Pohybové ústrojí

Pokroky ve výzkumu, diagnostice a terapii



Vydává
Společnost pro pojivové tkáně ČLS J. E. Purkyně z.s.
Ortopedicko-protetická společnost ČLS J. E. Purkyně z.s.
Ambulantní centrum pro vady pohybového aparátu, s.r.o.

ročník 31 / 2024 číslo 2

EMBASE / Excerpta Medica | Bibliographia medica Čechoslovaca

ISSN 2336-4777

ORLING

ZALOŽENO ROKU 1992

BIOAKTIVNÍ KOLAGENNÍ PEPTIDY REGENERUJÍ

Kolagen je nezbytný pro pohyblivost kloubů, stabilitu kostí, odolnost a pevnost vazů a šlach a také pro zdravé svaly a hojně se vyskytuje i v cévách, meziobratlových ploténkách, hematoencefalické bariéře a rohovce, dentinu a střevní stěně – kolagen je životně důležitá složka celého těla.



Kolagenní peptidy zvyšují syntézu kloubního kolagenu a proteoglykanů

Nejen sportovci jsou ve zvýšené míře náchylní ke kloubním problémům a léčba se u nich nijak neliší od jejího zvládání u běžné populace. Hlavním cílem je minimalizovat bolestivost a zlepšit funkčnost kloubů. Klinická studie provedená v Penn State University testovala účinek kolagenních peptidů na studenty sportovních škol, kteří trpěli kloubními problémy v důsledku mechanické zátěže. V porovnání s kontrolní skupinou došlo u studentů, kteří užívali kolagenní peptidy, k **výraznému snížení kloubních potíží a také ke zlepšení pohyblivosti.** Tyto pozitivní účinky byly patrné zejména u účastníků s problémy kolenních kloubů pocházejících z mechanické zátěže. *(Clark K. , Sebastianelli W., Flechsenhar K., Aukermann D., Meza F., Millard R., Deitch J., Sherbondy P., Affiliations A., 24-Week study on the use of collagen hydrolysate as a dietary supplement in athletes with activity-related joint pain, Curr Med Res Opin, 2008 May;24(5):1485-96)*

Významný je i vliv kolagenních peptidů na hustotu kostí, zejména u osob s osteoporózou či osteopenií, potvrzeno už v roce 2010 pilotní studií s doplňkem stravy Calcidrink®.

V této studii se řešil „Vliv suplementace kolagenními peptidy, vápníkem a vitaminem D, resp. Calcidrinkem® na úbytek kostní hmoty a remodelaci kosti u postmenopauzálních žen s osteopenií“ *(Ortopedie 2010, Gabriela Šimková, Revmatologická ambulance 1. PP Kladno)*. Výsledky byly velmi nadějné. U žádné pacientky se nevyskytly během sledovaného období jednoho roku žádné nové nízkozátěžové zlomeniny. Cílem bylo prokázat účinek pravidelného užívání přípravku Calcidrink (vitamin D, kalcium a kolagenní peptidy) na snížení úbytku kostní hmoty u postmenopauzálních žen s osteopenií. Výsledky studie tento efekt potvrdily.

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Prof. MUDr. Milan Adam, DrSc. byl první, kdo objevil obrovský potenciál kolagenních peptidů a v průběhu let jej další vědci a lékaři opakovaně prokázali a ještě rozšířili oblasti použití, pro které jsou kolagenní peptidy vhodné.



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ročník 31, 2024, číslo 2 | datum vydání: 31. 12. 2025

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Pohybové ústrojí. Pokroky ve výzkumu, diagnostice a terapii.

ISSN 2336-4777 (od roku 2013 pouze on-line verze)
Vydává Společnost pro pojivové tkáně ČLS J. E. Purkyně z.s.
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Při příležitosti sympozií je dvakrát ročně vydáváno supplementum.

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LOCOMOTOR SYSTEM

Advances in Research, Diagnostics and Therapy

Published by The Society for Connective Tissues, Czech Medical Association of J. E. Purkyně, Prague, Society for Prosthetics and Orthotics, Czech Medical Association of J. E. Purkyně, Prague, Czech Republic and Centre for Defects of Locomotor Apparatus Prague, Czech Republic.

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Submitted papers: Locomotor System will review for publication manuscripts engaged in diagnostics and interdisciplinary treatment of genetic and metabolic skeletal disorders, limb anomalies, secondary osteoporosis, osteo/spondyloarthritis and another disorders that negatively influence development and quality of locomotor apparatus during human life. Both papers on progress in research of connective tissue diagnostics, medical and surgical therapy of multiple congenital abnormalities of skeleton mainly in the fields of paediatric orthopaedic surgery and plastic surgery, orthotics and prosthetics treatment, and papers dealing with biomechanics, clinical anthropology and paleopathology are appreciated.

The journal has an interdisciplinary character which gives possibilities for complex approach to the problems of locomotor system. The journal belongs to clinical, preclinical and theoretical medical branches which connect various up-to-date results and discoveries concerned with locomotor system. You can find the volumes of Locomotor System journal at http://www.pojivo.cz/cz/pohybove-ustroji/ since 1997 (free of charge). Since 2013 only electronic edition of the journal is available. That is why we recommend to all subscribers and those interested apply at http://www.pojivo.cz/en/newsletter, enter personal data, titles and e-mail address where the journal will be mailed.

Abstracts of presented papers are excerpted in EMBASE/Excerpta Medica (from the year 1994) and in the Bibliographia medica Čechoslovaca (from the year 2010). We prefer the manuscripts to be prepared according to Uniform Requirements for Manuscripts Submitted to Biomedical Journals (Vancouver Declaration, Brit med J 1988; 296, p. 401–405).

Věnování čísla 1 a 2 časopisu Pohybové ústrojí, 31, 2024

31. ročník časopisu Pohybové ústrojí – pokroky ve výzkumu, diagnostice a terapii (PÚ), 2024 je věnován jubilantům, kterým byl udělen Diplom Čestné členství ve Společnosti pro pojivové tkáně České lékařské společnosti J.E. Purkyně (ČLS JEP

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MUDr. Ivanovi Hadrabovi (65 let)

a jubilantům, kterým byl udělen Diplom Čestné členství v České lékařské společnosti J.E. Purkyně:

Associate Professor Michael Bellemore, MD, A.M.F.R.A.C.S. (71 let)

Professor Dr. Med. Hans Zwipp (75 let)

Piet van Loon, MD (70 let)

Odborné životopisy jmenovaných jubilantů byly publikovány v Suplementu 1 a Suplementu 2 časopisu Pohybové ústrojí 31, 2024, která byla vydána při příležitosti symposia 29. Kubátovy dny a The 26th Prague-Lublin Symposium.

Suplementum 1 a 2 s abstrakty příspěvků a video záznamy přednášek jsou dostupné na webových stránkách obou symposium organizujících společností **www.pojivo.cz** a **www.ortoprotetika**.cz.

Dedication of issue 1 and 2 of the journal Locomotor System, 31, 2024

The 31st issue of the journal Locomotor System - Advances in Research, Diagnosis and Therapy (LS), 2024 is dedicated to the jubilarians who have been awarded the Diploma of Honorary Membership in the Society for Connective Tissues of the Czech Medical Association: J.E. Purkynje

MUDr. Alena Maříková (60 years),

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and jubilarians who were awarded the Diploma of Honorary Membership in the Orthopaedic and Prosthetic Society of the Czech Medical Association: J.E. Purkynje:

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Associate Professor Michael Bellemore, MD, A.M.F.R.A.C.S. (71 years),

Professor Dr. Med. Hans Zwipp (75 years),

Piet van Loon, MD (70 years)

The professional biographies of the named jubilarians were published in Supplement 1 and Supplement 2 of the journal Locomotor System 31, 2024, which was published on the occasion of the 29th Kubát Days and The 26th Prague-Lublin Symposium.
Supplement 1 and 2 with abstracts of the papers and video recordings of the lectures are available on the websites of both symposium organizing companies **www.pojivo.cz** and **www.ortoprotetika.cz**

**POHYBOVÉ ÚSTROJÍ –
POKROKY VE VÝZKUMU, DIAGNOSTICE A TERAPII, 31, 2024, č. 2**

Datum vydání: 31. 12. 2025

OBSAH

SLOVO ČTENÁŘŮM – EDITORIAL 121

OBRÁZEK NA TITULNÍ STRANĚ A POPIS

Píchová Renata
Scintigrafie skeletu pomocí techneciem značených fosfátových
komplexů (osteotropní radioaktivní látka) 127

DOPIS EDITOROVI

Karski Tomasz, Karski Jacek
Ortopedická zkušenost s DMSO terapií (krátký popis) 131
Všetička Jan
Vlastní zkušenost s DMSO a co nám říká AI 133

PŘEHLEDOVÉ PRÁCE

van Loon P.J.M., Soeterbroek A.M., Grotenhuis J.A. Smit T.H.
Zdravotní problémy způsobné hypokinezií, sezením a životem v digitálním světě dětí
„přecivilizovaných společností. Nebo jak nám kulturní evoluce způsobila „idiopatickou“
skoliózu (Esej) 137

PŮVODNÍ PRÁCE

KAZUISTIKY

Zwipp Hans
Calcaneogenese se sekundárním alograftem „Achilles tendon-bone" pro náhradu ztracené funkce. Kasuistika – výsledek po 12 letech 152

Krulišová Veronika, Zemková Daniela, Mařík Ivo, Paszeková Helena, Michalovská Renáta, Vlčková Zdeňka
Nová sestřihová varianta genu *FGFR3* – kauzální varianta kostní dysplazie u dvou pacientů s překrývajícími se fenotypy achondroplazie a hypochondroplazie 167

Mařík Ivo, Zemková Daniela, Maříková Alena, Šumník Zdeněk, Souček Ondřej, Krulišová Veronika, Hudáková Olga
WNT1 osteogenesis imperfecta: Případová studie české dívky 194

ZPRÁVY

Krawczyk Petr
Subkatedra ortopedické protetiky a podiatrie na IPVZ 223

Informace o Společnosti pro pojivové tkáně ČLS JEP 226

Přihláška řádného člena Společnosti pro pojivové tkáně ČLS JEP 227

Přihláška řádného člena Ortopedicko-protetické společnosti ČLS JEP 227

SMĚRNICE AUTORŮM 230

OBSAH ROČNÍKU 2023 235

OBSAH ROČNÍKU 2024 241

LOCOMOTOR SYSTEM –
ADVANCES IN RESEARCH, DIAGNOSIS AND THERAPY, 31, 2024, No. 2

Date of issue: 31. 12. 2025

CONTENT

A WORD TO READERS – EDITORIAL 124

TITLE PICTURE AND DESCRIPTION

Píchová Renata
Bone Scintigraphy Using Technetium-labeled Phosphate Complexes (Osteotropic Radiotracer) 129

LETTER TO EDITOR

Karski Tomasz, Karski Jacek
Orthopedic experience of therapy by DMSO (short description) 131
Všetička Jan
Personal experience with DMSO and what AI tells us 133

REVIEW ARTICLES

van Loon P.J.M., Soeterbroek A.M., Grotenhuis J.A. Smit T.H.
Health issues by hypokinesia, sitting and living in a digital world of children in "overcivilized" societies. Or how cultural evolution brought us „idiopathic" scoliosis (ASSAY) 137

ORIGINAL PAPERS

CASE REPORTS

Zwipp Hans
Calcaneogenesis with secondary Achilles tendon-bone-allograft for repair of the loss of hindfoot function. A 12 years case report 152

Krulišová Veronika, Zemková Daniela, Mařík Ivo, Paszeková Helena, Michalovská Renáta, Vlčková Zděnka
A novel splicing variant of *FGFR3* gene - a causal variant of bone dysplasia in two patients with overlapping phenotypes of achondroplasia and hypochondroplasia 167

Mařík Ivo, Zemková Daniela, Maříková Alena, Šumník Zdeněk, Souček Ondřej, Krulišová Veronika, Hudáková Olga
WNT1 osteogenesis imperfecta: Case study of a Czech girl 194

NEWS

Krawczyk Petr
Subdepartment of Orthopaedic Prosthetics and Podiatry at the Institute of Postgraduate Medical Education (IPME) 223

Information on the Society for Connective Tissues, Czech Medical Association J.E. Purkynje, Prague, CZ 228

Membership application of The Society for Connective Tissues, Czech Medical Association J.E. Purkynje, Prague, CZ 229

Membership application of The Orthopaedic and Prosthetic Society, Czech Medical Association J.E. Purkynje, Prague, CZ 229

INSTRUCTIONS FOR AUTHORS 233

CONTENTS OF VOLUME 2023 238

CONTENTS OF VOLUME 2024 244

SLOVO ČTENÁŘŮM

Vážení čtenáři, autoři a inzerenti!

