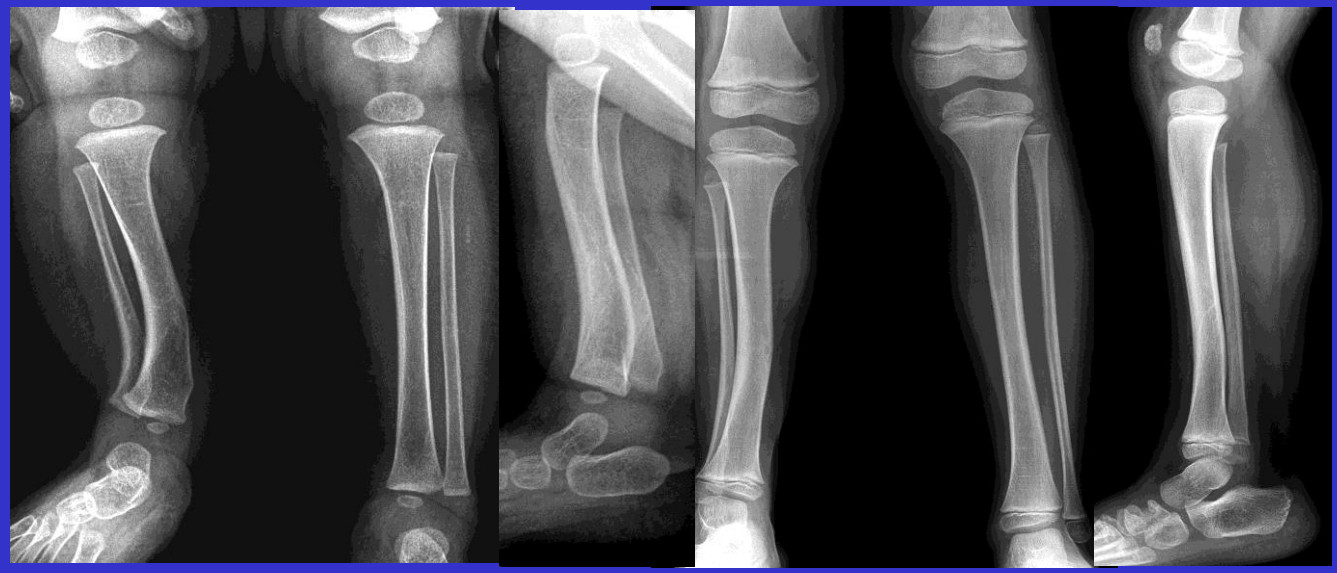
Results

- **8. partial tibial aplasia – „tibalisation“ of fibula**
- **9. congenital posteromedial bowing of tibia**

Partial tibial aplasia, type 3B



Posteromedial bowing of tibia

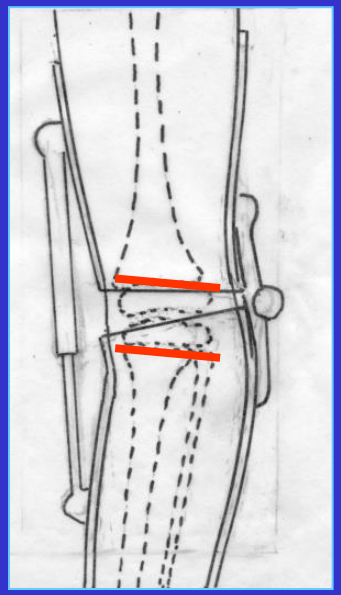


3 yrs.

8 yrs.

Utilization of the functional adaptation of bones in orthotic treatment

Orthotic treatment which is based on the three point balanced principle that takes advantage mainly of the 3rd fundamental mechanism of functional adaptation of bones – i.e. according to **Hüter and Volkmann law** the physis creates a new bone tissue into axial pressure direction (central line).



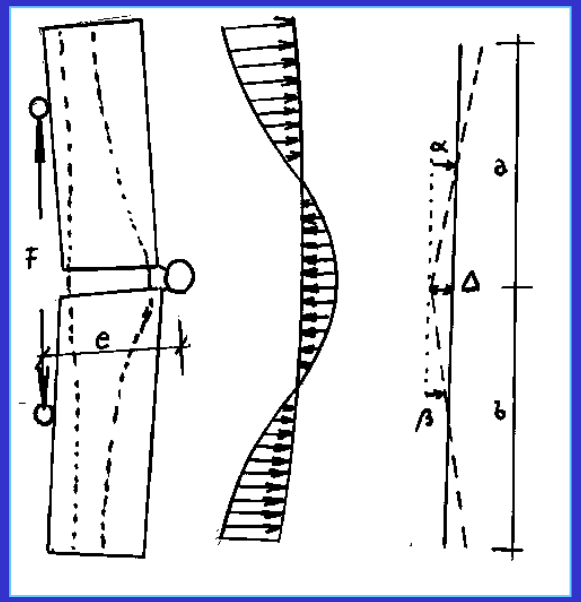
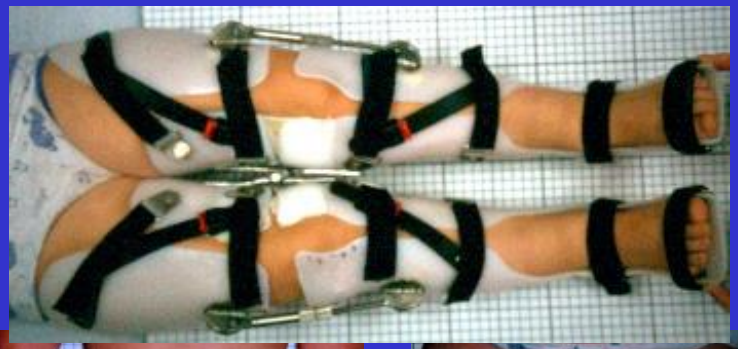


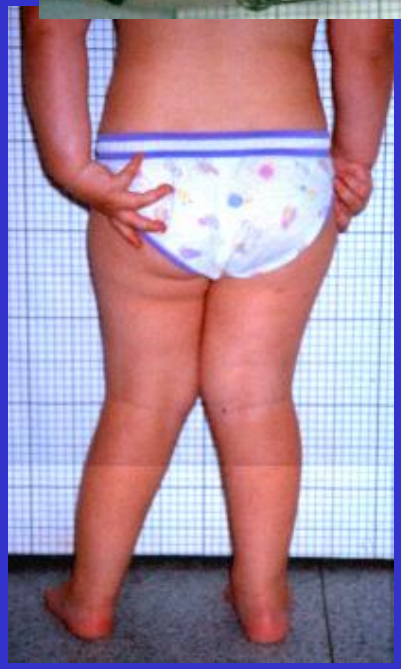
Fig. Force effect of orthosis by the three point principle causing bending pre-stressing. The result is the growth of long bone – physis - into the direction of the pressure resultant

