6th International Anthropological Congress of Dr. Ales Hrdlicka 150TH anniversary of birth.
"All mankind is of one origin"

INTERDISCIPLINARY COLLABORATION IN THE STUDY OF THE CHILDREN'S MUSCULOSKELETAL SYSTEM: facts, reflections, conclusions.

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HUMPOLEC 2019

INTERDISCIPLINARY COLLABORATION IN THE STUDY OF THE CHILDREN'S MUSCULOSKELETAL SYSTEM

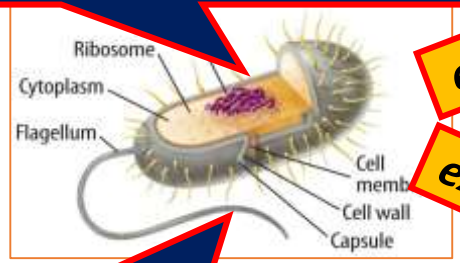
INTRODUCTION

EVOLUTION OF THE MUSCULOSKELETAL SYSTEM

The MUSCULOSKELETAL SYSTEM (MSS) or the LOCOMOTOR SYSTEM (LMS), is the BASIS of ALL LIFE on EARTH

First support is the cell plasma membrane (≈4 billion years ago, the first non-nuclear cells – prokaryotes)

*Futuyma D.J. **Evolution**. 2nd ed. 2009. Sinauer Associates, Sunderland, Massachusetts.*



The first motor mechanism is the plasma membrane flagellum

endoskeleton

exoskeleton

2.5 million years ago (on evolutionary time – 2 seconds) the mankind was "created" and "put on feet"

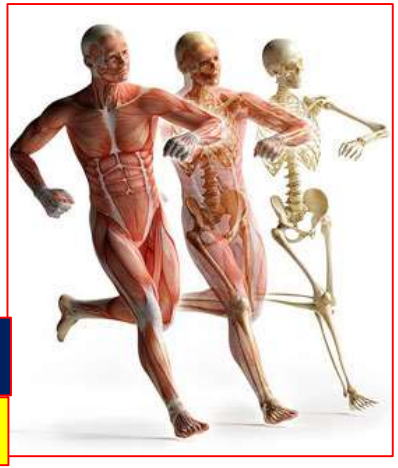
TASKS OF THE MUSCULOSKELETAL SYSTEM

MSS or LMS is an INTEGRAL PART of the HUMAN ORGANISM

Support & Protection

Mobility

“Fight-or-Flight”



Metabolic

”Collection, Storage and Distribution” of chemical elements necessary for life

The dry residue of inorganic matter contains: calcium, phosphorus, magnesium, aluminum, fluorine, manganese, plumbum, strontium, iron, potassium, zinc, barium, lithium etc.

The dry residue of the organic matrix consists of proteins (collagen), carbohydrates, fats etc.

INTERDISCIPLINARY COLLABORATION IN THE STUDY OF THE CHILDREN'S MSS

PART ONE

WHAT DO WE ALREADY KNOW ABOUT MSS?

THROUGH the PRISM of HISTORY

INTERDISCIPLINARY COLLABORATION IN THE STUDY OF THE CHILDREN'S MSS

CLASSIC ANATOMY (Anc. Gr. Ἀνα + Τέμνω) is the OLDEST METHOD of RESEARCH MSS

The BASIS of KNOWLEDGE ABOUT the CLASSICAL ANATOMY of MSS has gone from ALKMEON of Croton to SORANUS of Ephesus, from GALEN of Pergamon to Briton William GARVEY, from a SIMPLE DESCRIPTION to the TOPOGRAPHIC ANATOMY of Nikolas PIROGOV.

Alkmaion** (6th – 5th c. BC) from **Croton

Soranus** (98-138) from **Ephesus

***Galenus** (129-217) from **Pergamon**. His manuscript "**On the designation of parts of the human body**" for 14 centuries were the main sources of basic medical anatomy knowledge*

***William Harvey** (1578-1657)*
***Nikolay Pirogov** (1810-1881)*


Ἀλκμαίων


Soranus


Galenus


Harvey

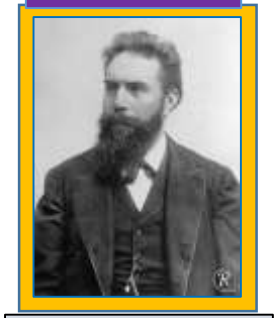

Pirogov

INTERDISCIPLINARY COLLABORATION IN THE STUDY OF THE CHILDREN'S MSS

MODERN ANATOMY – NONINVASIVE TECHNOLOGY

X-ray, CT and MRI DIAGNOSTICS

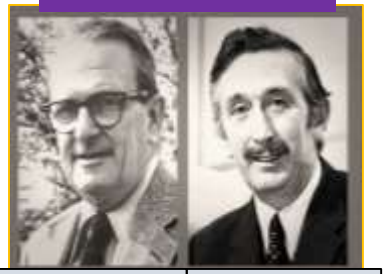
X-ray ANATOMY



Wilhelm Conrad Röntgen, 1845-1923

First Nobel Prize 1901

COMPUTER TOMOGRAPHY /CT/



Godfrey Newbold Hounsfield, 1919-2004

Allan McLeod Cormack, 1924-1998

Nobel Prize 1979

MAGNETIC RESONANCE IMAGING /MRI/

Paul Christian Lauterbur, 1929-2007

Sir Peter Mansfield, 1933-2017

Nobel Prize 2003

INTERDISCIPLINARY COLLABORATION IN THE STUDY OF THE CHILDREN'S MSS

MODERN ANATOMY – NONINVASIVE TECHNOLOGY

ULTRASOUND DIAGNOSTICS

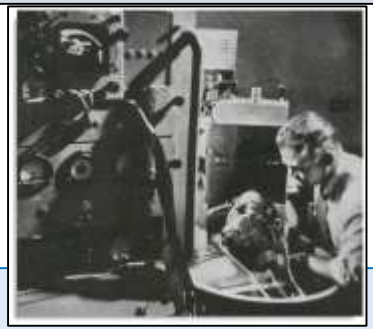
The **PHYSICAL BASIS of the METHOD** - opened in 1880 by the **Curie Brothers** (*Paul-Jacques /1856-1941/ and Pierre /1859-1906/*) piezoelectric effect arising in quartz crystal under mechanical action.

After 2 years, the reverse process was obtained - the generation of sound in a crystal under electrical influence.

Brothers Paul-Jacques and Pierre Curie

Karl Theodore Dussik, 1908-1968

For the first time the effect of different tissue echogenicity was used in 1947 by a psychoneurologist from Vienna K.T. Dussik for the diagnostics of brain tumors.