Děkujeme za Vaši nezastupitelnou pomoc při tvorbě mezioborového odborného recenzovaného časopisu „Pohybové ústrojí – pokroky ve výzkumu, diagnostice a terapii (dále PÚ).

Všechna čísla časopisu (včetně Suplement) vydaná od roku 1997 najdete ve formátu PDF na webové doméně Společnosti pro pojivové tkáně České lékařské společnosti J. E. Purkyně z.s. (SPT ČLS JEP) http://www.pojivo.cz/cz/ pohybove-ustroji/ (bezplatný přístup).

Časopis PÚ byl v roce 2008 zařazen Radou pro výzkum, vývoj a inovace vlády ČR na Seznam recenzovaných neimpaktovaných periodik vydávaných v České republice. Od roku 2013 je časopis PÚ vydáván pouze v elektronické formě (v roce 2014 bylo přiděleno nové ISSN 2336-4777). V souvislosti se změnou v elektronickou formu vydávání v roce 2013 časopis nedopatřením vypadl z tohoto Seznamu. Od roku 2015 je elektronická forma Pohybového ústrojí opět na Seznamu recenzovaných neimpaktovaných periodik.

Od roku 2016 vydáváme v časopisu PÚ příspěvky přijaté po recenzi jako číslo 1 a 2, dále dvě Suplementa obsahující souhrny nebo abstrakta ze symposií Kubátovy dny a mezinárodního symposia Praha-Lublin.

Nedostatek příspěvků je příčinou zpožděného vydání i tohoto 2. čísla časopisu PÚ, 31, 2024.Těšíme se na Vaši spolupráci a tvůrčí připomínky v roce 2024.

Obrázek na titulní straně *ukazuje scintigrafii skeletu pomocí techneciem značených fosfátových komplexů (osteotropní radioaktivní látka),* která verifikuje přestavbové změny ve skeletu mladé ženy s *genochondromatózou, typ 2*.

Dopis editorům *poskytuje čtenářům základní informace o DMSO (dimethylsulfoxid), který vzniká jako vedlejší produkt výroby celulózy ze dřeva a který má mnohostranné použití. Autoři uvádějí vlastní zkušenost v oblasti ortopedických poruch a nemocí pohybového aparátu;*

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Kasuistika *Calcaneogenese se sekundárním alograftem „Achilles tendon-bone" pro náhradu ztracené funkce dokumentuje vynikající dlouhodobý výsledek rekonstrukční operace otevřené dislokace kalkanea 3. stupně (typ 5) provedené za 9 měs po úrazu. Úraz byl komplikován infekcí měkkých tkání, osteoitidou a nekrózou. Léčení si vyžádalo kalkanektomii, resekci Achillovy šlachy a volný vaskularizovaný transfer svalu latissimus dorsi;*

Další dvě kazuistické práce *jsou věnovány raritním genetickým kostním chorobám: jednak nové kauzální variantě sestřihu genu FGFR3 u dvou českých pacientů s překrývajícími se fenotypy achondroplazie a hypochondroplazie a jednak velmi raritní WNT1 osteogenesis imperfecta – OI typ 15.*

V ***rubrice Zprávy*** *se čtenáři seznámí s činností Subkatedry ortopedické protetiky a podiatrie na Institutu postgraduálního vzdělávání ve zdravotnictví (IPVZ), která byla obnovena v říjnu 2022 a která zahájila v r. 2023 certifikované kurzy určené pro výchovu další generace odborníků v oboru ortopedická protetika.*

Suplementum 1 a 2 *časopisu Pohybové ústrojí, 31, 2024 s abstrakty příspěvků a video záznamy* ***všech přednášek symposia*** *29. Kubátovy dny a The 26th Prague-Lublin symposia, jsou dostupné na webových stránkách organizujících společností: www.pojivo.cz a www.ortoprotetika.cz.*

Posláním časopisu PÚ je, jako v minulých letech, uveřejňovat vědecké práce zabývající se diagnostikou a mezioborovým léčením genetických kostních chorob, vrozených defektů končetin, sekundární osteoporózy, osteo/spondylartrózy, ale i jiných chorob, které ve svých důsledcích negativně ovlivňují růst, vývoj a kvalitu pohybového ústrojí v průběhu lidského života. Ceněny jsou práce vycházející z výzkumu pojivových tkání na všech úrovních poznání, práce orientované na biochemickou, morfologickou, genetickou a molekulární diagnostiku chorob pohybového ústrojí. Zvláštní pozornost je přikládána pracím z oblasti ortopedické a antropologické biomechaniky, neuroadaptačním změnám skeletu v období růstu, řízené remodelaci pojivových tkání, studiím muskuloskeletálních a neuronálních interakcí v závislosti na léčebných metodách (kalciotropní léky, rehabilitace, ortoticko-protetické a operační léčení aj.) a v neposlední řadě studiím antropologickým a paleopatologickým. Oceňujeme především interdisciplinárně zaměřené práce. V anglickém jazyce jsou publikována sdělení zahraničních i našich autorů. Žádaným doplněním obsahu časopisu jsou zprávy ze sjezdů a konferencí. Zveřejňujeme oznámení o životním výročí členů RR časopisu, SPT ČLS JEP z.s., OPS ČLS JEP z.s. a významných osobností, sdělení o prioritních pozorováních, ze studijních a poznávacích cest aj.

V každém ročníku najdete směrnice pro autory příspěvků, kterým věnujte prosím pozornost při tvorbě Vašich vědeckých sdělení. Souhrny prací publikovaných v časopisu jsou excerpovány v EMBASE / Excerpta Medica (od r. 1994) a v Bibliographia medica Čechoslovaca (od r. 2010).

K prosazení časopisu Pohybové ústrojí mezinárodně přispívá citovat práce publikované v našem časopisu v příspěvcích posílaných do zahraničních impaktovaných časopisů. Pro zvýšení meziná-

rodního zájmu o časopis PÚ je žádoucí získávat původní kvalitní práce a kazuistiky v angličtině. Souhrny všech prací doporučujeme psát co nejvýstižněji, strukturovaně, česky a anglicky (objectives, methods, results and discussion), s klíčovými slovy.

Těšíme se na Vaši spolupráci a tvůrčí připomínky v roce 2025

Redakční rada

A WORD TO READERS

Dear readers, authors and advertisers!

Thank you for your indispensable help in the creation of the interdisciplinary peer-reviewed journal Locomotor System - Advances in Research, Diagnosis and Therapy (journal LS).

All issues of the journal (including the Supplement) published since 1997 can be found in PDF format on the web domain of the Society for Connective Tissues of the Czech Medical Association J. E. Purkyne (SCT CMA JEP) http://www.pojivo.cz/cz/ pohybove-ustroji/ (free access).

In 2008, the journal was included by the Council for Research, Development and Innovation of the Government of the Czech Republic in the List of peer-reviewed non-impacted periodicals published in the Czech Republic. Since 2013, the journal has been published only in electronic form (in 2014, a new ISSN 2336-4777 was assigned). In connection with the change to electronic publication in 2013, the journal inadvertently dropped from this List. Since 2015, the electronic form of the journal Locomotor System is again on the List of peer-reviewed non-impacted journals.

Since 2016, we have been publishing papers accepted after peer review as Issues 1 and 2, as well as two Supplements containing summaries or abstracts from the Kubát Days and International Symposia.

The lack of contributions is the reason for the delayed publication of this second issue of PÚ, 31, 2024.

*The **image on the cover** shows skeletal scintigraphy using technetium-labeled phosphate complexes (osteotropic radioactive substance)* to verify skeletal remodeling in a young woman with *genochondromatosis type 2*.

*The **letter to the editors** provides readers with basic information about DMSO (dimethyl sulfoxide), which is produced as a by-product of wood cellulose production and has many uses. The authors share their own experience in the field of orthopedic disorders and diseases of the musculoskeletal system;*

SOCIETY FOR CONNECTIVE TISSUES J.E.Purkyně PRAGUE • CZECH REPUBLIC
CZECH SOCIETY FOR PROSTHETICS AND ORTHOTICS J.E. PURKYNĚ PRAHA • CZECH REPUBLIC
CZECH MEDICAL ASSOCIATION J.E. PURKYNĚ
AMBULANT CENTRE for defects of locomotor apparatus limited liability company

*The **review paper** draws attention to health problems caused by hypokinesia, sedentary lifestyles, and life in the digital world of children in „overcivilized societies";*

*The **case study** of calcaneogenesis with secondary allograft „Achilles tendon-bone" to replace lost function documents the excellent long-term result of reconstructive surgery for open dislocation of the calcaneus, grade 3 (type 5), performed 9 months after the injury. The injury was complicated by soft tissue infection, osteitis, and necrosis. Treatment required calcaneectomy, Achilles tendon resection, and free vascularized transfer of the latissimus dorsi muscle.*

*The **other two case studies** are devoted to rare genetic bone diseases: a new causal variant of the FGFR3 gene in two Czech patients with overlapping phenotypes of achondroplasia and hypochondroplasia, and the very rare WNT1 osteogenesis imperfecta – OI type 15.*

*In the **rubric Reports**, readers will learn about the activities of the Subdepartment of Orthopedic Prosthetics and Podiatry at the Institute for Postgraduate Medical Education (IPME), which was reestablished in October 2022 and launched certified courses in 2023 designed to educate the next generation of experts in the field of orthopedic prosthetics.*

***Supplements 1 and 2** of the journal Pohybové ústrojí, 31, 2024, with abstracts of contributions and video recordings of all lectures from the 29th Kubát Days (2024) and The 26th Prague-Lublin symposia, (2024) are available on the websites of the organizing companies: www.pojivo.cz and www.ortoprotetika.cz.*

The mission of the journal is to publish scientific papers dealing with the diagnosis and interdisciplinary treatment of genetic bone diseases, congenital defects of the limbs, secondary osteoporosis, osteo/spondylarthritis, as well as other diseases that adversely affect the growth, development and quality of the musculoskeletal system during human life. Works based on research on connective tissues at all levels of knowledge, works oriented on biochemical, morphological, genetic and molecular diagnostics of musculoskeletal diseases are valued.

Particular attention is paid to works in the field of orthopaedic and anthropological biomechanics, neuroadaptive changes of the skeleton during the growth period, controlled remodelling of connective tissues, studies of musculoskeletal and neuronal interactions in relation to therapeutic methods (calciotropic drugs, rehabilitation, orthotic-prosthetic and surgical treatment) and, last but not least, anthropological and palaeopathological communications. We particularly appreciate the interdisciplinary work. Communications by foreign and national authors are published in English. Reports from congresses and conferences are a welcome addition to the content of the journal. In the news section, we publish announcements of life anniversaries of members of the editorial board of the journal, Society for Connective Tissues CMA JEP & Society for Prosthetics and Orthotics CMA JEP and important personalities, announcements of priority observations, study and discovery trips, etc.

In each edition, you will find guidelines for authors of papers, which please pay attention to when drafting your scientific communications. Summaries of papers published in the journal are excerpted in EMBASE / Excerpta Medica (since 1994) and in Bibliographia medica Čechoslovaca (since 2010).

The citation of papers published in our journal in papers sent to foreign impacted journals contributes to the promotion of the journal Locomotor System internationally. In order to increase the international interest in the journal of Locomotor System, it is desirable to obtain original high quality papers and case reports in English. Abstracts of all papers are recommended to be written as concisely as possible, structured, in Czech and English (objectives, methods, results and discussion), with key words.