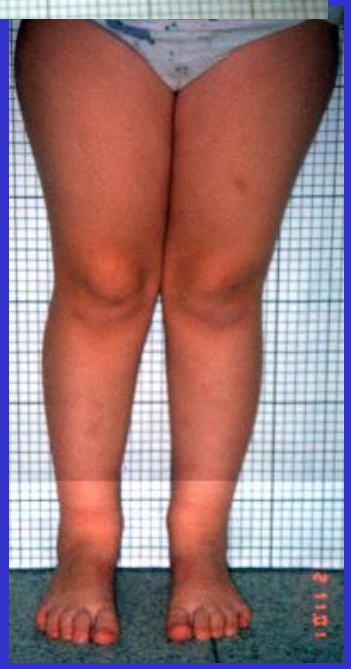
(Čulík and Mařík 2001)

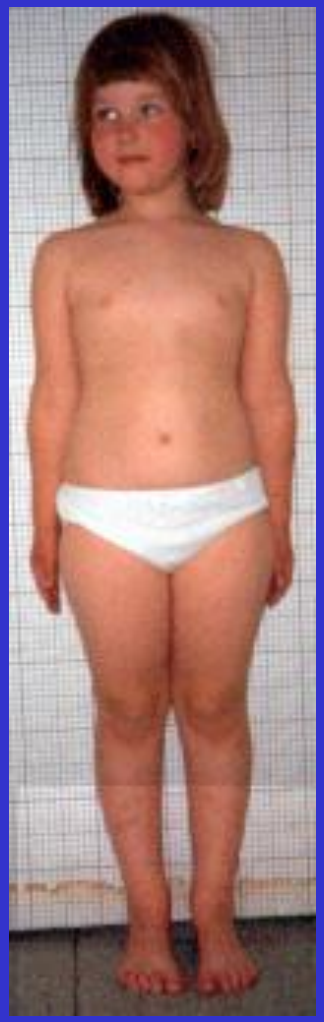
Utilization of the functional adaptation in orthotic treatment

„Idiopathic“ valgosity of knee joints: 3 yrs. girl, obesity (> 97.P), hyperlaxity, high bone turnover