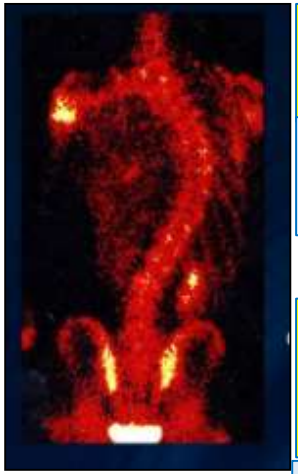


The first device /somascope/ for medical ultrasound scanning designed in 1949 by Douglass Howry /USA/.

INTERDISCIPLINARY COLLABORATION IN THE STUDY OF THE CHILDREN'S MSS

OSTEOSCINTIGRAFY

DIAGNOSTICS of INTRAVITAL /in vivo/ FUNCTIONAL STATE of BONE TISSUE



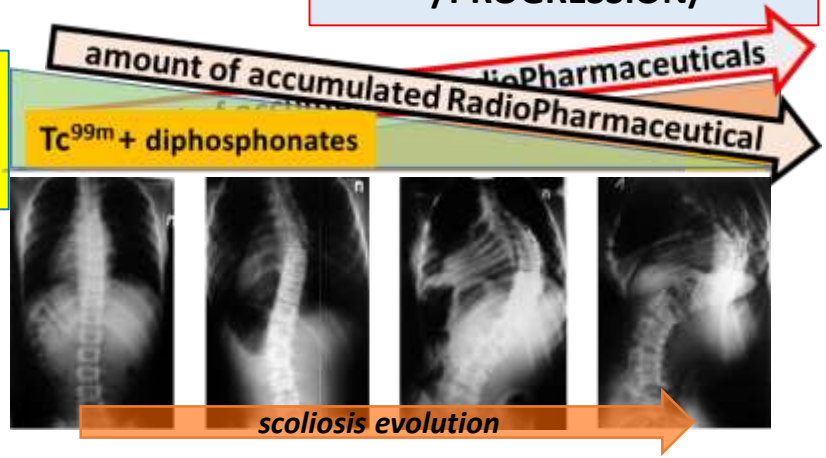
In the 70^{s} of the XXth century – Sr^{85} (T1/2 - 64 days).

RPhP acceptor – Hydroxylapatite crystals

Since the 80^{s} of the XXth century – osteotropic diphosphonates + Tc^{99m} (T1/2 - 6.1 hours).

RPhP acceptor – phage row cells (from our point of view)

On the EXAMPLE of the SPINE 3D DEFORMATION ALL VARIANTS of the INTENSITY of OSTEOGENESIS are DESCRIBED CORRELATING with CHARACTER of SCOLIOSIS EVOLUTION /PROGRESSION/

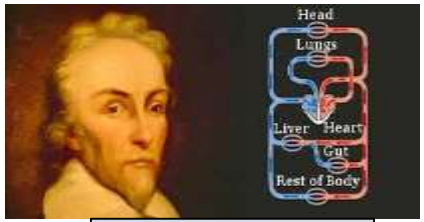


INTERDISCIPLINARY COLLABORATION IN THE STUDY OF THE CHILDREN'S MSS

FUNCTIONS of the MSS

FUNCTIONS (*Lat*. **functio**) **of systems, organs and tissues in humans is studied by the science called PHYSIOLOGY**.

The official date of occurrence of physiology can be considered 1628, when the English physician, anatomist and physiologist **W. Garvey** published his treatise **"Anatomical study on the movement of the heart and blood in animals".**



William Harvey, 1578-1657

The first textbook on ***PHYSIOLOGY*** **("Fundamenta physiologiae humani")** was published by the Swiss scientist ***Albrecht von Haller*** in 1747.

At the end of the XVIII c. (1791) Italian scientists ***Luigi Galvani*** laid the foundations of the theory of **"animal electricity"**.

At 1820 ***Jiří Procháska*** published **"Physiologie, oder Lehre von der Natur des Menschen"** /"Physiology, or the science of the nature of man"/.

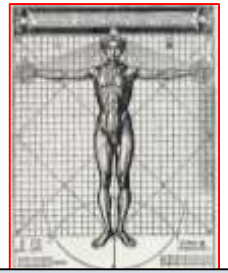
Albrecht von Haller, 1708—1777

Luigi Galvani, 1737-1798

Jiří Procháska, 1749-1820

INTERDISCIPLINARY COLLABORATION IN THE STUDY OF THE CHILDREN'S MSS

PHYSIOLOGY of MOVEMENT /BIOMECHANICS/



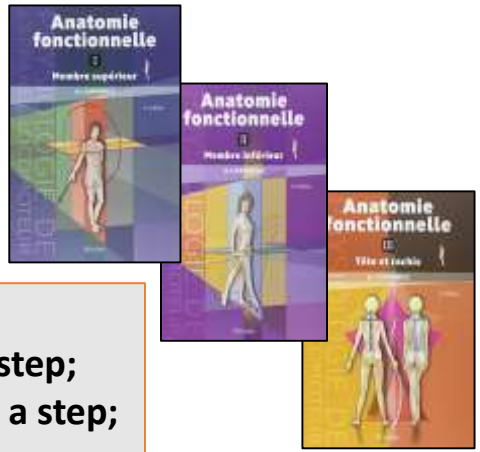
Man by Marcus Vitruvius Pollio, 80-20 BC

Vitruvian Man by Leonardo da Vinci, /1492/

From Vitruvius to Kapandji

Adalbert Ibrahim Kapandji, 1928-2019

Three volumes of the "Anatomie fonctionnelle"



The MAIN RESEARCH METHODS of BIOMECHANICS of MSS:

IHNOMETRY - βήμα + μέτρο - measurement of spatial characteristics of a step;
PODOMETRY - πόδι + μέτρο - measurement of temporal characteristics of a step;
GONIOMETRY - γωνία + μέτρο - measurement of the joint motion angle;
DYNAMOMETRY - δύναμη + μέτρο - measurement of the muscle strength;
STABILOMETRY - κοινό κέντρο βάρους + θέση - registration of the position of the common center of pressure on the plane of the support upon standing;
ELECTROMYOGRAPHY – ηλεκτρονίου + μυς + μέτρο - registration of surface EMG.