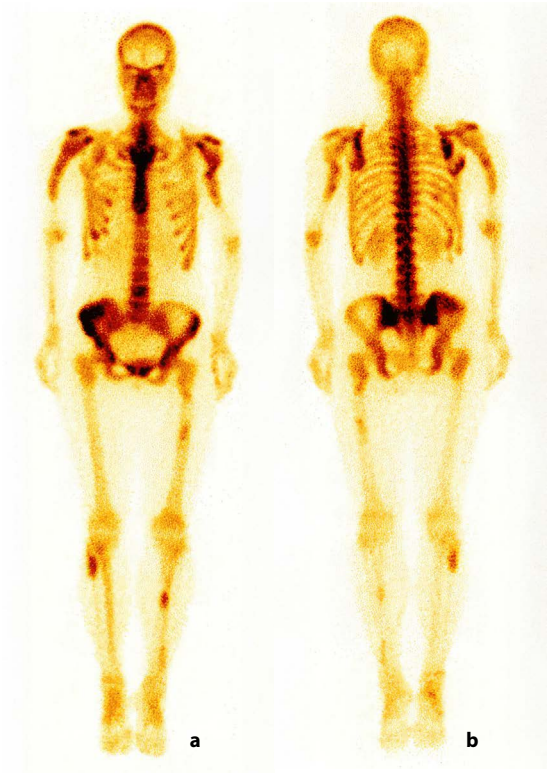
We look forward to your cooperation and creative comments in 2025.

Editorial Board

OBRÁZEK NA TITULNÍ STRANĚ ČASOPISU: SCINTIGRAFIE SKELETU POMOCÍ TECHNECIEM ZNAČENÝCH FOSFÁTOVÝCH KOMPLEXŮ (OSTEOTROPNÍ RADIOAKTIVNÍ LÁTKA)

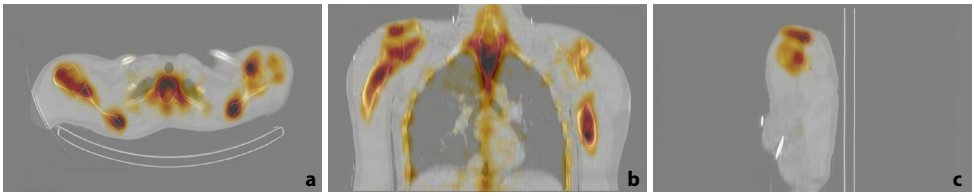
OBRÁZEK NA TITULNÍ STRANĚ ČASOPISU znázorňuje scintigrafii skeletu pacientky s raritní diagnózou genochondromatóza, typ 2 pomocí techneciem značených fosfátových komplexů, nejčastěji difosfonátů (99mTc –HDP). Pomocí osteotropního radiofarmaka lze scintigraficky zobrazit distribuci intenzity kostního metabolizmu. V oblasti patologických kostních ložisek s přestavbou kostní tkáně dochází ke zvýšení aktivity osteoblastů, která vede k zvýšené produkci krystalů hydroxyapatitů. Ty jsou substrátem, na jejichž povrchu se pevně váží značené fosfátové komplexy, a to buď přímo v patologickém ložisku nebo v reaktivní zóně kolem patologického ložiska. Obojí se scintigraficky zobrazí se zvýšenou akumulací osteotropního radiofarmaka (RF).

Jedná se o radionuklidové vyšetření, při kterém v časovém odstupu 2 hodin po nitrožilním podání radiofarmaka je pacient snímán scintilační kamerou celotělově (**obr. 1a, b**) a následně cíleně tomo-

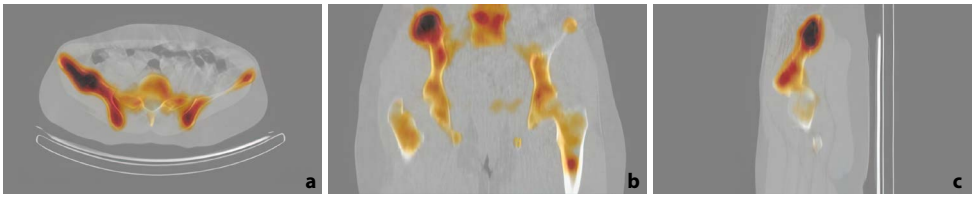


Obrázek 1a, b. Scintigrafie skeletu.

graficky na patologické oblasti skeletu pomocí SPECT/low dose CT (jednofotonová emisní počítačová tomografie/nízkodávková CT) (**obr. 2a, b, c; 3a, b, c**).



Obrázek 2a, b, c. Scintigrafie hrudníku.



Obrázek 3a, b, c. Scintigrafie pánve.

SPECT upřesňuje patologický nález zvýšením kontrastu sledovaného ložiska, čímž zvyšuje senzitivitu vyšetření. Hybridní zobrazení s CT je indikováno k upřesnění lokalizace (nízkodávkové) a strukturání morfologie kostní tkáně (plnohodnotné).

Pro správnou interpretaci je nutné znát fyziologickou distribuci osteotropního RF ve skeletu, podle věku, podle typu jednotlivých kostí a fyziologického zatěžování. U dospělých osob je fyziologicky vyšší akumulace RF v lebce, v osovém skeletu, sytěji se zobrazují klouby, naopak s nižší intenzitou dlouhé kosti. Vzhledem k tomu, že RF je vylučováno močovým systémem, fyziologicky se zobrazují ledviny a močový měchýř.

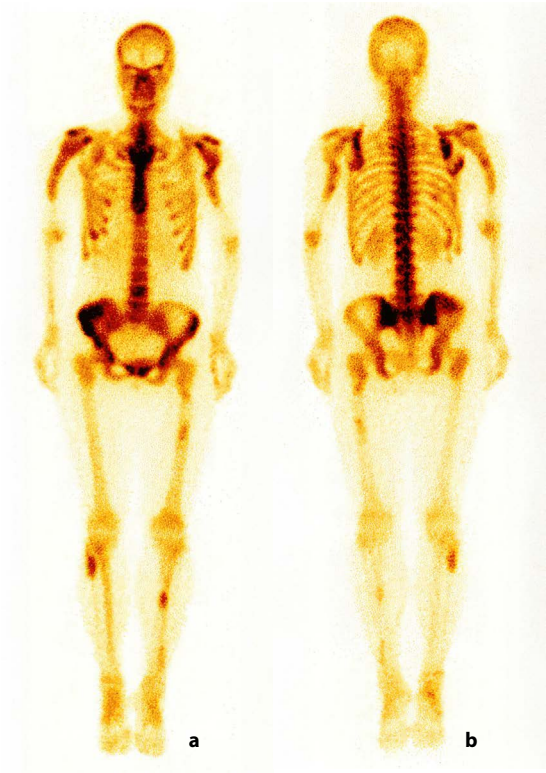
Patologický proces ve skeletu se nejčastěji projevuje zvýšeným hromaděním osteotropního RF, které odpovídá zvýšené osteogenezi (novotvorby či přestavby kostní tkáně), které může mít ložiskový nebo difuzní charakter.

MUDr. Renata Píchová
Klinika radiologie a nukleární medicíny
Fakultní nemocnice Královské Vinohrady a 3. Lékařská fakulta UK, Praha
E-mail: renata.pichova@fnkv.cz

THE FIGURE ON THE TITLE PAGE OF THE JOURNAL: BONE SCINTIGRAPHY USING TECHNETIUM-LABELED PHOSPHATE COMPLEXES (OSTEOTROPIC RADIOTRACER)

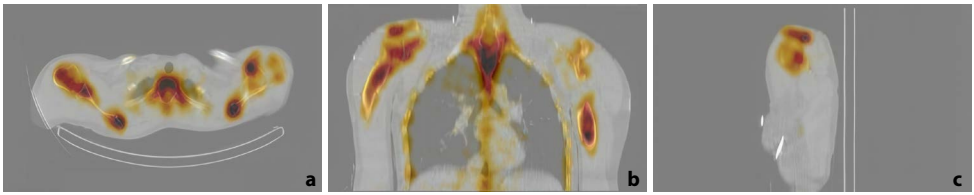
THE FIGURE ON THE COVER PAGE OF THIS JOURNAL shows scintigraphy of the skeleton of a patient with the rare diagnosis genochondromatosis type II using technetium-labeled phosphate complexes, most commonly diphosphonates (99mTc -HDP). Using an osteotropic radiotracer, the intensity distribution of bone metabolism can be displayed scintigraphically. In areas of pathological bone foci with tissue remodeling, there is an increase in osteoblast activity, leading to increased production of hydroxyapatite crystals. These crystals serve as a substrate on whose surface the labeled phosphate complexes bind tightly, either directly in the pathological deposit or in the reactive zone around the deposit. Both appear scintigraphically with increased accumulation of the osteotropic radiotracer (RF).

This is a radionuclide examination where, two hours after intravenous administration of the radiopharmaceutical, the patient is imaged with a whole-body scintillation camera (**Fig. 1a, b**) followed

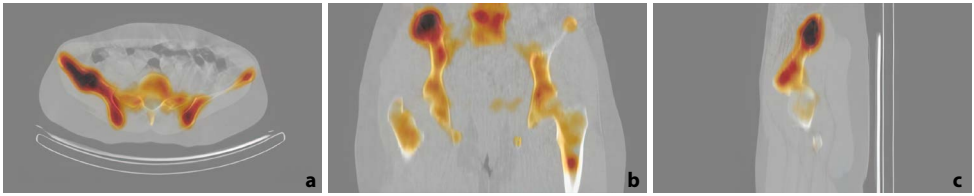


Obrázek 1a, b. Scintigraphy of the skeleton.

by targeted tomography of the pathological areas of the skeleton using SPECT/low dose CT (single-photon emission computed tomography/low dose CT) (**Fig. 2a, b, c; 3a, b, c**).



Obrázek 2a, b, c. Scintigraphy of the thorax.



Obrázek 3a, b, c. Scintigraphy of the pelvis.

SPECT refines the pathological finding by increasing the contrast of the observed lesion, thus enhancing the sensitivity of the examination. Hybrid imaging with CT is indicated to refine the localization (low-dose) and structuring of bone tissue morphology (full-dose).

For correct interpretation, it is necessary to know the physiological distribution of osteotropic RT in the skeleton, according to age, individual bone type and physiological loading. In adults, the physiological accumulation of RT is higher in the skull, in the axial skeleton, with more intense visualization in the joints, and lower intensity in long bones. Since RT is excreted by the urinary system, the kidneys and bladder are also physiologically imaged.

The pathological process in the skeleton is most often manifested as an increased accumulation of osteotropic RT, corresponding to increased osteogenesis (new formation or remodeling of bone tissue), which may have a focal or diffuse character.

Whole-body bone scintigraphy using technetium-labeled diphosphonates, conducted repeatedly in 2011, 2012, 2015, and 2017, demonstrated stationary pathologically increased bone remodeling in both humeri, the medial part of both scapulae, the right ala of the iliac bone, the subtrochanteric region and diaphysis of the left femur, the head of the right fibula, the diaphysis of the left tibia, the right 8^{th}-10^{th} ribs, and the right forearm.

Renata Pichova, MD
Department of Radiology and Nuclear Medicine
University Hospital Královské Vinohrady and Third Faculty of Medicine, Charles University, Prague
E-mail: renata.pichova@fnkv.cz

ORTHOPEDIC EXPERIENCE OF THERAPY BY DMSO (short description)

ORTOPEDICKÁ ZKUŠENOST S DMSO TERAPIÍ (krátký popis)

Karski Tomasz, Karski Jacek
Lublin, Poland

e-mail: tmkarski@gmail.com, jkarski@vp.pl

Keywords: DMSO. Blood circulation disturbances. Therapy. Legs. Brain.

Dear Editor,

We would like to inform you about a new therapy involving the use of DMSO (dimethyl sulfoxide).