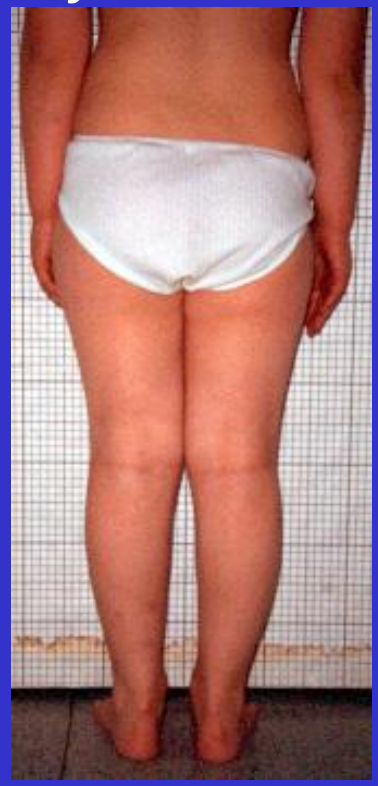






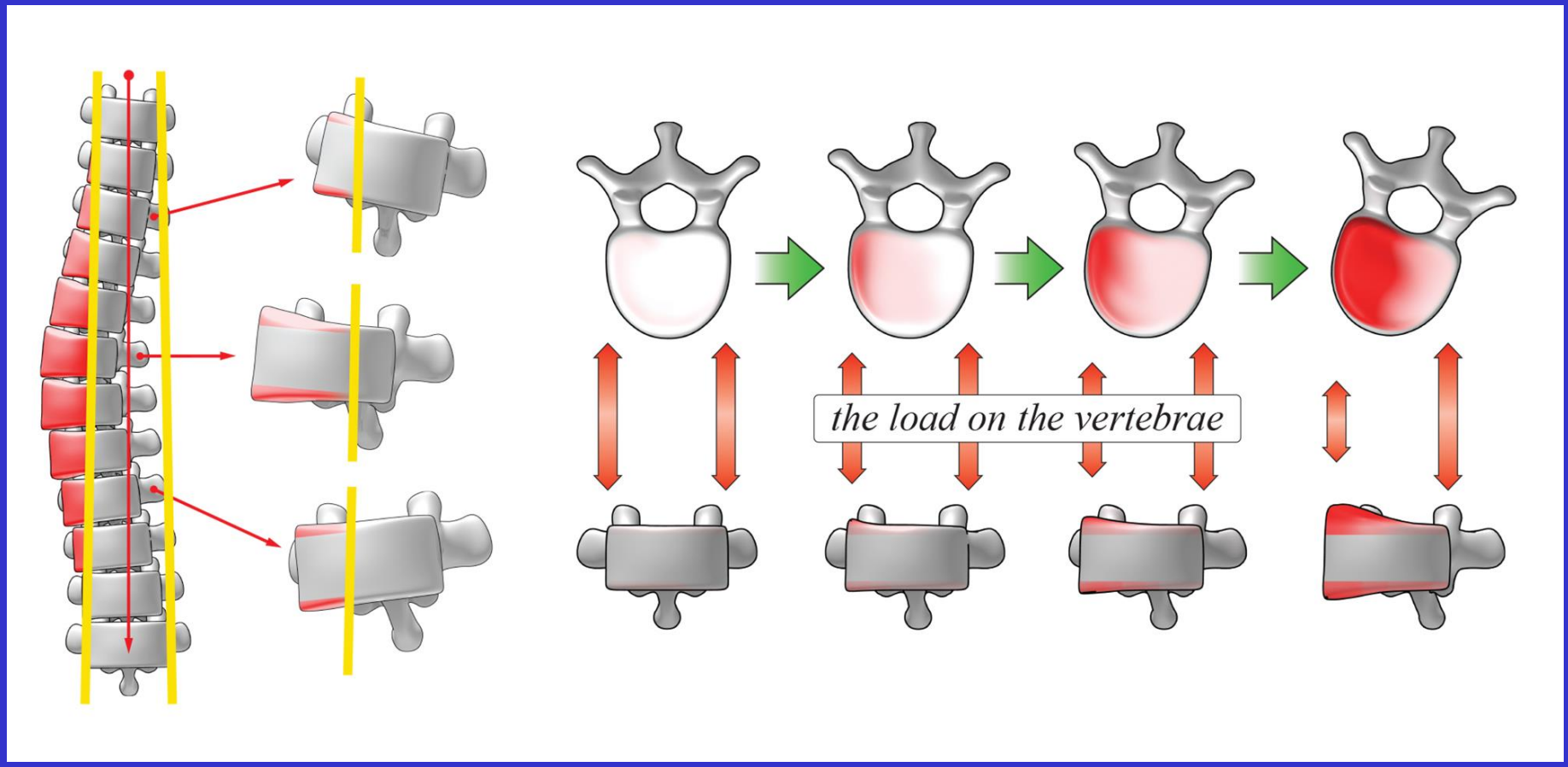


5 yrs.



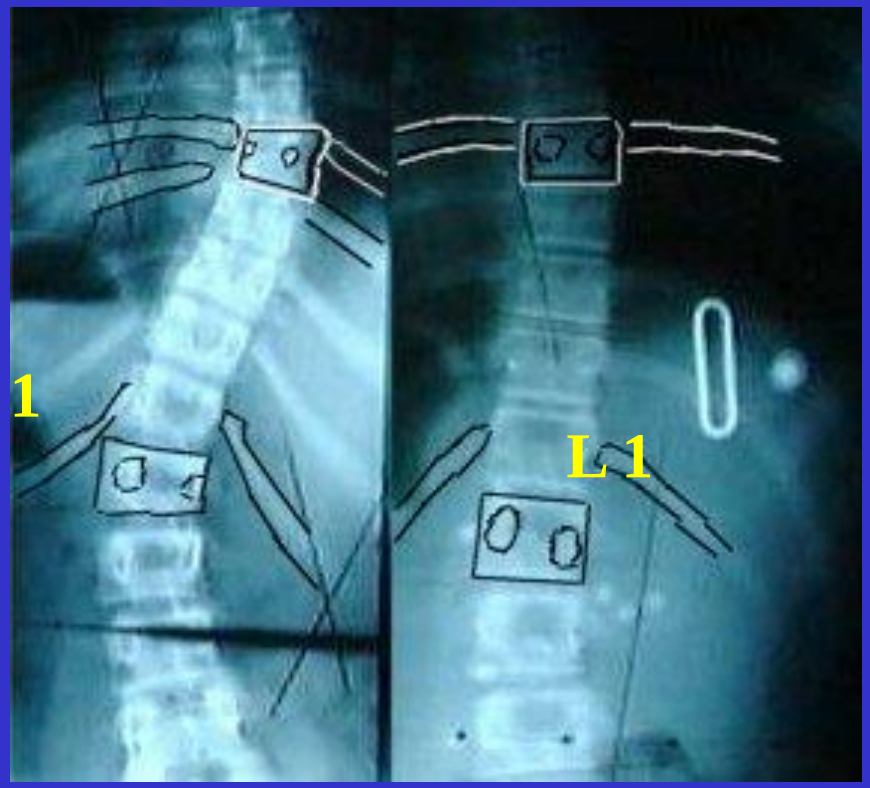
Utilization of the functional adaptation of bones in bracing of scoliotic patients

Mikhail Dudin et al. 2015. **Hüter-Volkmann´s Law** clarifies abnormal – pathologic wedging of vertebral bodies



Utilization of the functional adaptation of bones in bracing

Hüter-Volkmann´s Law use during **structural** idiopathic scoliosis correction by bracing



Corrected scoliosis by bracing

- disappearing of:

scoliosis

rotation

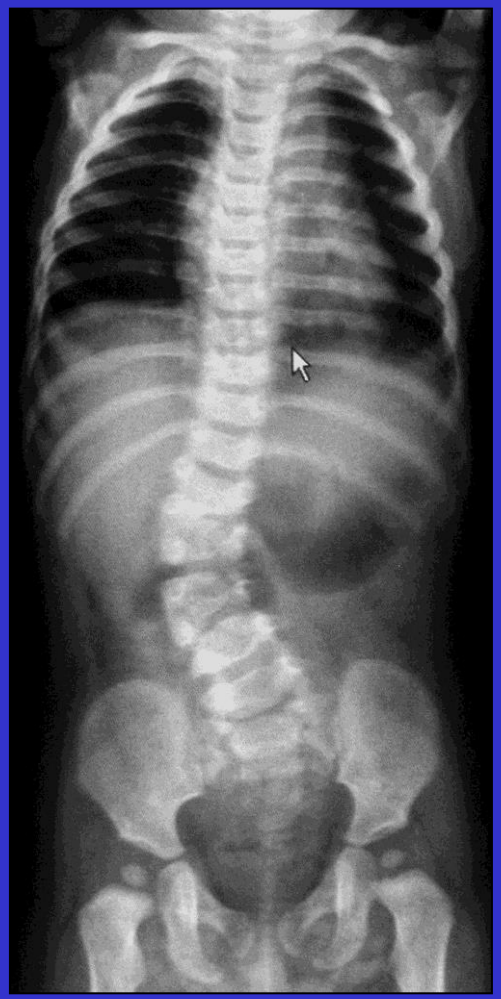
oblique inclination of ribs

wedging of vertebral bodies

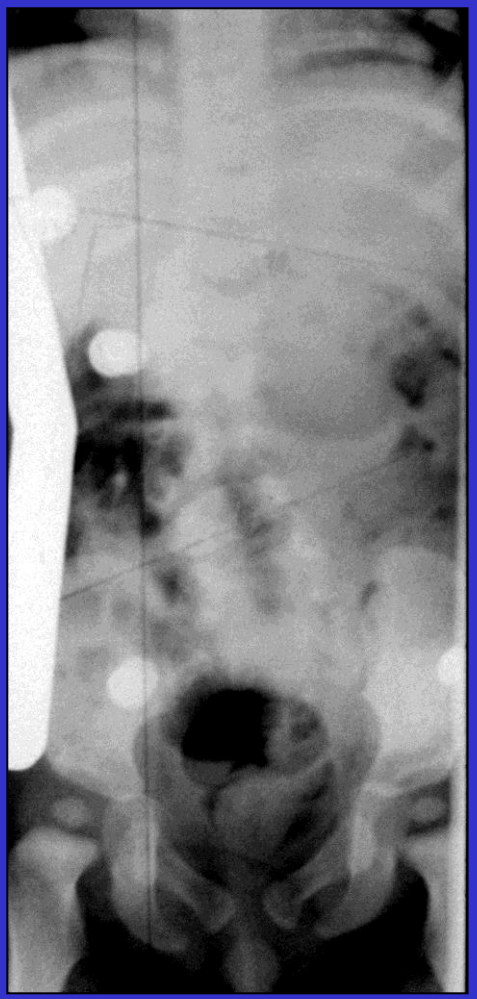
Utilization of the functional adaptation of bones in bracing