TODAY it is INDEPENDENT SCIENTIFIC DISCIPLINE

INTERDISCIPLINARY COLLABORATION IN THE STUDY OF THE CHILDREN'S MSS

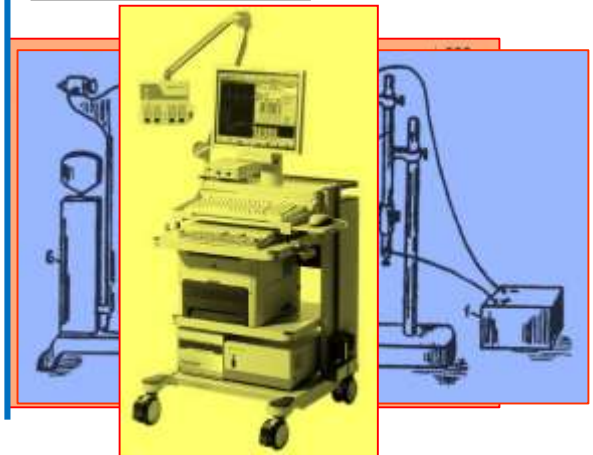
The SECOND HALF of the MSS "APPLE" are MUSCLES

Luigi Galvani, 1737-1798

The main method for studying the bioelectric potentials that arise in the skeletal muscles of humans and animals when muscle fibers are excited is

ELECTROMYOGRAPHY

(anc. Gr. ηλεκτρονίου + μυς + μέτρο)



In 1907 the German scientist Hans Edmund von Piper first applied the method of electromyography in relation to man

Piper H. Elektrophysiologie menschlicher muskeln, Springer-Verlag Berlin Heidelberg, 1912 : 61 p.

H.E. von Piper, 1877-1915

INTERDISCIPLINARY COLLABORATION IN THE STUDY OF THE CHILDREN'S MSS

THE FACTS:

MSS is a subject of INTERDISCIPLINARY study for at least 2.5 thousand years and in each era to achieve such goal as the progress of medical science were used the most modern diagnostic technology of that time .

REFLECTIONS:

– the resulting information from this work reflects preferential organ's macro- and microanatomy

– the main part of the information reflects the state of MSS in an adult person

– the lack of data on the age-related anatomical and physiological features of children's and adolescent MSS has quite a few objective reasons.

INTERDISCIPLINARY COLLABORATION IN THE STUDY OF THE CHILDREN'S MSS

REFLECTIONS:

ONE of the REASONS is the MISTAKEN NOTION that CHILDREN are SMALL ADULTS

The MAIN PECULIARITY of a CHILD'S BODY is that MATURATION and GROWTH are NON-LINEAR.

INTERDISCIPLINARY COLLABORATION IN THE STUDY OF THE CHILDREN'S MSS

PART TWO

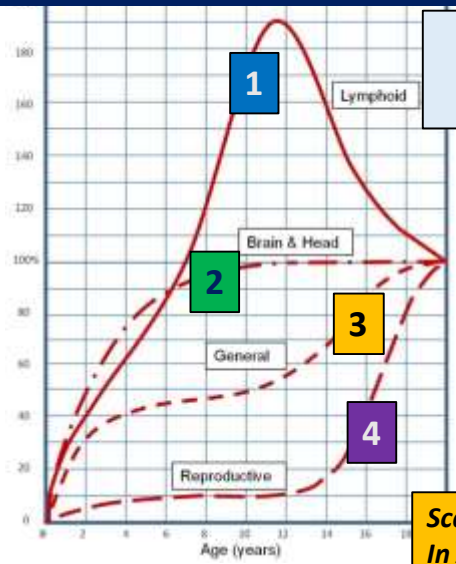
CHILDREN

INTERDISCIPLINARY COLLABORATION IN THE STUDY OF THE CHILDREN'S MSS

The PROCESS of MATURATION of CHILD'S BODY SYSTEMS

The FIRST MOST IMPORTANT CHARACTERISTIC is a DIVERSE, NON-LINEAR SPEED of MATURATION of the MAIN SYSTEMS of a CHILD'S BODY, which is DETERMINED by the ROLE of each of them in the PROCESS of INDIVIDUAL DEVELOPMENT.
At the VERY BEGINNING of the LIFE PATH – a DEFENSE SYSTEM (lymphoid or immune) is NEEDED, and the last in this row is the REPRODUCTIVE SYSTEM.

Richard Everingham Scammon, 1883-1952



Types of postnatal growth curves as percentage of total growth Increment from birth to 20 years.

Ratio of growth rates of various tissues (according to Scammon):

- 1 – lymphoid /protection/
- 2 – nervous /adaptation/
- 3 – general development /physical maturation/
- 4 – reproduction /procreation/

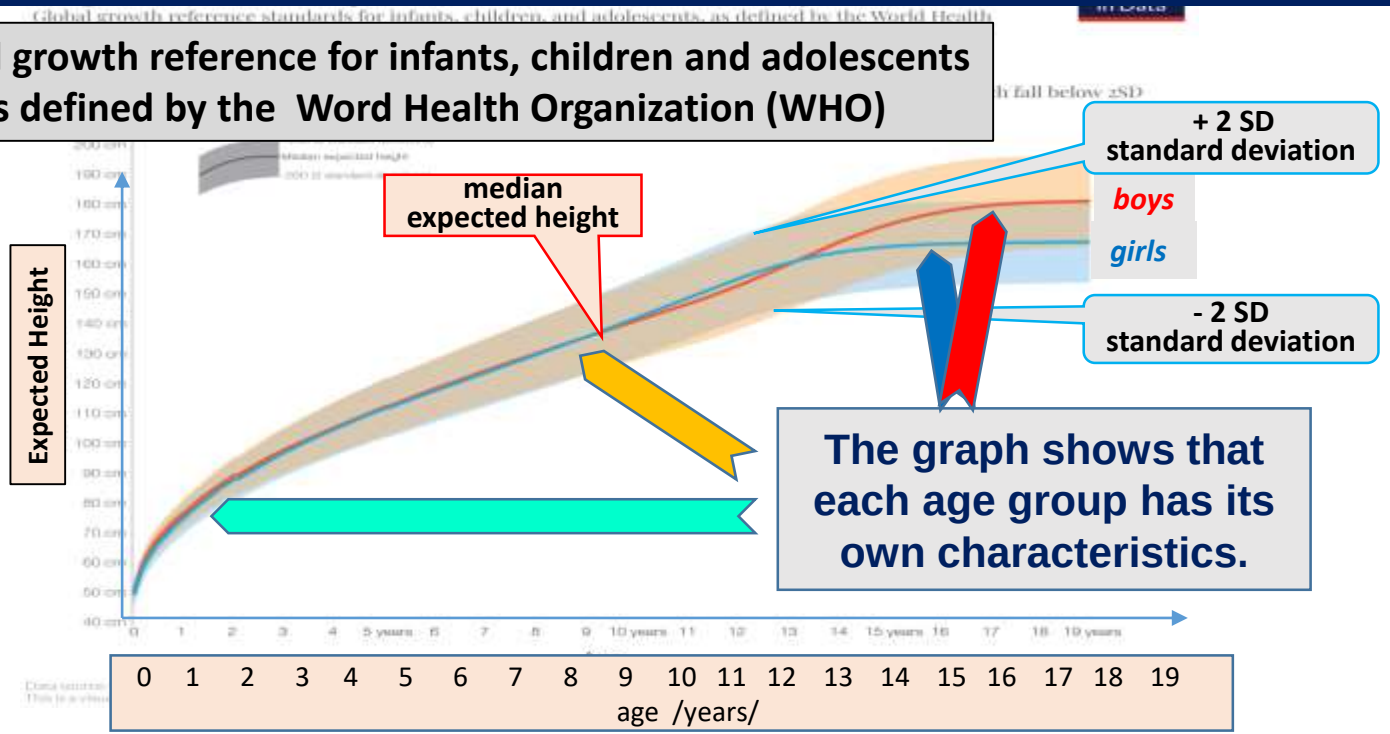
Scammon R.E., The ponderal growth of the extremities of the human fetus. In American Journal of PHYSICAL ANTHROPOLOGY, 1930: Vol.15, issue 1 : pp. 111-121.