Introduction

Very frequently orthopaedic surgeons and rehabilitation doctors must treat patients with blood circulation disturbances in / of lower extremities. Similarly – is in therapy of patients with locomotor system disorders connected with improper brain or peripheral nervous system function – and these – also connected with blood circulation disturbances. The new therapy is connected with using of DMSO (Di – Methyl – Sulfone – Oxygen). DMSO – is discovered in XIX century – by chemist Alexander Zaytsev (Russia). Next was introduced to medicine in XX century in USA and Germany. DMSO makes improvements of circulation in the lower limbs and other parts of the human body. Authors short presentation is also for other possibilities in therapy of illnesses typical in internal medicine.

Clinical symptoms in the situation of blood circulation disturbances in lower extremities

It is a problem with older people. Clinically – pain in the feet, especially in toes – mostly in big toes. The problem of pain is mostly in the night – mostly in the second part of the night. The feet are cold, colour of skin changes – mostly in the big toes – it is dark, brown. In extreme cases – this blood circulation disturbances are the cause of amputation of the legs. Here we inform – (taken from Internet) – every year in Poland there are 30.000 limb amputations for vascular reasons. In England – 25.000. In the Czech Republic 12.000. DMSO protects limbs from amputation.

How to use DMSO [Di Methyl Sulfo Oxygenium Oxide – in the form – of a liquid on the legs.

a. Dilute half of DMSO and half with water. b. Apply this liquid on the skin of your feet, toes, shins and knees. c. Do not spill on your clothes until the liquid is absorbed into the tissues – approximately 20–30 minutes. d. DMSO in the vessels/capillaries dissolves cholesterol and atherosclerotic deposits – it opens the vessels. e. Returns normal blood circulation. f. Circulation in the limbs returns – no more pain problems, no danger of amputation.

How to use DMSO [Di Methyl Sulfo Oxygenium (Oxide)] **– to make blood circulation better in the brain**

Add DMSO – two or three small teaspoons to water in a plastic bottle – together with IRIGASIN salt [this salt is for the sinuses – known to all doctors in all countries – (the plastic bottle you can buy in a Chemistry)]. Mix and shake the water with IRIGASIN and with DMSO. Put cannula to the hole of the nose – press the bottle – allow the incoming mixture to flow / existing flowing though sinuses. From the sinuses to the brain vessels is short distance. Now this will not be only a healing effect on the sinuses by / through IRIGASIN – but – DMSO – from the par-nasal sinuses is absorbed into the brain vessels – it restores circulation – there will be no stroke. Please remember – Cerebral incidents – strokes, Parkinson's, Alzheimer's – USA 795.000 people annually, UK 100.000 people, Poland stroke – 70.000 and Parkinson – 90.000 people.

Prophylaxis / therapy of Internal intestinal illnesses

Prescription of using: a. Half a glass of mineral water + Turmeric (in Polish KURKUMA) – buy at a grocery store, b. add a pinch of peppers, c. add a teaspoon or half a teaspoon of honey, d. squeeze a whole lemon (in polish cytryna) / into a glass of water. e. Mix. Drink. f. Regulates the digestive tract. Anti-cancer effect, anti-sclerotic effect.

Discussion and Conclusion

Using DMSO for therapy or prophylaxis of orthopaedic and neurology illnesses and disfunctions is for us (Authors) known only for 2 years (the information came from an American citizen coming to Lublin Mr. Krzysztof W.). In Poland this was unknown till now (many – T. Karski – phone discussions with Colleagues in Warsaw, Poznan, Bialystok, Kraków, Lublin – they never listen about DMSO). This – DMSO method of prophylaxis we use for us (Authors) personally and – plus – only in / for some patients coming to our Out-Patients Clinic. Our personal experiences (2 years) have shown – that DMSO for the legs and the brain have given very positive results.

Text for translation prepared by Prof. Tomasz Karski and Dr Jacek Karski – on material of Internet and on the Book of Dr Hartmut P. A. Fischer (German doctor and scientist) – the original title of the Book "*Das DMSO – Handbuch: Verborgenes Heilwissen aus der Natur*". **The Book is translated into Polish by Katarzyna Jurczak.**

The author's text of / about information of DMSO – translation from Polish into English – Mr. David Poynton / UK / Lublin

Authors address:
Prof. Dr. med. Tomasz Karski, Ph.D.
home +48 81 742 63 71 | handy +48 604 933 234 (for SMS)
E-mail: tmkarski@gmail.com | www.ortopedia.karski.lublin.pl

Dr med. Jacek Karski, Ph.D.
home +48 81 746 90 60 | handy +48 604 406 291
E-mail: jkarski@vp.pl

TO THE EDITOR

Sir, let me share my own experience with the use of DMSO. I suffered from chronic sinusitis and after a conference (The 26th Prague-Lublin symposium, Praha 2024) where Prof. Karski gave a presentation on this substance, I tried it. I used a highly diluted solution in water and a regular Rhino Horn nasal canister according to the recommendations found on the website. The effect was very fast - within a few days the problems subsided and the condition improved for a long time. I repeated this procedure with success for other infections.

I have not used DMSO for musculoskeletal problems, so I cannot comment on this in more detail.

For an objective assessment of DMSO and its use in medicine, I consulted AI and I want to quoting the general overview:

1. DMSO (Dimethyl Sulfoxide) Report

DMSO, or **Dimethyl Sulfoxide**, is an organic sulfur compound that exists as a clear liquid. It was originally discovered in the 19th century as a byproduct of wood processing (paper production). Today, it is used as an **industrial solvent**, but due to its unique properties, it is also utilized in scientific research and **alternative medicine**.

2. Effects of DMSO on the Organism

DMSO possesses several key mechanisms of action that explain its potential use:

- **Excellent Solvent and Transport Medium (Carrier):** It is a **bipolar** solvent that mixes well with both water and fats (oils). The most important property is its ability to **rapidly penetrate the skin** (and other biological membranes) without damaging them. This allows it to **transport** other active substances deeper into tissues and the bloodstream, thereby **increasing their efficacy**.
- **Anti-inflammatory and Analgesic Effects:** It helps to **suppress inflammation** and **alleviates pain** (analgesic). These effects are primarily used for musculoskeletal issues.
- **Antioxidant:** It acts as a **powerful scavenger of free radicals**, protecting cells from damage caused by reactive oxygen species.
- **Support for Healing and Regeneration:** It promotes the **rapid absorption of edema** and **bruises** and accelerates the healing of wounds and the smoothing of scars.

3. Uses in Medicine (Official and Alternative)

Official Medicine

In the United States (approved by the FDA) and some other countries, DMSO is **officially approved as a drug** for the treatment of one specific indication:

- **Interstitial Cystitis (Painful Bladder Syndrome):** It is applied **directly into the bladder** as an irrigation to alleviate symptoms.

Alternative and Experimental Use

In **alternative medicine** and scientific research, DMSO is studied and used (often as an unapproved drug or as a technical substance/topical supplement) for a wide range of ailments, especially:

- **Musculoskeletal Diseases:** Arthritis, osteoporosis, rheumatic, and degenerative joint diseases, sports injuries (muscle pain, swelling).
- **Skin Problems:** Warts, acne, eczema, fungi.
- **Healing Support:** Scars, bruises, burns.
- **As a Carrier:** Improving the absorption of other topically applied substances (e.g., magnesium oil, herbal extracts).

4. Potential Risks and Safety

Although DMSO is considered a relatively safe substance (especially compared to some pharmaceuticals), it is essential to adhere to strict guidelines and be aware of the risks:

a) Odor and Taste

- **Strong Garlic/Oyster Odor and Aftertaste:** This is the most common and noticeable side effect. The smell is caused by a metabolic product of DMSO, which is released through breath and sweat.

b) Transport of Undesirable Substances

- Risk of Toxin Absorption: Due to its ability to act as a carrier, DMSO can rapidly transport into the body not only beneficial substances but also impurities, toxins, or undesirable chemicals from the skin, clothing, or low-quality plastic containers (DMSO can dissolve some plastics!). *Therefore, it is necessary to use **only highly pure DMSO** (**pharmaceutical grade 99.9%**) and ensure that the skin and application tools are absolutely **clean and free of plastics**.*

c) Skin Irritation

- **Redness, Itching, or Burning:** Especially when using an **undiluted** or too concentrated solution. It is recommended to start with a lower concentration (e.g., diluted with distilled water or Aloe Vera gel) and perform a **tolerance test** on a small skin area.
- **Allergic Reactions:** Although rare, allergy must be ruled out.

d) Unapproved Use

- **Lack of EU Approval:** For most indications (other than Interstitial Cystitis, where an approved drug exists), DMSO is **not approved as a medicine** for human use in the EU. Products available over-the-counter are often sold for technical, laboratory, or cosmetic purposes (but should be of pharmaceutical grade).

Consultation with a physician is always recommended before any therapeutic use of DMSO (especially internal use).

Recommended Concentrations for DMSO

The recommended concentration of DMSO primarily depends on the **application site** and the **sensitivity of your skin**. Most recommendations (especially from alternative medicine and publications on DMSO) are based on anecdotal experience, not officially approved clinical studies for every specific indication.

It is always crucial to start with a **lower concentration** and perform a **tolerance test**.

5. Overview of Recommended Concentrations for Topical Application

The table below summarizes **guideline recommendations** for diluting 99.9% pure DMSO:

DMSO Concentration	Area/Purpose of Application	Description and Reason for Concentration
1%–5%	Sensitive areas (around eyes, thin skin)	Very low, used for minimal penetration and maximum gentleness.

DMSO Concentration	Area/Purpose of Application	Description and Reason for Concentration
30%–50%	Face, Neck, Head area	Moderate concentration suitable for thinner and more sensitive skin. Often used for migraines or jaw problems.
50%–70%	Entire body, Torso, Muscle aches	Common concentration for broad application. A good balance between efficacy and tolerability.
70%–80%	Joint pain, Arthritis, Rheumatism	Concentration used for penetrating deeper tissues (joints, tendons). Recommended for thick skin (knees, elbows, shoulders).
80%–90%	Skin growths, Warts, Scars	Higher concentration for localized, more aggressive use. May cause significant redness and burning.
100% (Undiluted)	Generally Not Recommended	Applied only exceptionally for very stubborn skin issues or locally in veterinary medicine. Highly irritating!

Important Rule: The thinner and more sensitive the skin (face, inner arm), the **lower** the concentration you should use. The thicker the skin and the deeper the problem (joints), the **higher** the concentration may be.

6. How to Properly Dilute DMSO

For dilution, you should only use **pharmaceutical grade DMSO (99.9%)** and always dilute it with **distilled (demineralized) water**, or possibly with high-quality **magnesium oil** or **Aloe Vera gel**.

Critical Safety Recommendations:

1. **Use Only Glass and Ceramics:** DMSO is a powerful solvent. It must **never** come into contact with common plastics (PET, PVC, etc.) or rubber, as it could dissolve toxins from these materials and transport them into the body. Use exclusively **glass or ceramic containers** for dilution and application.
2. **Clean Skin:** Before application, thoroughly wash the skin with un-perfumed soap to remove any impurities, cosmetics, creams, or perfumes that DMSO could transport inwards.
3. **Tolerance Test:** Always start by applying a small amount to a small area of skin (e.g., the forearm). If you feel only slight warmth or itching within 15–30 minutes, this is acceptable. If you feel severe burning, redness, or swelling, immediately wash the area with cold water.