Hüter-Volkmann´s Law use during **congenital** scoliosis correction by **special brace with regulated force effect**

Hemivertebra L2 & L5 on right side



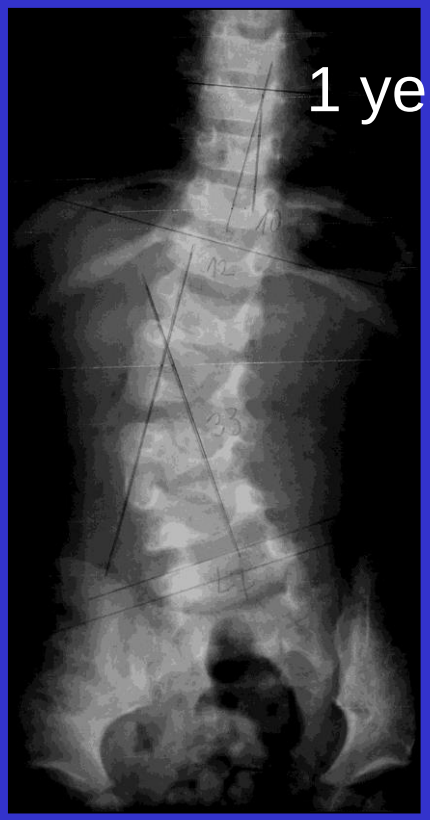
14 mo.



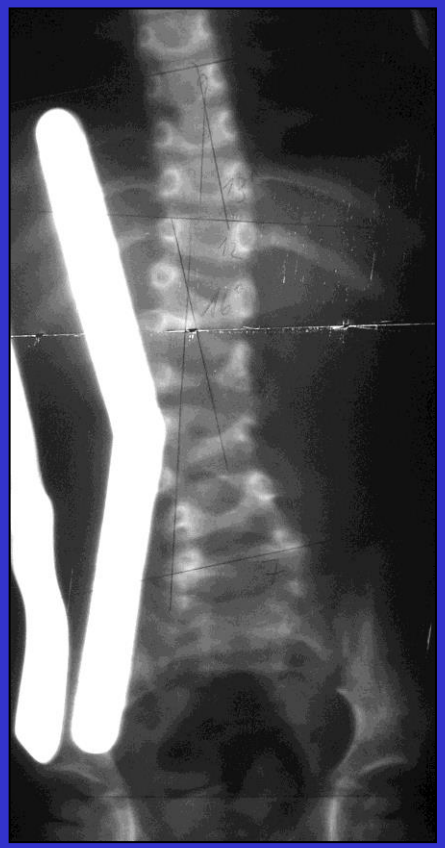
Utilization of the functional adaptation of bones in bracing

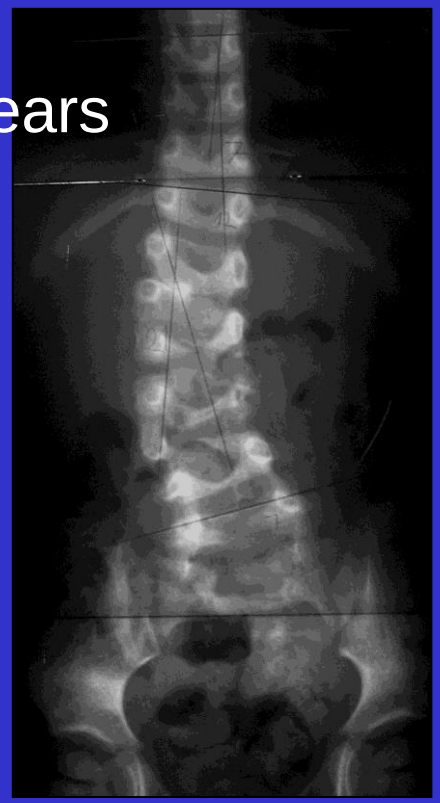
Hüter-Volkmann´s Law use during hemivertebra L2 & L5 correction by **special brace with regulated force effect**