INTERDISCIPLINARY COLLABORATION IN THE STUDY OF THE CHILDREN'S MSS

GROWTH PROCESS

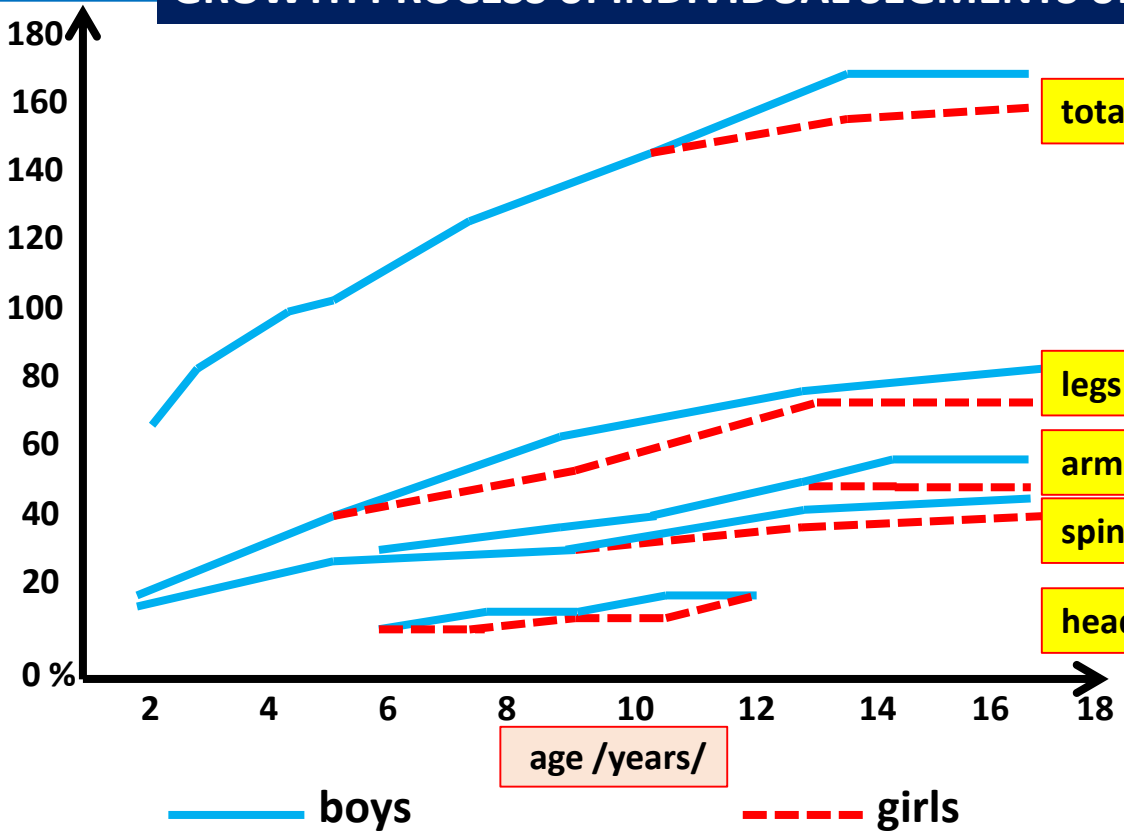
The SECOND PECULIARITY of a CHILDREN'S MSS is the CONSTANT PROCESS of GROWTH

Global growth reference for infants, children and adolescents as defined by the Word Health Organization (WHO)



INTERDISCIPLINARY COLLABORATION IN THE STUDY OF THE CHILDREN'S MSS

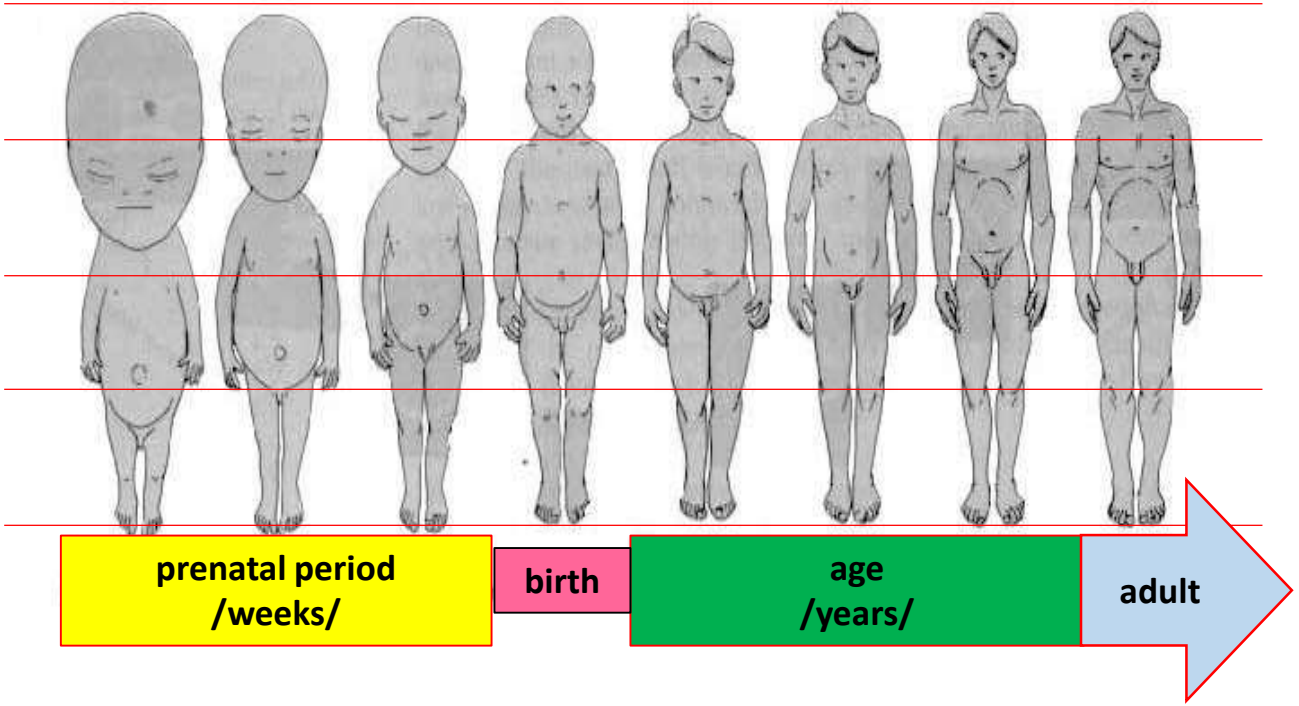
GROWTH PROCESS of INDIVIDUAL SEGMENTS of MSS