Authors address:
Jan Všetička, MD
Clinical geneticist
EUC laboratoře CGB, a.s, Kořenského 1210/10, 703 00 Ostrava – Vítkovice.
E-mail: jan.vseticka55@gmail.com

HEALTH ISSUES BY HYPOKINESIA, SITTING AND LIVING IN A DIGITAL WORLD OF CHILDREN IN "OVERCIVILIZED" SOCIETIES. OR HOW CULTURAL EVOLUTION BROUGHT US „IDIOPATHIC" SCOLIOSIS (ASSAY)

ZDRAVOTNÍ PROBLÉMY ZPŮSOBNÉ HYPOKINEZIÍ, SEZENÍM A ŽIVOTEM V DIGITÁLNÍM SVĚTĚ DĚTÍ „PŘECIVILIZOVANÝCH SPOLEČNOSTÍ. NEBO JAK NÁM KULTURNÍ EVOLUCE ZPŮSOBILA „IDIOPATICKOU" SKOLIÓZU (ESEJ)

P.J.M. van Loon[1], A.M. Soeterbroek[2], T.H. Smit[3]

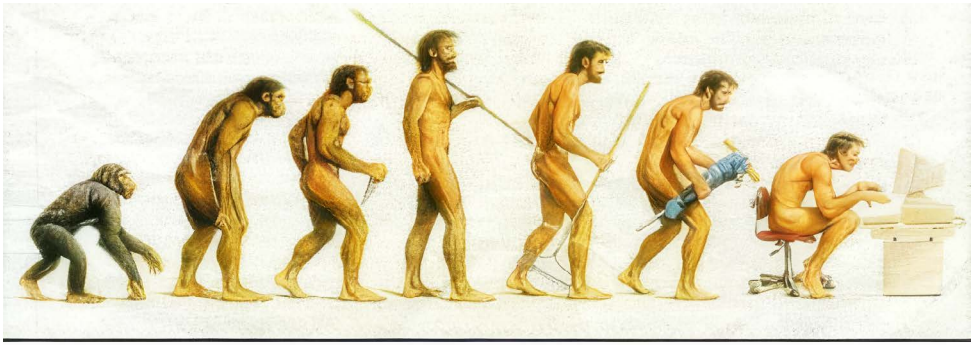
[1] Orthopedic surgeon, Proktovar, Hengelo, the Netherlands

[2] Analyst, Chairman Posture Network Netherlands

[3] Em. prof. neurosurgery Radboud University Nijmegen;4: Professor Tissue Engineering; Mechanobiology of development and disease; Amsterdam UMC UMC

INTRODUCTION

Each era in history of mankind and each part of the world has had and will have its own frequently present health conditions, because of the way we live. Many of these conditions can disappear too in the case of infectious diseases, but not if caused by the broader negative aspects of civilisation on our body health. Maybe important in this is the way we increasingly misunderstood or forgot the importance of providing our children full help and support with the healthy natural development and the lifelong quality of our neuromusculoskeletal system. The increase in spinal problems and even („idiopathic") scoliosis seems part of that decline and is there to stay in the „overcivilized" societies. Accelerated transformation of rural living societies into urban, sedenatary and techdriven societies (like Korea and China) will make musculoskeletal conditions, thus also spinal problems „pandemic" (**1**). We try to explore and combine different parts of scientific knowledge in a changing environment to understand the global decline of health and the pandemic spinal problems from pain to scoliosis (**2**).



Somewhere, something went terribly wrong

Fig. 1: A well known cartoon. But what do we know about the patho-anatomy and patho-physiology of what happened with our body by this cascade in civilization?

EVOLUTION AND MEDICINE

Every book on history of Medicine can give ample examples of these unhealthy conditions and the more homo sapiens started to spread out over the world, the more genetic, infectious and manmade environmental causative factors will be spread over the continents. The way humans organised their way of living, from hunting and gathering in free nature to live in blocks of flats staring to screens will alter their possibilities to achieve full health (**3**). Sitting (on chairs) became such a lifestyle factor that conquered the world after it started as prevailing activity for the masses first in „Western countries" were obligation of schooling brought everybody to read and write in sitting positions. Effects of too much sitting is unhappily nowadays not good enough researched in childhood on its influence on the individual health, or conclusions out of historic research became forgotten or underestimated in its importance (**4**).

For the development of individual health only basic biological needs has to be provided like enough food, all needed nutritions, water, warmth and light from the sun, free locomotion, shelter and of course proper caretaking of adult animals for their offspring (**5**). But all animal life is defined by its possibility to move(locomotion), or it is crawling, swimming, flying or walking. But only men sedated in houses, cities and in the last two centuries increasingly on chairs and sofa's, nowadays mainly sloughed and slumped in posture, still not aware of its negative effects on their durable health (**6**).

ONTOGENESIS VS PHYLOGENESIS

The individual development of unborn animal life from the fertilised egg until birth in vertebrates is called embryology and part of ontogenesis. Since the full exposure and broad accetaption and expansion of the evolution theory (Charles Darwin, Alfred Russel Wallace, Jean Baptiste de Lamarck) in which all species started once from unicellulair life, the biologic scientist call it phylogenesis. Since the end of the 19th century the biomedical scientific world equate the ontogenesis of the

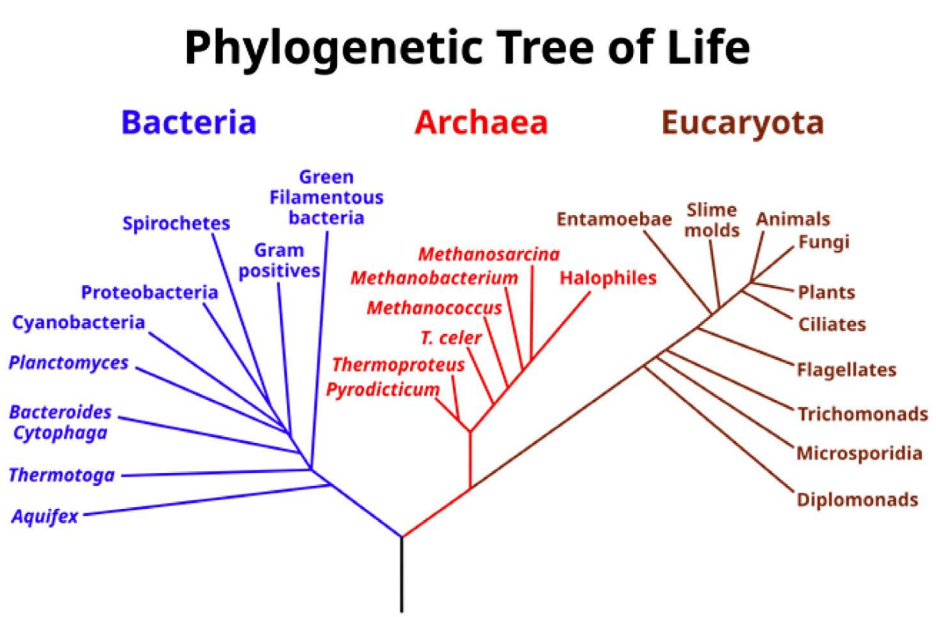


Fig. 2: Phylogenesis in evolution from the first monocells towards an extreme wide variety in multicellulair organisms. Homo Sapiens is only a very small species in the Animal Kingdom.

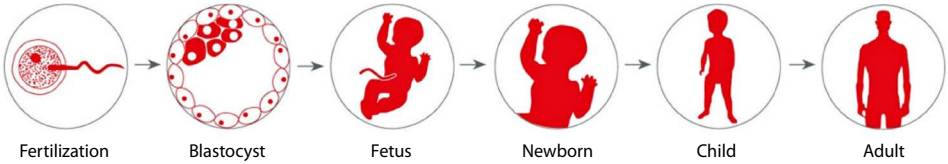


Fig. 3: A condensed infographic presentation of the pathway between the fertilized eggcell towards adulthood of man. The only difference between the phylogenesis of man and his ontogenesis is the timesapn: millions versus 18–20 years.

living individual with the phylogenesis of their species. The presence of homo sapiens in the long history of life on earth is only a minuscule part but he managed, with accelaration of his possibilities to innovate techniques and conditions, to himself a myriad of negative consequences. So modern medicine has to react on many new exogen factors, conditions and events that influence their epigenetics (**7**). Sedentary lifestyle (hypokinesia excecuted in chairs) as a chosen and climatechange by excessive CO_2-production as a non chosen factor are some of the greatest cultural evolutionary threats of durable health of people (**8**).

GROWTH AND ANATOMY. FORM FOLLOWS FUNCTION

The early embryologic stages between the foetus of a human, chicken, pig or frog are very similar in the first six weeks. The basic formation of the organsystems and development of interdependant functionality of organs is similar in the embryologic period and postnatal period in all. It is only the human child that takes about 18 years to reach full maturity of all interdependant organ systems, including its central nervous system, including the neurocognitive functions of their brain. But with apperently forgetting the most profound and indisputable axiom in biology: „Form follows function": „it is all you do, perform or undergo actively that forms your adult anatomy and your health", the prognosis for a durable health in adulthood had not improved. „If you don't use it you loose it" is a wellknown consequence of not accomplish that natural morphogenesis (**9**).

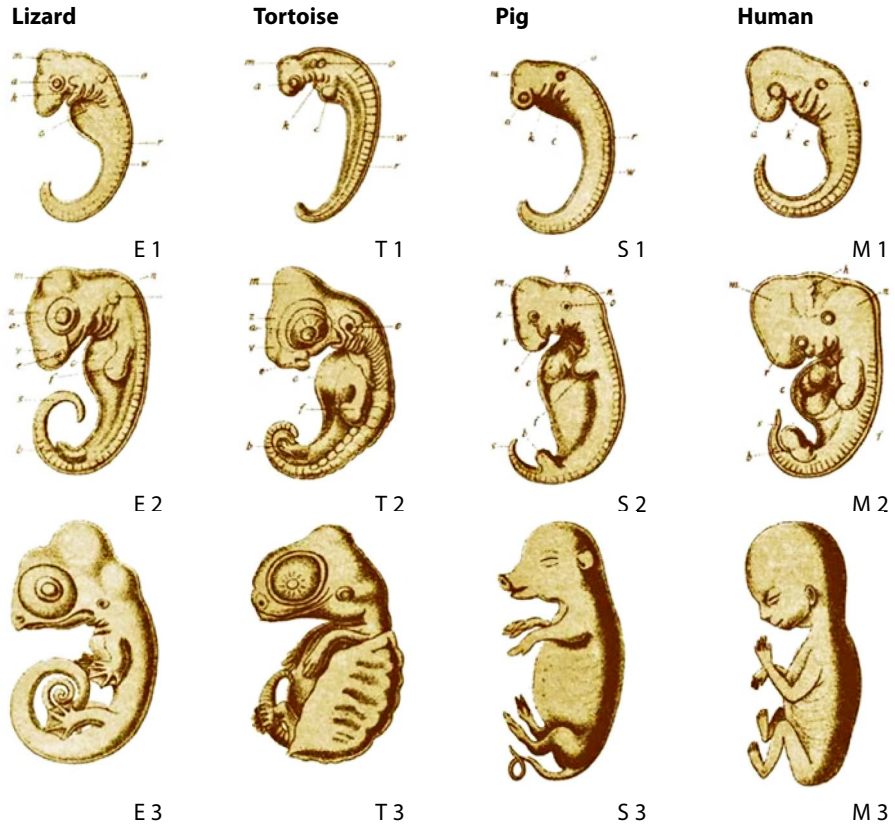


Fig. 4: In the first 6 weeks after gestation the development of the embryo is very similar between different vertebrates, like here in lizards, the turtle, the pig and the human embryo.
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Modern men seems to be the only species that hinders (by all aspects of sedentary lifestyle) their offspring the natural urge for free locomotion and the urge to freely investigate its environment and world. Even baby's are immobilised in chairlike products, that prevent them to get rid of the foetal kyphosis where they were born with. Puer ludens became puer sedens.

Gradual development towards the end-anatomy of the outside (posture) and the form and function and realtions of the inside organs of the newborn and growing child is a complex, but understandable process. The complete processing of all biochemical substances controlled by the neurohormonal system and the autonomous nervous system is dependant of good coordination and cooperation of a well adjusted nervous system as a true „learning machine" together with an optimal working system of heart, vessels and blood circulation. Where we speak of Homoiostasis of all aspects of contents in cellfluid, tissuefluid and the contents in blood of all sorts of biochemical substances, we speak also of homoiostasis in all biomechanic factors that provide balance and optimal locomotion in the continuous play with gravity, when we are awake. It is called propriocepsis and should be an optimal learning process of interaction of the nervous system, including sight, hearing and smell, and the musculature as it is attached on a very „intelligent" way on all the elements of the skeleton, to make complex locomotion possible, as is needed for example in complex hunting actions or nowadays sports, like tennis or gymnastcs (**10**). But all locomotion and balances a long learning process, that start already a few weeks after birth. But the civilization has its costs: modern men is the only species that introduces hypokinesia in their childs life that hinders the learning processes (of growth) to reach optimization.