Correction of Cobb´s angle on 12° after 20 months of bracing



T12 - 33°dx - L7



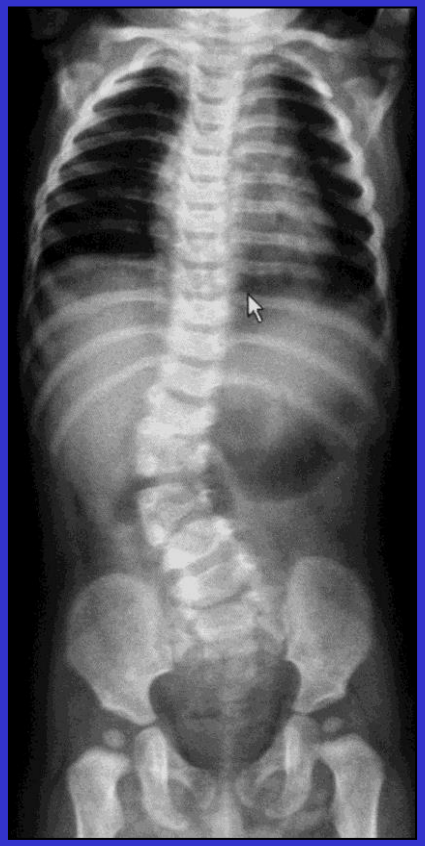


T12 - 21°dx - L7

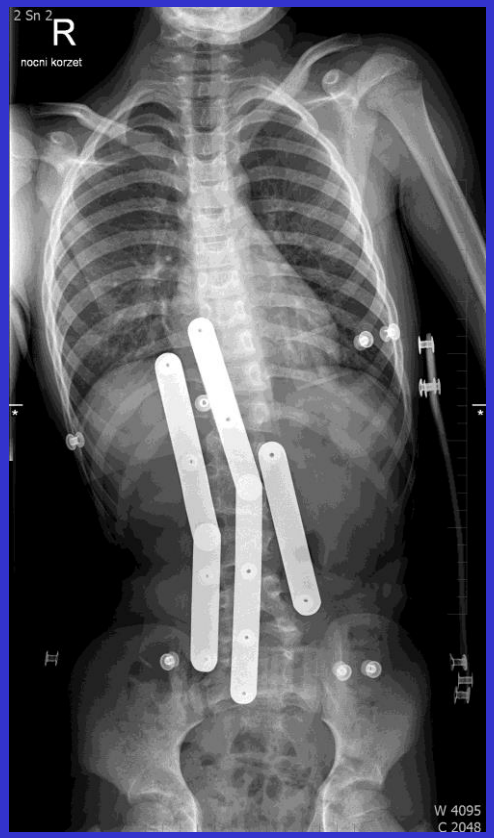
Utilization of the functional adaptation in bracing

Hüter-Volkmann´s Law use during hemivertebra L2 & L5 correction by **special brace with regulated force effect**

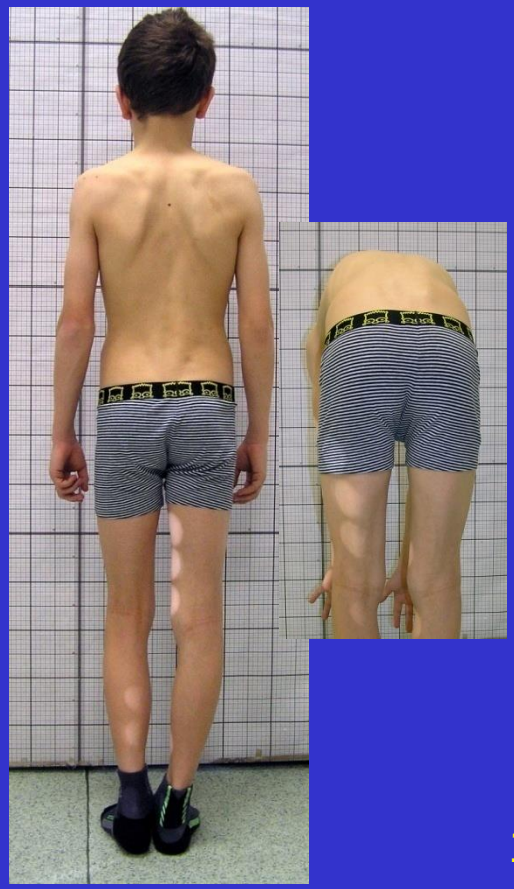
Correction of Cobb´s angle on 15° after 10 years of bracing

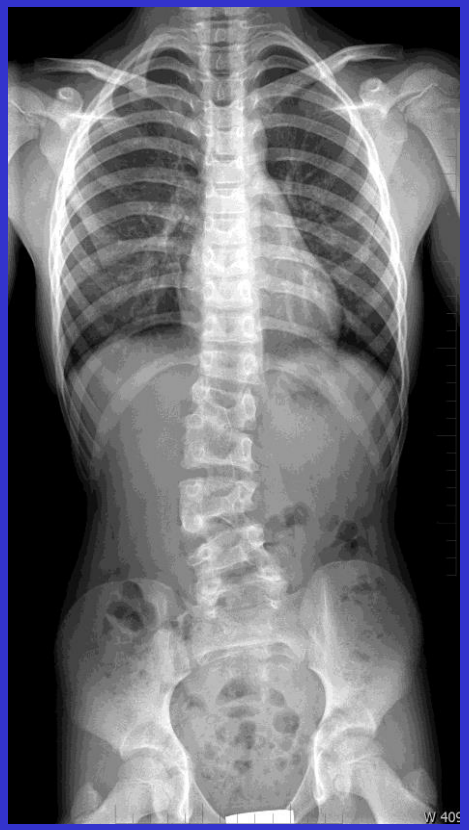


1 rok: T12 - 33°dx - L7



11 let: T12 - 8°dx - L7



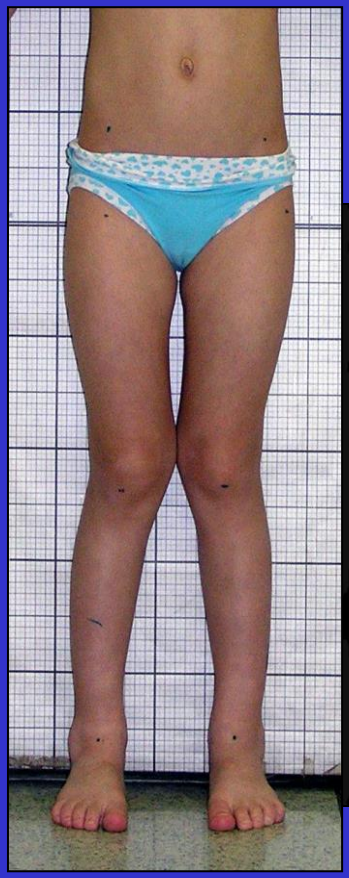


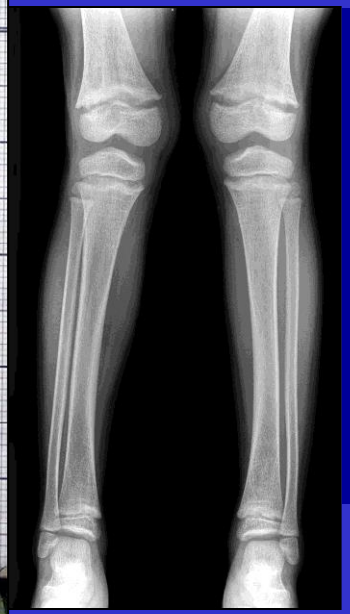
11 let: T12 - 18°dx - L7

Utilization of the functional adaptation during partial epiphysiodesis

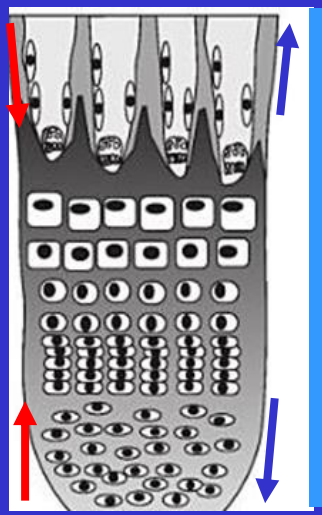
Hüter-Volkmann´s Law use during 8 plate „guided growth“