The MOST IMPORTANT FEATURE of GROWTH PROCESS is it's ALLOMETRY (Anc. Gr. άλλο + μέτρο)

INTERDISCIPLINARY COLLABORATION IN THE STUDY OF THE CHILDREN'S MSS

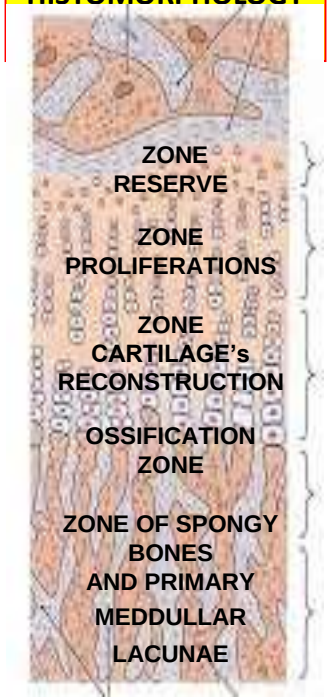
SUMMARY ILLUSTRATION of ALLOMETRIC GROWTH PROCESS



INTERDISCIPLINARY COLLABORATION IN THE STUDY OF THE CHILDREN'S MSS

PHYSIOLOGY of BONE GROWTH

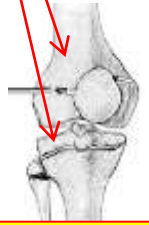
GROWTH ZONES HISTOMORPHOLOGY



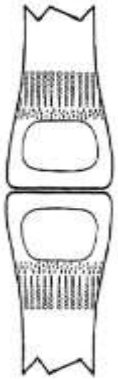
skeleton's scintigraphy

growth zones

spine

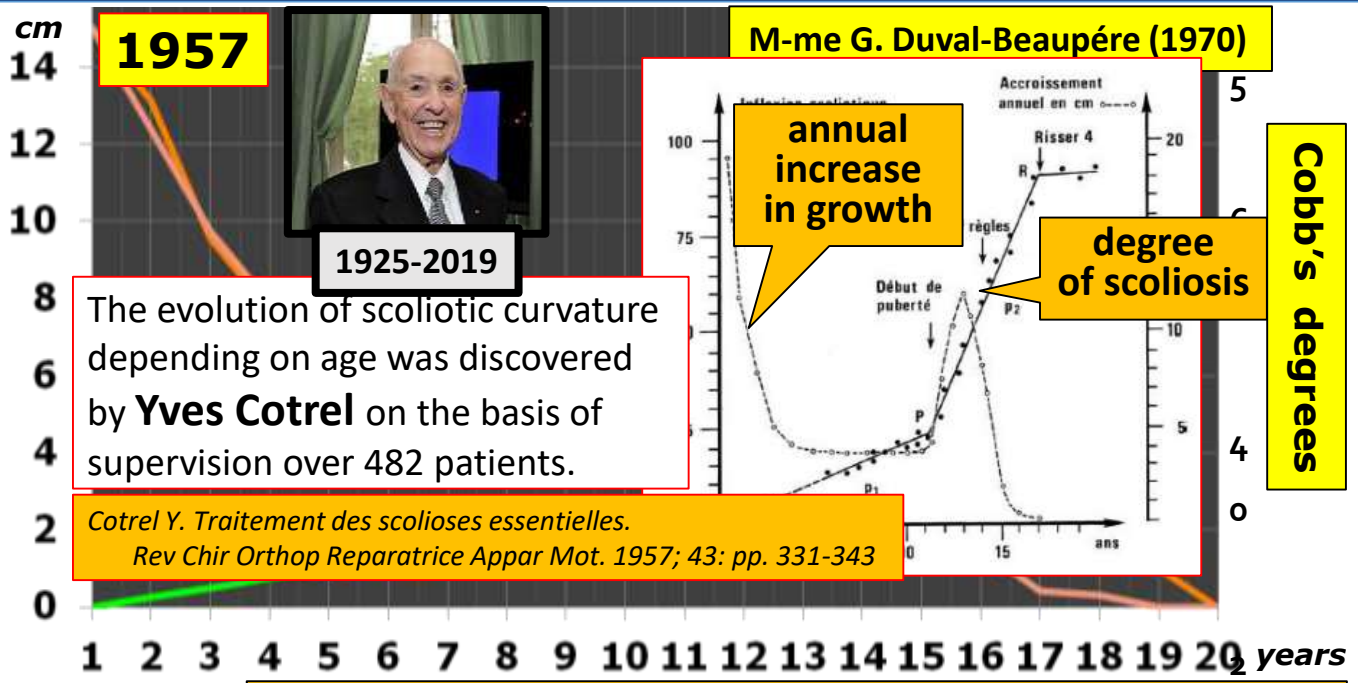


tubular bones



INTERDISCIPLINARY COLLABORATION IN THE STUDY OF THE CHILDREN'S MSS

The MOST STRIKING EXAMPLE of the RELATIONSHIP of GROWTH and DISEASE



The evolution of scoliotic curvature depending on age was discovered by **Yves Cotrel** on the basis of supervision over 482 patients.

Cotrel Y. Traitement des scolioses essentielles.
Rev Chir Orthop Reparatrice Appar Mot. 1957; 43: pp. 331-343

Duval-Beaupère G. Maturation indices in the surveillance of scoliosis.
Rev Chir Orthop Reparatrice Appar Mot. Jan-Feb 1970; 56(1): pp. 59-76

INTERDISCIPLINARY COLLABORATION IN THE STUDY OF THE CHILDREN'S MSS

THE FACTS:

Lack of knowledge about child and adolescent anatomical age norm makes it:

– difficult to diagnose diseases of MSS,

– difficult to create the theories of their pathogenesis.