NATURAL LAWS IN HUMAN BALANCE

Scoliosis seems to be a peculiar variation or deviation of our continuous play with gravity in balance and locomotion during the period of growth as a bipedal very upright animal with a heavy skull. In this lifelong play with gravity any substance, anorganic, organic or living material from cell to complete organisms have to obey Natural Laws (**11**). Certainly in Growth, the fact that an organism, like we bipedals, grow against gravity upward and can keep our vertical position with balancing our heavy skull above our feet, shows that tension to pull masses upward and keep it there while standing and walking must be the decisive force to achieve that. It need respect, that Nature made it possible that muscles that can only shorten themselves, are able to „pull" the weight of the skeleton and especially the heavy human skull vertical and upright exactly above the feet. It was Leonarda da Vinci in his biomedical writings and drawings that gave us the undisputed definition of natural posture: there should be a vertical line down from the ear, along the head of the shoulder, the centre of the trochater, the knee and the foot/ankle.

Negative influence on that process of reaching natural anatomy and balance, and prologed sitting as main „activity"during hypokinesia as the main disturber, will give sagittal and coronal imbalance in loading and tensions, leading to deformations. This complex matter is well described in Vladimir Janda's work on „Muscular Imbalance": in a kyphotic posture your abdominal muscles, your glutei and upper spinal erectors will be hypotrophic and the lower spinal extensors, the hamstrings and

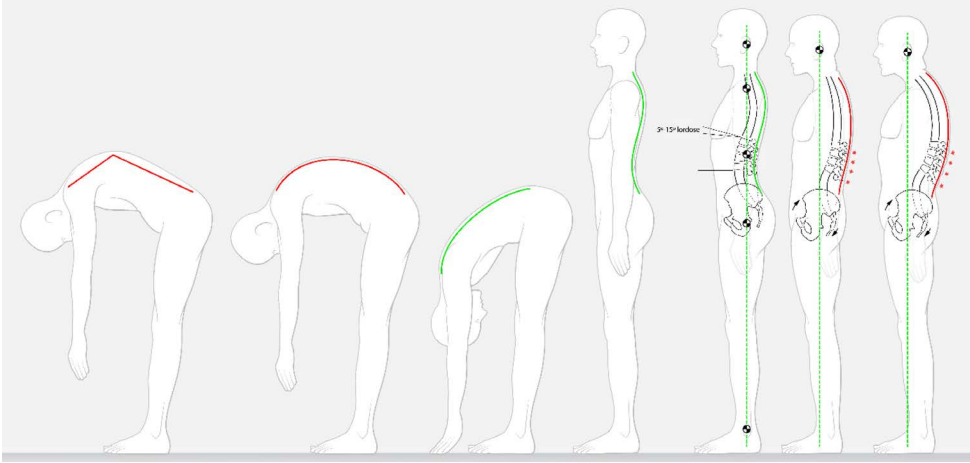
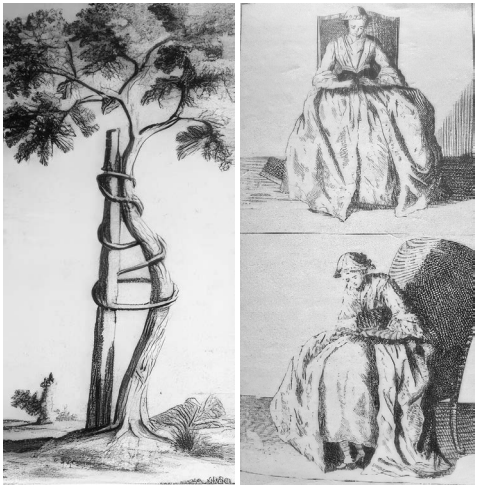


Fig. 5: Infographic on a natural posture (green) as the give definition by Leonardo da Vinci: The plumbline from the ear will pass the center of the shoulder, the center of bodymass, centre of the hip , knee and ankle. In red a moderatie sagital imbalance and a more massive imbalance by hyperkyphosis that ends ditally in the higher lumbar area or even lower. The lack in flexibility in the Finger Floortest is caused by increased tightness in neuromuscular structures (drawings Erik Crins).

calve muscles will be hypertrophic or qualified as „tight" (**12**). In an own survey on posture and tight hamstrings in 248 adolescent schoolchildren (14–18 years) about 60% had bilateral short hamstrings and about 60% did show an abnormal hyperkyphotic curve (angular or arcuate) assessing the Adam's bending test from lateral (**13**). No information was get on the duration of sitting hours, but for the Dutch youth it's proven otherwise that they are European Champions in sitting!



CROOKED WOOD AND BONE

There is ample evidence that osseous tissue (bone)in a young animal/child and wood in growing trees react in a simular way in the process of growth to external deforming forces that can deform the structural integrity of the organism. In men it is the very recent addiction of sitting on chairs or heavy physical labour in childhood that can deform the alignement of

Fig. 6: The allegoric drawing of a young crooked tree protected and guided in further growth by a pole in the book Orthopaedia of Nicolas Andry. He already depicted sitting of girls on chairs (in rich families) as a spine deforming factor of great importance.

the skeleton by creating overloads and shearloads on cartilage and discs. In trees it is the influence of winds and storms that can lead to malformation. In the very first book of Orthopaedics of Nicolas Andry (Paris 1741), his famous drawing of a crooked tree tight with ropes on a vertical pole became the logo of this field of medical direction and all orthopaedic societies worldwide. But it is misunderstood as being a form of treatment of deformations, while it was meant as nothing more than an allegory on this preventive action to put poles along very young trees, as to protect them preventivily from growing crooked against the deformative forces of winds and storms. It has lead to the subtitle of Andry's book: „Orthopaedia, or the art to prevent and correct all difformities of the child's body, by all means and possibilities disposable to the fathers and the mothers and all people involved in raising children" (**14**).

ASYMMETRY IN LOADS AND TENSIONS

In manmade structures of different parts and materials, like bridges, houses, cars etc. etc., equilibrity in loads and tensions and quality and strength of the materials provide what was called in architecture by Buckminster Fuller as "Tensegrity". In fact all Natural Laws in Mechanics by Isaac Newton and Dynamics (energy, springs!) by Robert Hooke can be seen incorporated in living structures too. In manmade structures miscalculations in the use of the mathematic certainty of these laws or underestimate gradual loss of quality in the used materials can make the structure sensitive for early or late collaps. Lack of knowledge nowadays of the fact that in the period of growth the human child has to build up optimal quality of the materials (bone, cartilage, discs, fascial and tendon) structures and an optimal quality of its structural integrity by balanced tensions makes its body sensitive for early or late collapse or invalidating shortcomings.

Also spiralizing of parts of living structures, like scoliosis in men are a consequence of unbalance in structural integrity with local increased tension or tightness in muscular structures (Janda) and researched and described in the plant kingdom (D'Arcy Wentworth Thompson, Felix Paturi, Claus Mattheck) (**15**).

DISAPPEARANCE OF KNOWLEDGE ON HUMAN SPINAL GROWTH DISORDERS

But for understanding gross anatomic malformation developing in the whole process of postnatal growth, like scolioisis, more knowledge on Growth, an indispendable part of all life in the vegetable and animal kingdom and all the tissues that are part of movement/ locomotion as the other indispendable part of all life in animals, the biomedical scientific world has to wait for two researchers, the orthopaedic surgeon Murk Jansen from Leiden (NL) and the neuroradiologist Milan Roth of Brno (CZ) to understand scoliosis more properly. Of both their work, vast and impressive research done on scoliosis and bone deformation, around 2000 nothing was left or could be found in the new (and now prevailing) digital biomedical search systems like PubMed! It was by coincidence

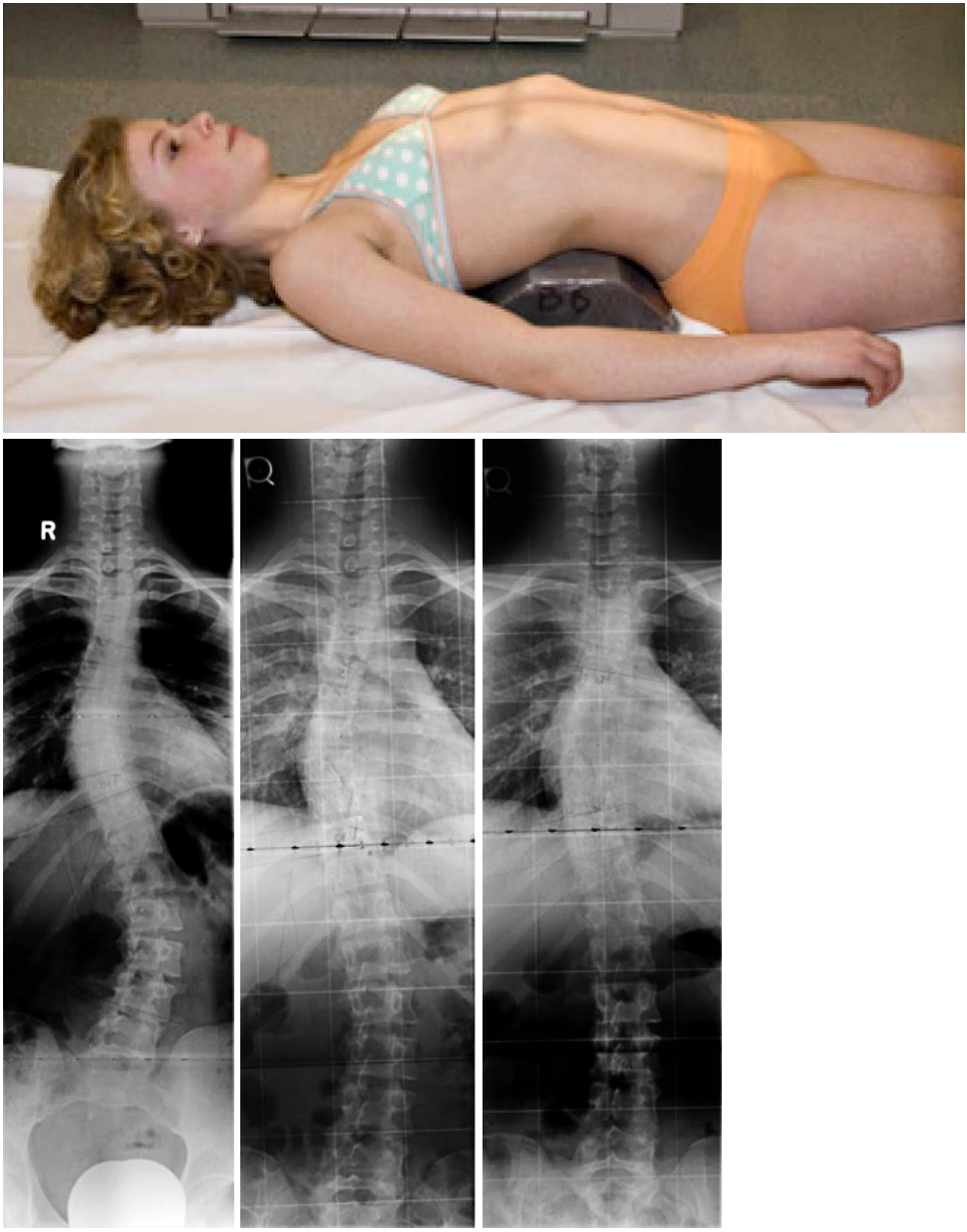


Fig. 7: Correcting the ever present kyphosis at the thoracolumbar spine (Th10-L2) in scoliosis was proven and published and was implemented in the brace technique called TLI (Thoracolumbar Lordotic Intervention).

that both their research in medical science were discoverd and came together in a proces of reversed engeneering after invention (by serendipity) that correction of scoliosis could be achieved by extending and creating lordosis of the thoracolumbar spine (Th10-L2) by the first author (PvL) (**16**, **17**, **18**). Both historic researchers stressed, that the bony anatomy, functionality of and muscular attachements on the thoracolumbar spine (Th10–L2) as is the typical human position of the conus medullae at the centre of this form the quintessence of optimal human locomotion and balance.