7 years girl with **hypophosphatemic rickets -** correction during 12 months

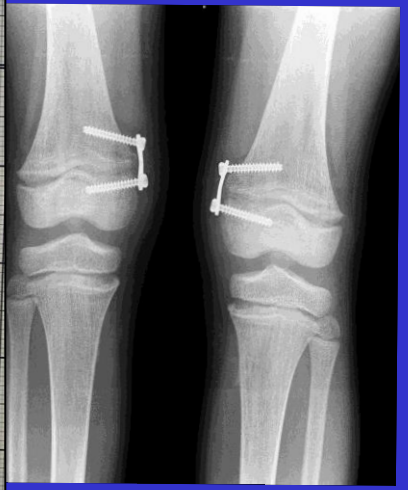




stress causes restriction of growth



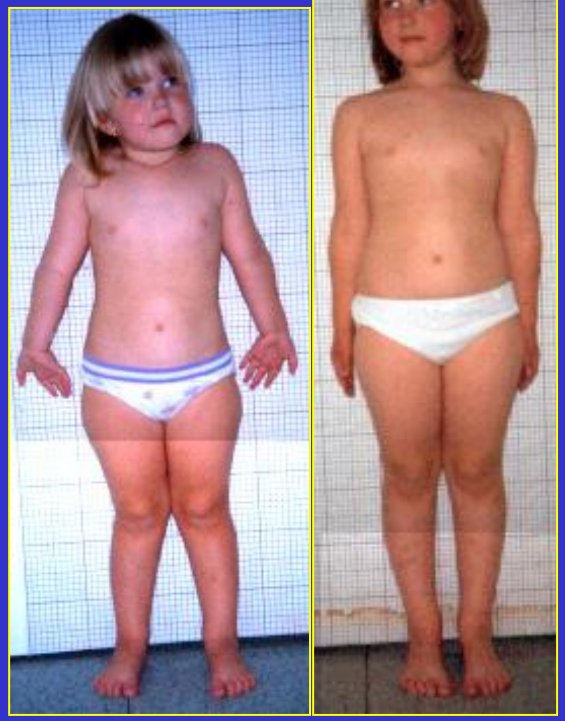
unloading of physis accelerate growth



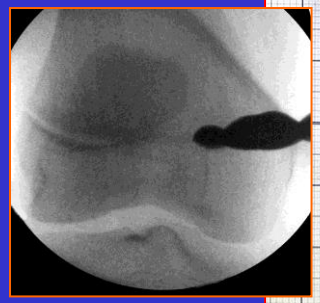
Utilization of the functional adaptation during partial drilling epiphysiodesis

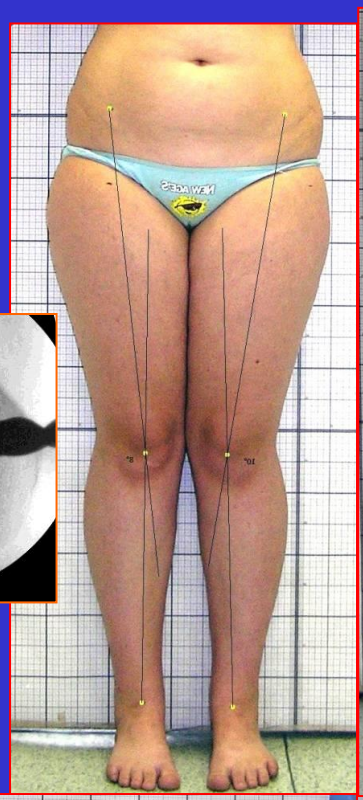
„Idiopathic“ valgosity of knee joints:
13.5 yrs. girl, obesity, hyperlaxity
Right: **result of drilling** medial partial epiphysiodesis of distal femur bil.

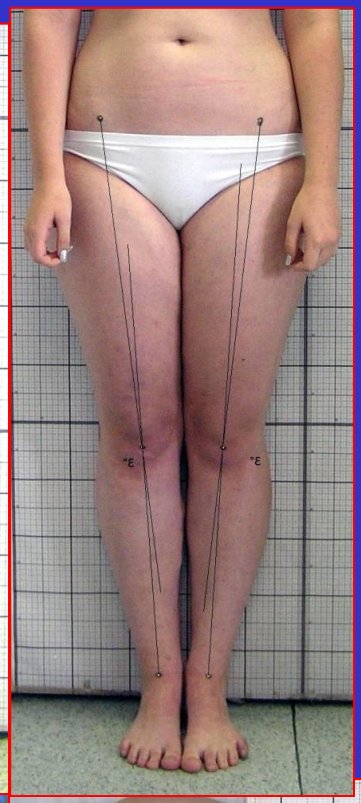
3 yrs.



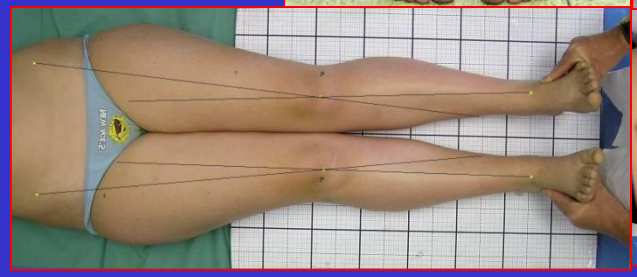
5 yrs.







13.5 yrs.



15 yrs.

Functional adaptation of bones

Discussion

- The described fundamental laws of bone remodelling secure healthy organism an ability to **adapt shape and solidness of skeleton to varying living condition.**
- In patients with some **GSD** and **bone dysplasias**, the modelling and remodelling, bone resorption and apposition (it means function of osteoclasts, osteoblasts and osteocytes) are in some way abnormal – attenuated and/or accelerated
- Abnormal shape and above described deformities of skeleton in individuals with bone dysplasias are results of modelling and remodelling of genetic predetermined pathologic bone tissue (due to contain as abnormal collagen chains and proteoglycans as disorders of calciophosphate metabolism, etc.) with **abnormal material properties**.