A DIRECT CONSEQUENCE of these TWO FACTS is the ABSENCE of PATHOGENETIC TREATMENT

NOTE:

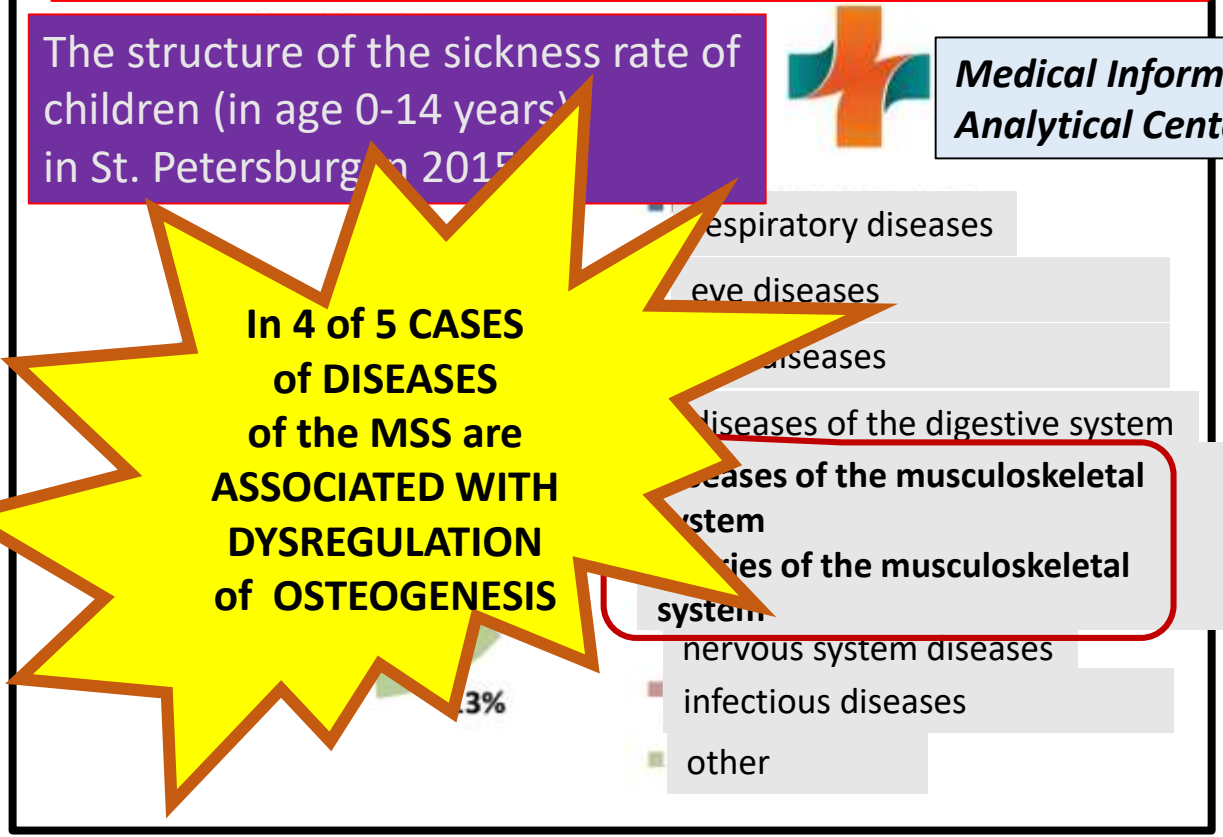
- **The ABILITY of BONE TISSUE to "COLLECT, PRESERVE and SUPPLY the NECESSARY CHEMICAL ELEMENTS" of the HUMAN BODY is VITAL.**
- **Then PARTIAL DISTURBANCES in these PROCESSES LEAD to SYSTEMIC LESIONS of other SYSTEMS and TISSUES.**
- **Therefore, FURTHER IDENTIFICATION of MOLECULAR MECHANISMS related to BONE METABOLISM will not ONLY PROVIDE a BETTER UNDERSTANDING of these PROCESSES, but also DETERMINE NEW TREATMENT STRATEGIES for BOTH SKELETAL and SYSTEMIC DISEASES.**

INTERDISCIPLINARY COLLABORATION IN THE STUDY OF THE CHILDREN'S MSS

MUSCULOSKELETAL SYSTEM: its DISEASES and INJURIES

The structure of the sickness rate of children (in age 0-14 years) in St. Petersburg in 2015

Medical Information Analytical Center of SPb



In 4 of 5 CASES of DISEASES of the MSS are ASSOCIATED WITH DYSREGULATION of OSTEOGENESIS

INTERDISCIPLINARY COLLABORATION IN THE STUDY OF THE CHILDREN'S MSS

DEFINITION of the term "DISEASE"

DISEASE are a state of a living organism subject to damage to the anatomy /structure/ or function of one or more organs under the influence of internal or external factors and manifested in the reactive /response/ mobilization of compensatory-adaptive mechanisms.

THE FACTS:

The DISEASES of MSS are based on generalized or local disorders in the REGULATION of OSTEOGENESIS

HOWEVER
it should be remembered that the "performers" of OSTEOGENESIS are only three types of cells:
OSTEOBLASTS, OSTEOCYTES and OSTEOCLASTS.

INTERDISCIPLINARY COLLABORATION IN THE STUDY OF THE CHILDREN'S MSS

BONE CELLS

Embryonic Stem Cells (ESC)

Multipotent Stem Cells (MSC)

Del Fattore et al., 2010

Hematopoietic Stem Cells (HSC)

Mesenchymal Stem Cells (MSC)

Ott S., 2004;
Hirvonen M.J. et al., 2013

Osteocytes are osteoblasts, "buried" in a bone matrix
(≈95% of all cells present in the skeleton).
Young skeleton – ????

Dallas S.L. et al., 2013

related to cell macrophages

Ott S., 2004;
Hirvonen M.J. et al., 2013

OSTEOBLAST

OSTEOCYTES

OSTECLAST

INTERDISCIPLINARY COLLABORATION IN THE STUDY OF THE CHILDREN'S MSS

MUTUAL INFLUENCE of BONE CELLS

INTERDISCIPLINARY COLLABORATION IN THE STUDY OF THE CHILDREN'S MSS

THE FACTS:

BONE is LIVING TISSUE which is SUBJECTED to PERMANENT DYNAMIC MODELING in CHILDREN and REMODELING in ADULTS

It /BONE/ CONSISTS of EXTRACELLULAR MATRIX and BONE CELLS at DIFFERENT STAGES of DIFFERENTIATION

(Ham A.W., Cormack D.H., 1983; Baron R., Kneissel M., 2013; Pogoda P. et al., 2005)

- **BIOCHEMICAL and HISTOCHEMICAL RESEARCHES of OSTEOGENESIS PROCESSES SHOW its MAIN VALUE for the SOLUTION of all the MAIN TASKS of MSS: SUPPORT, PROTECTION, MOBILITY ("Fight-or-Flight") and MAINTAINING LOCAL and BODY HOMEOSTASIS**
- **HORMONAL REGULATION is MOST STUDIED TODAY**
- **LESS but SUFFICIENT VOLUME of INFORMATION about NEUROTROPHIC MECHANISMS has ALREADY BEEN RECEIVED**

INTERDISCIPLINARY COLLABORATION IN THE STUDY OF THE CHILDREN'S MSS

PART THREE

NEW HORIZONS

INTERDISCIPLINARY COLLABORATION IN THE STUDY OF THE CHILDREN'S MSS

ELISA - OUR BASIC KEY to NEW HORIZONS

UNDOUBTED SUCCESS in the STUDY of NEURO-HORMONAL REGULATION in the HUMAN BODY is DIRECTLY RELATED to ELISA, the RATIONALE and DEVELOPMENT of which has been AWARDED numerous Nobel Prizes.