It were the two World Wars and the Cold War that were responsible of neglectance and disapearance of their pediatric orthopedic research on deformities, because of focus on traumatology and rehabilitation But the underlying geopolitical battle took care of the exclusion of their opponents (neutral) biomedical science.

ASYMMETRIC ROTATIONAL FORCES IN THE BIPEDAL HUMAN WITH UPRIGHT SPINES

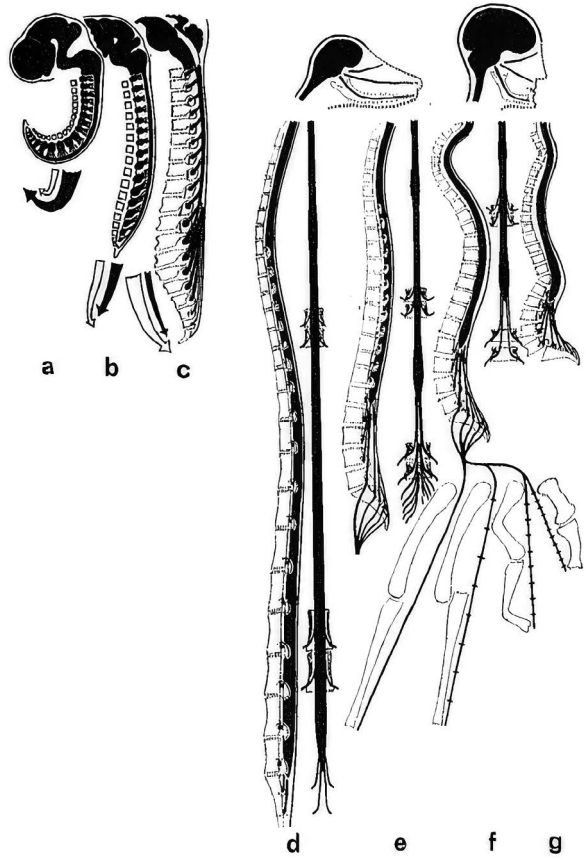
For his monography on scoliosis, published in Leiden in 1912, Murk Jansen (1867–1935) in his introduction, he could draw out of vast orthopeadic and biomechanical knowledge build up in almost two centuris in European (French, English, but mainly German) published textbooks and research literature in journals on development of healthy posture and also since 1950 dealing with the negative effects of sitting in childhood on that development of physical healthy anatomy. Clinical experience and observations made already clear to keen physicians that (too) early and longstanding



Fig. 8: The very important but neglected monography of the Dutch orthopedic surgeon Murk Jansen on scoliosis (1912) revealed very intriguing studies in cadavers, in vivo and animal experiments that provided clearity of the prence of a stiffening kyphotic thoracolumbar spine (der Sitzbuckel in young children) that will result in scoliosis as the asymmetric forces of the left and right crurae diaphragmatica will create left directed rotational forces.



Fig. 9: Portrait of Prof. Milan Roth (1923–2006) at his 80th birthday. He concepted as a neuroradiologist after astonishing observations on the central cord in spines with scoliosis pneumomyelography in a longstanding and intensive research the Osteoneural Growth Relations in which the possible discongruency of the mitotic growth of the somatic cells and the growth by stretch of the neural cells by all means that hinders this growth by stretch of nervous cells is responsible for skeletal deformities in the first place the spine with its very mobile segmentation. In his drawings he was able to show the events in time in the period of growth.



passive sitting of baby's and toddlers creates kyphosis at the thoracolumbar spine (der Sitzbuckel). This although the endemic „English disease" or rhachitis got a lot of blame too in causing skeletal deformities. In deducting the different internal anatomy and position of organs in bipedal (heart leftsided, liver rightsided) he confirmed with cadaveric studies (with the famous British orthopedic surgeon Robert Jones from Liverpool) that the anatomy of the two crurae diaphragmatica was asymetric and that the left one looks firmer and must be stronger. This can explain the existence of asymmetric strength breathing in favour of the left crux. With in vivo experiments with suspended toddlers and in animal experiments (hares with same left right lateralisation of organs) he could show this consequent left sided rotational force in ventilation (**19**, **20**).

It was Roth that discovered firstly on pmeumomyelography that the position and caliber of the central cord was abnormal with long contact zones of the cord and rootcomplex with the bony envelop in the spinal canal in scoliosis. He spent more than 30 years of research and all sort of experiments to show that any form hindering the growth by stretch of the nervous cells gives all sorts of deformations of the skeleton. Lack of oxygen, the most important substance for the nervous cell, like on birth, will end up in a myriad of skeletal malformation, called Cerebral Palsy. His work on a broad spectrum of discongruent osteoneural growth conditions was described condensed but very revealing in his book Neurovertebral and Osteoneural Growth Relations (1985). But his main focus was on the spinal deformities, where scoliosis stayed the most intriguing until now (**21**, **22**, **23**, **24**).

SEDENTARY LIFESTYLE; EXPANDING THREAT TO HUMAN HEALTH AND THE SPINES. THE ADDICTION TO SCREENS

Sedentary lifestyle is based on two very related parts: hypokinesia and sitting. Hypokinesia is not using your muscles in order to move your joints for prolonged times in a day and for longer periods in your life. It puts our metabolism of all biochemical substances in a restposition. By that. no or almost no neurotransmitter transfer in neuromuscular and interneural synapses has impact on the general neurotransmitter metabolism, with consequences for the metabolism in the neurohormonale apparatus too. During the period of growth this hyokinesia must have extensive consequences for all processes of growth, that are normally processes of optimization, where all morphogenesis and physiogenesis of healthy organsystems is dependant on. The most impressive work on consequences of hypokinesia on health was done by prof. Jana Parizkova of Prague. She showed that young rats under hypokinetic circumstances during growth do live shorter. Even offspring of pregnant rats under hypokinetic circumstances did live shorter than of normal moving pregnant rats. Lack of creating a suficient amount of sysnapses to connect all nerve cells to the new somatic cells must be part of the explanation, that an organism can decline much earlier (**25**).

Lack of movement in adults can be involuntary (prolonged bed rest, neuromuscular conditions, living in outerspace like astronauts) or voluntary by our massive timespending on chairs and sofa's at home or at „work", endless travelling in chairs that promote kyphosis (cars, busses, trains, airplanes) lead to serious decline in quality and health of bone, muscles and connective tissue.

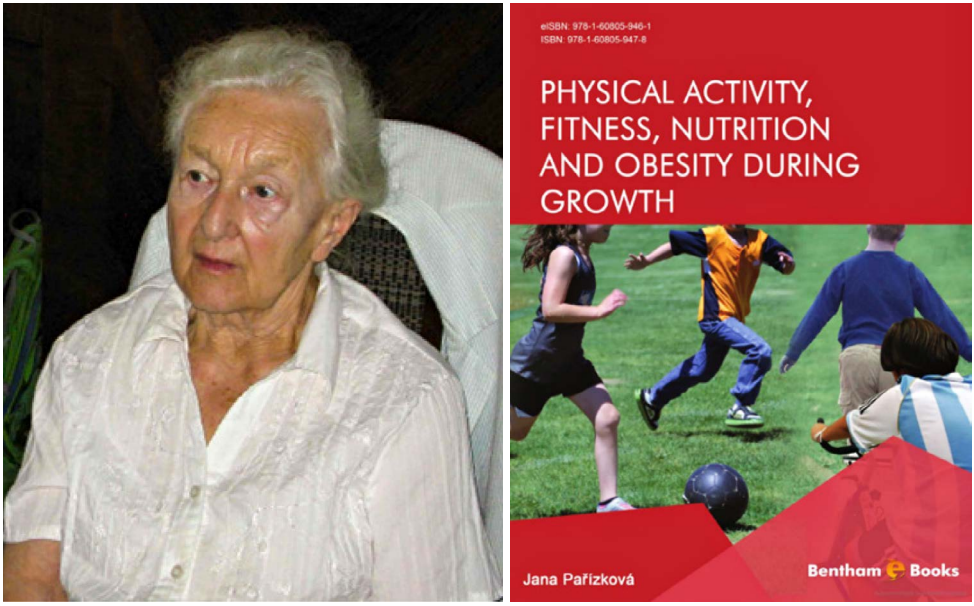


Fig. 10: Very impressive clinical epidemiological studies and animal experiments in rats on hypokinesia were done by Prof. Jana Pariskova of Charles University of Prague.

Epidemiological studies on osteoporosis, sarcopenia an injuries of tendons, fascia and ligaments do show this decline. But the first two were studied in older people and not in youngsters as are the injuries. But in the period of growth too much sitting plays her own distinctive role in morphogenesis (**26**, **27**).

But Homo sapiens entered as homo sedens an new era with technology, in which now much arousal is raised in the world of concerned parents by the impressive warning psychologists and psychiatrists delivered when the impact of constant input of digital content on smartphones, tablets and smart-tv sets, was aggravated by the brain -poisoning influence of social media content becomes clear an is made responsible for the exponential increase of neurocognitive and neurodegenerative conditions (**28**, **29**). It seems that modern Medical science, in all its efforts too cure or mitigate all the „lifestyle dependant"health conditions forgot the knowledge on raising children towards a more optimal anatomy and functionality'as the most powerfull preventive medicine you can get. It looks it's done by neglecting the knowledge on what an overload of sitting and abnormal sitting postures as slumping and sloughing will do in terms of deformation with the child's body from „bad posture'to scoliosis (**30**, **31**).

The general health of peoples is jeopardised by this missing of preventive knowledge in raising children properly into good health, resulting in pandemic chronic diseases or conditions of all organ-

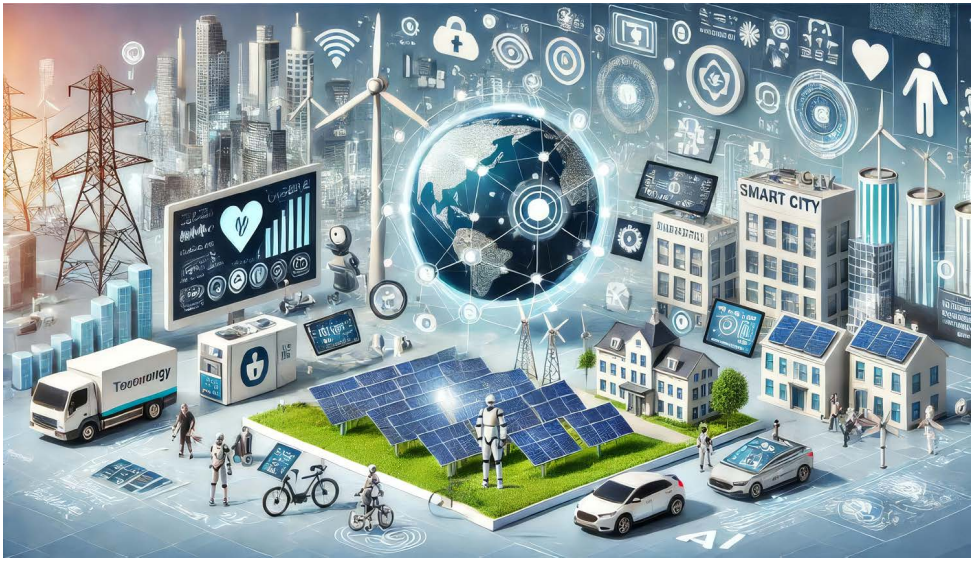


Fig. 11: Infographic of all sorts of technology that is implemented in modern life. From the introduction of the train, cars, television, computers towards smartphones and now AI, the most prevailing posture in using this all is sitting, mainly sloughed and slumping with minimal use of muscles (hypokinesia).

systems. Understandig by everybody, that growth should be an optimization of structural integrity with tension as a steering force, obeying all Natural Laws in biomechanics (**32**).