Functional adaptation of bones

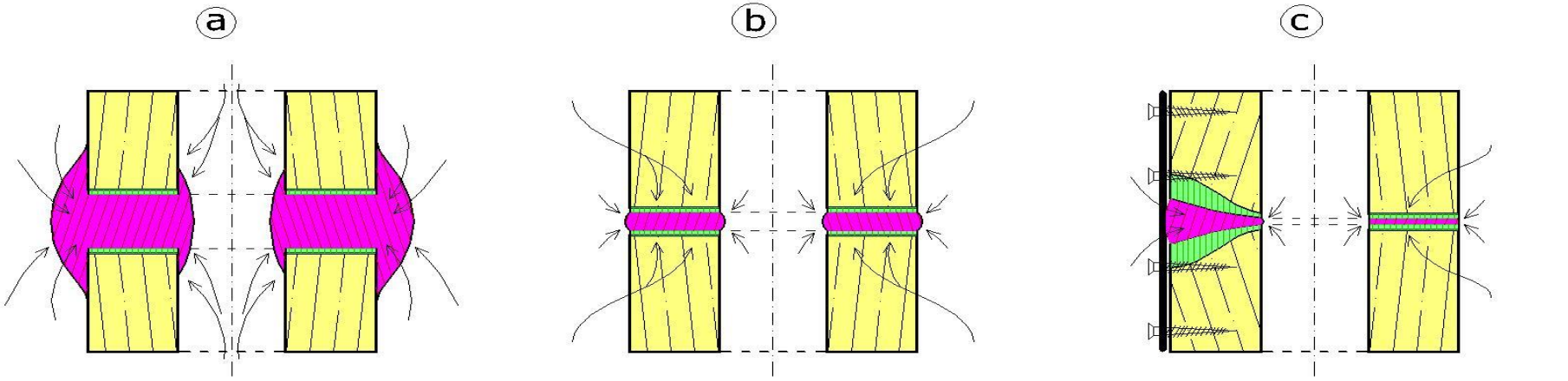
Conclusions

- At various genetic skeletal disorders (bone dysplasias, etc.), the **functional adaptation of bones is affected in different levels**, from the normal course to the pathological one. The remodelling is genetically predetermined. In these cases we observe various deformities of the skeleton.
- Orthotic treatment which is based on the three point balanced principle takes advantage of the three fundamental mechanisms (laws) of functional adaptation of connective tissues.
- We have many years ongoing experience with treatment of spine deformities by bracing and knee and shank deformities by orthosis with bending pre-stressing and/or by surgical method so-called guided growth. Both methods of **orthotic and surgical treatment** use **Hüter-Volkmann law** i.e. the **3rd mechanism** of functional adaptation of bones.
- efficiency of **orthotic treatment** and **physiotherapy** on remodelling of locomotion system is explained by **deformation-rheological theory** (Sobotka & Mařík, 1993)