Ilia Iv. Mechnikov 18

Paul Ehrlich, 915

Nobel Prize 1908 y.


Rodney R. Porter, 19

Gerald M. Edelman, 14

Nobel Prize 1972 y.


Nobel Prizes 1977 y.

alyn S. 1921-

Solomon A. Berson, 1918-1972



Baruj Benacerraf, 1920-201

Jean Dausset,

George D. Snell, 903-1996

Nobel Prize 1980 y.

ELISA
(Enzyme-Linked-Immuno-Sorbent Assay)
is a simple technology, with high specificity, reagent availability and stability.

Currently, due to its relatively low cost and environmental safety, ELISA has moved into the category of standard, "routine" methods for the qualitative and quantitative analysis of substances.

INTERDISCIPLINARY COLLABORATION IN THE STUDY OF THE CHILDREN'S MSS

HORMONAL REGULATION of OSTEOGENESIS (OG)

UVR

SKIN

pituitary

pineal gland

Liver + Kidney

Vit D3

ICF 1

GH + IGF 1

Clt

T4

gonads

Estr

Prg

Andr

active growth process

cyto[illegible]esis

OCt

Ocl

Csl

Prt

Insufficient growth process

Melatonin /from APUD system/

TODAY TRUSTWORTHY INFORMATION about CONCENTRATIONS of HORMONES is AVAILABLE

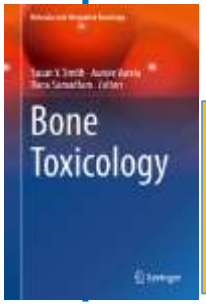
HOWEVER the COMPLEX MECHANISMS of the INTERACTION of OB, OCt and OCl, as well as the MULTI-LINK REGULATION of OG do not ALLOW us to STATE a LINEAR RELATIONSHIP between HORMONE LEVELS and MACRO-BIOLOGICAL EFFECTS

INTERDISCIPLINARY COLLABORATION IN THE STUDY OF THE CHILDREN'S MSS

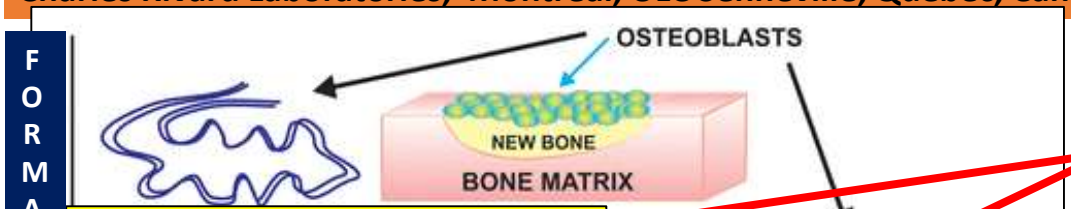
COLLAGEN EXCHANGE SCHEME

Charles Rivard Laboratories, Montreal, ULC Senneville, Quebec, Canada

Professor Charles-Hilaire Rivard



Varela A., Jolette J. Bone Toolbox: Biomarkers, Imagine Tools, Biomechanics and Histomorphometry. Toxicologic Pathology, vol. 46, 5: pp. 511-529.
First Published July 4, 2018. Review Article



Osteocalcin (BGP, Bone-Gla-protein). Bone Matrix protein produced by Obl during mineralization. Incorpoated in to BM and released during resorption.

Carboxy- and Aminoterminal Propeptides (PICP and PINP)

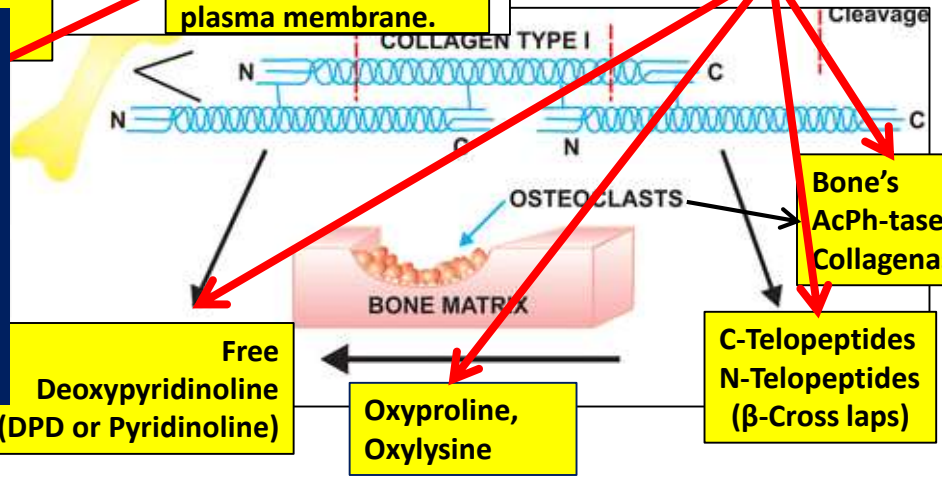
SYNTHESIS

Bone's AlkPh-tase, assciated with osteoblast plasma membrane.

MARKERS of BONE TURNOVER

RESORPTION

RESORPTION



Bone's AcPh-tase, Collagenase.

Free Deoxypyridinoline (DPD or Pyridinoline)

Oxyproline, Oxylysine

C-Telopeptides N-Telopeptides (β-Cross laps)

INTERDISCIPLINARY COLLABORATION IN THE STUDY OF THE CHILDREN'S MSS

MARKERS of MUTUAL INFLUENCE of BONE CELLS

Synthesis - OB

OSTEOBLASTS interact with OSTEOCLASTS via RANK/RANKLigand
(Harada S., Rodan G.A., 2003; Teitelbaum S.L., Ross F.P., 2003)

- **BGP** (Bone-Gla-protein, *OSTEOCALCIN*)
- **PGE2** (prostaglandin E2) **NO** (nitric oxide) and **ATP**, which stimulate activity of OB (SOST antagonists)
- **PICP** and **PINP** (finite C- and N-propeptides Collagen 1)
- **AlkPh** (alkaline phosphatase)
- **Clt** **GH** **VitD3 (RVD3)**
- **NGF** **FbGF**

Resorption - OCl

- **RANK** (TNFSF11) + **RANKLigand**, **OPG** (osteoprotogerin)
- Terminal C- and N-telopeptides (Beta-Cross laps)
- Oxyproline and Oxylysine DPD (urine deoxypyridinoline)
- IL-1, IL-3, IL-6, IL -11 (nterleukins-n)
- **AcPh** (acid phosphatase)
- Ptr as a Suppressor BGP synthesis
- Csl as a Suppressor of procollagen synthesis
- T4

Current balance – OCt

SCLEROSTIN (SOST)

SOST is an inhibitor of bone formation effect only in the presence of DKK1 (Dickkopf-1) by way to an inhibition of **OB** activity. **RANKL or OPG** (**osteoprotegrin**) as a stimulator or an inhibitor of **OCl** differentiation respectively. So, **RANKL** and **M-CSF**, **OPG**, endothelial **NO-synthase** and **TGFβ** (**transforming growth factor β**) to inhibit activity **OCl**

Pfeilschifter J.S. et al., 1988; Heino T.J. et al., 2002; Loveridge N.F. et al., 2002; Li X.Z. et al., 2011.

Mechanical loading can promote bone formation through down-regulation of SOST expression in osteocytes

The gonadal estrogen is an inhibitor of osteocyte apoptosis

Khosla S. et al., 2012; Rhee Y. et al.. 2013

INTERDISCIPLINARY COLLABORATION IN THE STUDY OF THE CHILDREN'S MSS

NEURO-TROPHIC REGULATION

The INTRODUCTION: Under the neuro-trophic regulation are understood the trophic influences of the neuron, which ensure the normal functioning of the structures innervated by it.

HISTORY. The first documented information about the anatomical relationship between nerves and bone on wood engraving was made by **Charles Etienne in Paris in 1545**. He showed how the nerves enter and exit the bones of the skeleton. A more specific study of bone innervation expected the availability of technology to study this issue in more detail.

The **Russian scientist A. Otelin in the his atlas of 1965** indicated the presence of nerve endings in the cortical bone. A year later, **Cooper R.R. et al.** in his publications **1966 and 1968** in the **JBJS** and **Science** presented the results of electron microscopy, according to which the cortical bone is well innervated.

The following year, **Calvo W. and Fortez-Vila J. (Am J. Anat,1969)** differentiated myelinated and non-myelinated fibers associated with arterial vessels and venous sinuses in the bone.

Finally, in **1986, Hohmann E.L. et al. (Science, 1986)** reported immunohistochemical localization of a **vasoactive intestinal peptide (VIP)** containing sympathetic fibers in the bone.

This was the beginning of a steady stream of research on various types of nerves in bone tissue.

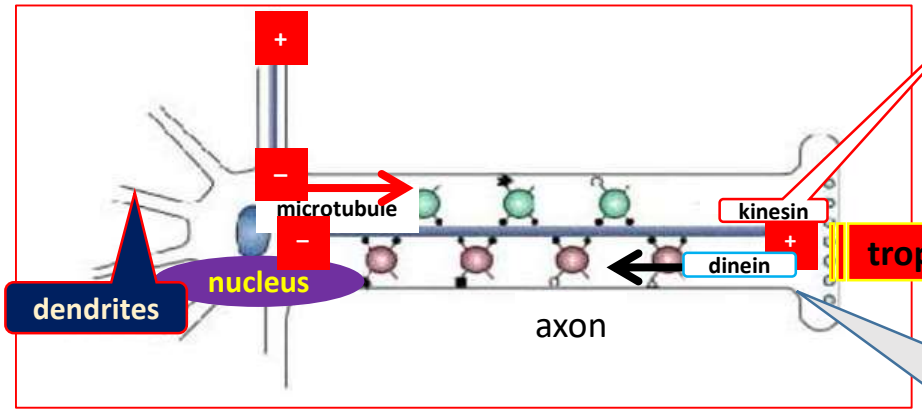
INTERDISCIPLINARY COLLABORATION IN THE STUDY OF THE CHILDREN'S MSS

NEURO-TROPHIC REGULATION

How does the implementation of neuro-trophic regulation happen?

The answer to this is given by a well-substantiated model of the transport axonal.

The transport axonal is the movement along the axon of nerve cell of various biological material /trophogenes, informones/. The transport of material from the body of the neuron to the synapse is called anterograde and in the opposite direction – retrograde.



Kinesins are motor proteins that move from the minus ends of microtubules to the plus ends and usually moving the "load" from the center of the cell to the periphery.

Dyneins are motor proteins that move from the plus ends of microtubules to the minus ends and usually moving the "load" from the periphery to the center of the cells.

Two type of the transport axonal are described.
SLOW with speed 1-3 mm/day and FAST with speed about 400 mm/day.

INTERDISCIPLINARY COLLABORATION IN THE STUDY OF THE CHILDREN'S MSS

NEURO-TROPHIC REGULATION

THE FACTS and REFLECTIONS:

We hope that the audience understands that in a short presentation time we cannot reflect all the information received by our colleagues in a new field for clinicians.

The analysis of the literature on this subject (more than 200 works) gave us reason to believe that a thorough study of neurotrophic regulation and their extrapolation to "clinical scenarios of changes in bone growth and metabolism require orthopedic scientists to rethink the fundamental orthopedic pathophysiology in the light of a recent understanding of the neuro-bone axis".

(Jones K.B. et al. Iowa Orthop J. 2004).

INTERDISCIPLINARY COLLABORATION IN THE STUDY OF THE CHILDREN'S MSS

CONCLUSION

1. MSS has been studied for several thousand years. The encyclopedists were the first on this path, and today a rather long series of biomedical and engineering disciplines are involved in such studies.

2. Meanwhile, in the huge database of information received, there are still many "white spots". At the same time, the largest number of such "spots" is observed in the field of information on children's MSS.

3. The most important reason should be considered two interconnected allometric processes that are observed only in children - the maturation and the growth of MSS.

4. Today, enough evidence has already been received to understand the physiology of these processes and the pathophysiolgy of diseases of MSS in children.
Further studies on the cellular and molecular levels are necessary.

5. Our presentation is a direct illustration of not only the new discoveries of colleagues working in the basic sciences, but also a call for expanding interdisciplinary cooperation in the study of children's MSS.

INTERDISCIPLINARY COLLABORATION IN THE STUDY OF THE CHILDREN'S MSS

We hope and believe that the last conclusion allows us to see new horizons and prospects in the development of children's orthopedics.

Doufáme a věříme, že poslední závěr nám umožňuje vidět nové obzory a vyhlídky ve vývoji dětské ortopedie.

Mamy nadzieję i wierzymy, że ostatni wniosek pozwala nam zobaczyć nowe horyzonty i perspektywy rozwoju ortopedii dziecięcej.

Мы надеемся и верим, что последний вывод позволяет нам увидеть новые горизонты и перспективы в развитии детской ортопедии.


WE THANK YOU FOR
YOUR ATTENTION!
DĚKUJEME ZA
VÁŠ POZOR!