Děkuji za pozornost = Thanks for your attention

Řízená remodelace u systémových vad v období růstu

Klasifikace tří základních druhů hojení svalkem

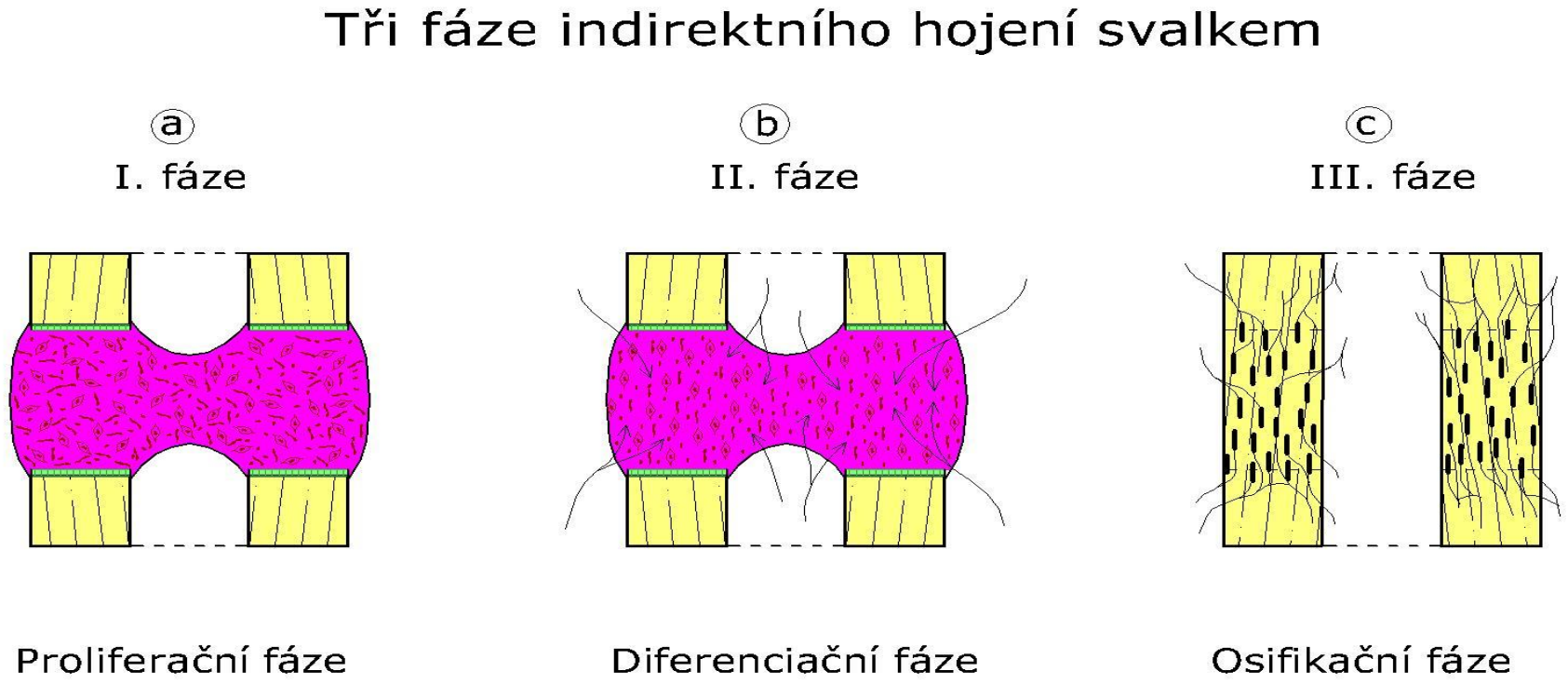


Indirekní (nepřímé) hojení svalkem

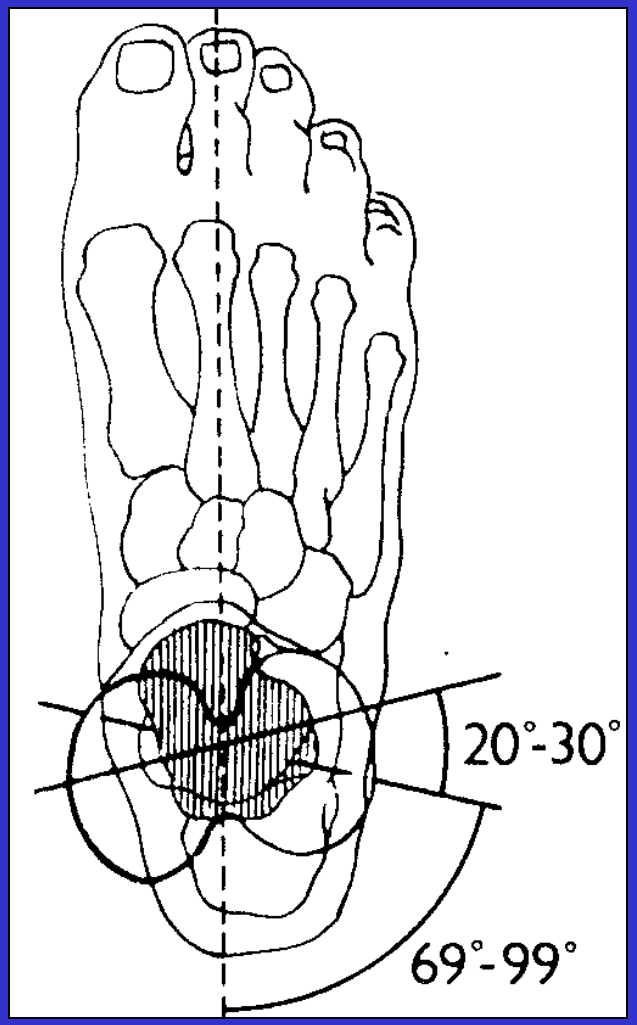
Direktní (přímé) hojení svalkem

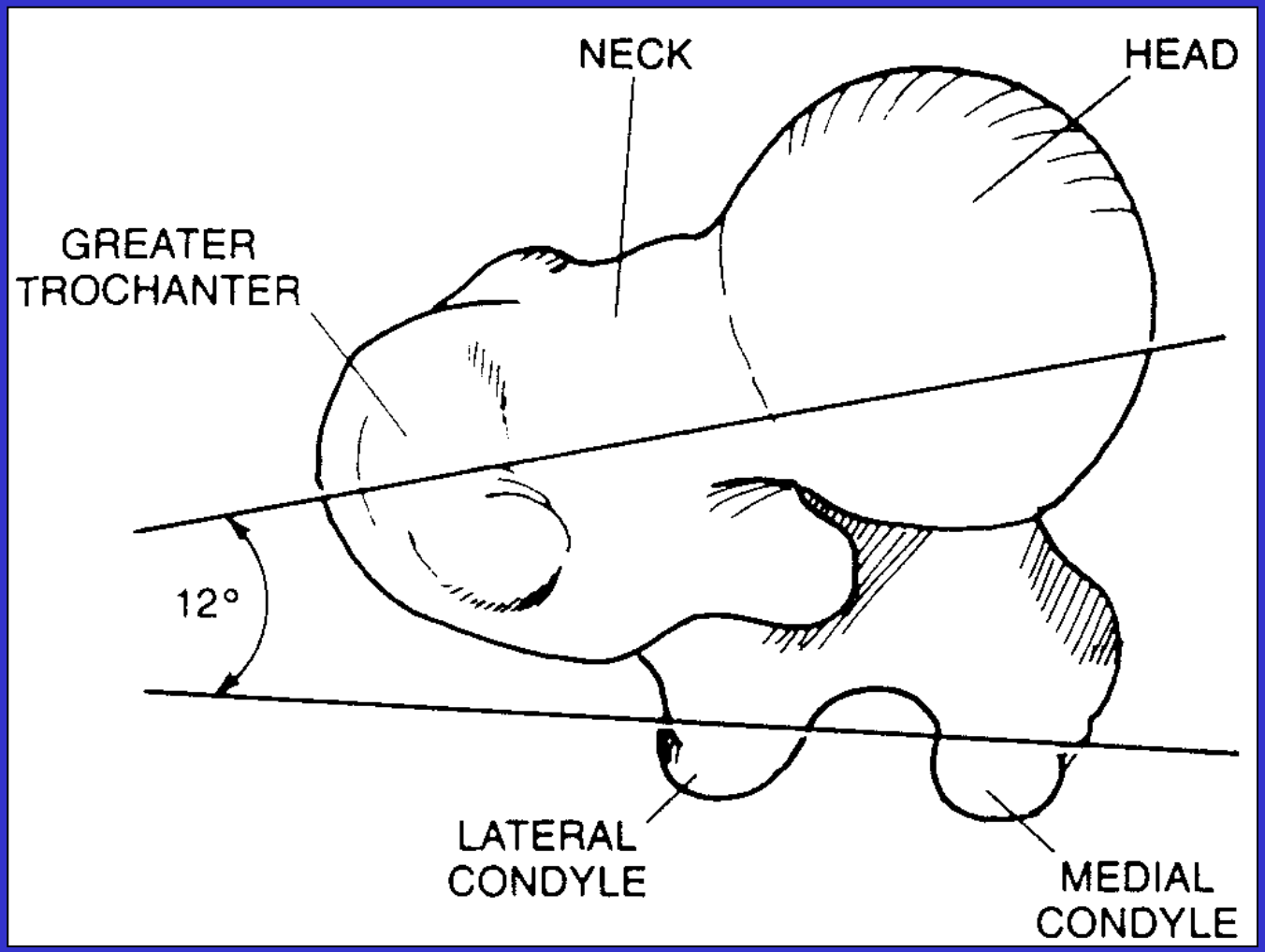
Angiogenní (štěrbinové) hojení svalkem

Řízená remodelace u systémových vad v období růstu



OPERAČNÍ & ORTOTICKÉ LÉČENÍ





Řízená remodelace u systémových vad v období růstu