But all piled up biomedical wisdom and science together did not have yet too much effect on the way modern homo sapiens looks to his own health or cope with it. Or is practising strategies to keep the children away from all health conditions, were they don't ask for!

Huge efforts by politics, authorities, scientists, physicians, educational systems, but above all parents are needed to save the childrens brains and neuromusculoskeletal system for further and irreparable decline of human health by our „overcivilization".

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Author Address:
P.J.M. van Loon
Orthopedic surgeon, Proktovar, Hengelo, the Netherlands
E-mail: pvanloon@planet.nl

CALCANEOGENESIS WITH SECONDARY ACHILLES TENDON-BONE-ALLOGRAFT FOR REPAIR OF THE LOSS OF HINDFOOT FUNCTION. A 12 YEARS CASE REPORT

CALCANEOGENESE SE SEKUNDÁRNÍM ALOGRAFTEM „ACHILLES TENDON-BONE“ PRO NÁHRADU ZTRACENÉ FUNKCE. KASUISTIKA – VÝSLEDEK PO 12 LETECH

Zwipp Hans

Center of Orthopedics and Traumatology of the University Hospital Carl Gustav Carus at the Technical University of Dresden, Germany

ABSTRACT

Background
Loss of complete hindfoot function caused by calcanectomy and resection of the Achilles tendon due to severest soft tissue and bone infection is very hard to repair.

Objective
Ilizarov's "calcaneogenesis" is possible including preservation of the ankle joint. Even after 3.5 years of functio laesa of the triceps surae muscle with fatty degeneration it can function again and be rebuilt almost normally.

Material and Methods
A 25-year-old motorcyclist suffered a 3rd degree open calcaneal dislocation fracture (type 5). Severest soft tissue infection, osteitis and necrosis required calcanectomy, resection of the Achilles tendon and a free vascularized latissimus dorsi muscle transfer. 9 months later in our unit, a talus corpus osteotomy with Ilizarov distraction created in the 1st step a "neo-calcaneus". In a delayed 2nd step a fresh-frozen Achilles tendon-bone block allograft was transplanted to regain active plantar flexion.

Results
The initial AOFAS score of 35 points was significantly improved to 70 points 12 years after step 1 and delayed step 2. After both operations the patient could walk without an orthosis and regained 88% of normal plantar flexion strength. Quantitative measurement of health outcome according to EQ-5D-5L was marked by the patient with 80 out of 100 points.

INTRODUCTION

Evolution took millions of years to develop the human foot as a prerequisite for upright walking. The human heel bone, as the largest tarsal bone, is attached on its back by the strongest tendon of the human body. The interaction of both guarantees free walking and has been a symbol of life in freedom since ancient times. This ingenious gift of nature can be lost to the individual within milliseconds if both elements of the hindfoot leverarm are lost due to an accident, as in the present case due to a following foudroyant infection and necessary radical debridement to save patient's life and extremity.

HISTORY, DIAGNOSES AND FINDINGS

A 25-year-old motorcyclist suffered a severe barytrauma of the left foot in a high-energy trauma caused by a collision with a tractor. After helicopter emergency care at the scene of the accident, primary care was provided at the regional university clinic. There, a third-degree open calcaneal dislocation fracture (type 5) on the left [**1**] with an ipsilateral cuboid impression fracture and multiple Lisfranc fractures was discovered radiologically (**Fig. 1a**), a left clavicle and left metacarpal fracture as secondary findings.



Fig 1. Radiologically serial fractures of the left hindfoot and midfoot (day of accident). **a** Calcaneal dislocation fracture (type 5, 3rd degree open) with cuboid impression fracture and Lisfranc fractures, x-ray taken on the day of the accident. **b** Emergency treatment with debridement, adaptive K-wire osteosynthesis, tibiotarsal transfixation and artificial skin coverage.

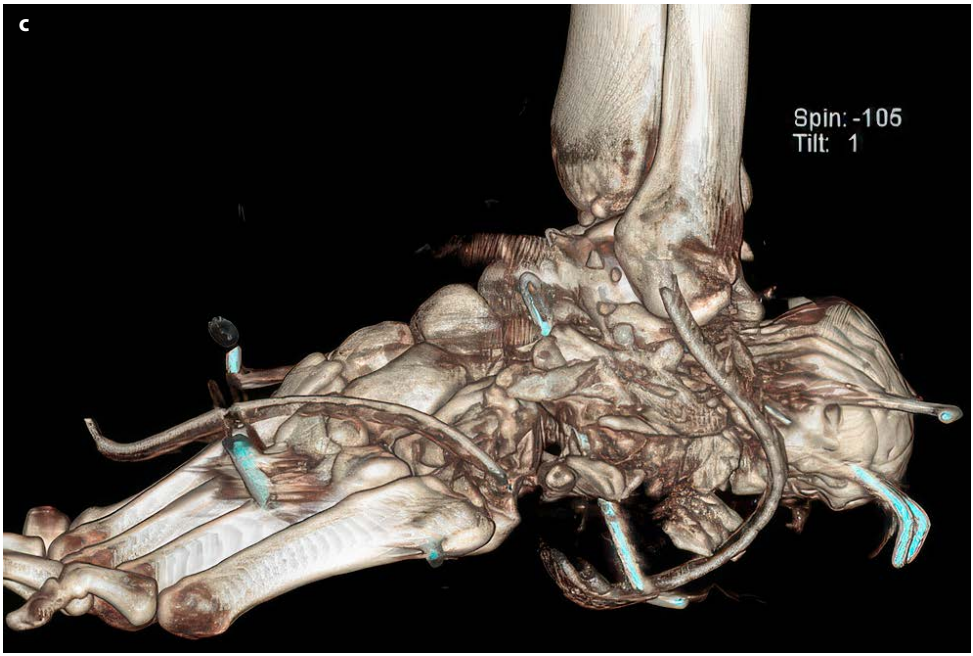


Fig 1. Radiologically serial fractures of the left hindfoot and midfoot. **c** CT scan control (2 days after accident).

An initial attempt to preserve the left hindfoot with debridement, adaptive K-wire osteosynthesis, relieving tibiotarsal transfixation of the foot and artificial skin coverage (**Fig. 1b, c**), failed due to a foudroyant mixed infection of the heel bone with the surrounding soft tissues. This required repeated radical debridements including at least calcanectomy, Achilles tendon resection and surrounding soft tissue structures. The fifth operation was a free transplanted latissimus dorsi muscle flap with partly large mesh graft areas to preserve the limb.

First presentation in our unit 6 months after the accident

On imaging there were only remnants of the anterior calcaneal process on the lateral side and the sustentaculum tali on the medial side (**Fig. 2a, b**). The patient was only able to walk with a very individually manufactured orthosis (**Fig. 2c**). The mirror table image (**Fig. 2d**) showed the absence of the bony heel, the pathological load bearing in the midfoot area and the massive flap expansion distally with a completely atrophied calf on the left.

Options of therapy

The patient was offered a purely conservative orthotic treatment, lower leg amputation with endo--exo-prosthetics and as a third alternative the Ilizarov calcaneogenesis with preserving his ankle



Fig 2a–b. Initial presentation in our unit 6 months after the accident with 5 previous operations, the last one as a latissimus dorsi free flap. **a, b** Lateral weightbearing images show the subtotal calcanectomy, a tibial inclination with one remaining K-wire. The CT scan (b) shows a questionable avascular necrosis or a severe demineralization of the talus.



Fig 2c. Initial presentation in our unit 6 months after the accident with 5 previous operations, the last one as a latissimus dorsi free flap. **c** special orthosis.

joint. The patient was informed that an Ilizarov lengthening procedure usually takes long time of treatment, involves numerous hospital stays, requires full cooperation of the patient, and that the outcome after talar osteotomy would be uncertain. The patient specifically wanted the third option, despite the effort and all the risks.

Preoperative judgement and indication for calcaneogenesis

After removal of a remaining K-wire (**Fig. 2a**) at his home hospital an Angio-MRI of the foot and distal lower leg could be performed. An avascular necrosis of the talus could be ruled out. Therefore an indication for calcaneogenesis became realistic. But neither remnants of the Achilles tendon nor remnants of the flexor hallucis longus tendon could be seen in the Angio-MRI.



Fig 2d, e. Initial presentation in our unit 6 months after the accident with 5 previous operations, the last one as a latissimus dorsi free flap. **c** special orthosis. **d** mirror table image (preoperative) with missing bony heel, midfoot load bearing (arrow). **e** 8 months after calcaneogenesis with noticeable hindfoot enlargement and dorsalization of load bearing (arrow).

THERAPY

Calcaneogenesis

Nine months after the accident, the talus was approached dorsocentrally in prone position of the patient. The body of the talus was osteotomized dorsally 1.5 cm above its posterior facet with a broad, sharp chisel as planned (**Fig. 3a**). The bone wedge, which narrowed distally, was grasped with 3 olive wires, and the Ilizarov fixator was then completed under sterile conditions in the supine position (**Fig. 3b–d**). After 5 days, the daily 1 mm transfer was started, and the patient and his father

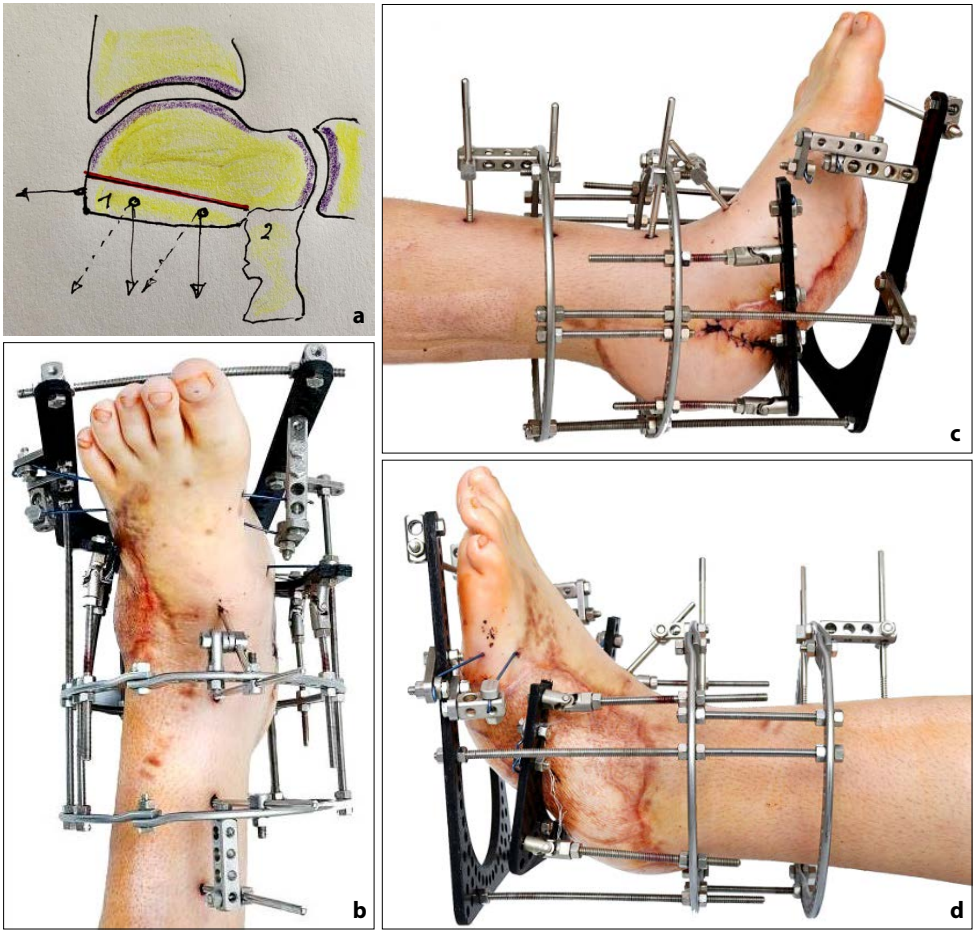


Fig 3a. Plan for the talar osteotomy, 9 months after the accident: 1 = wedge dorsal 1.5 cm, ventral 1 cm, 2 = lateral remnant of the anterior calcaneal process (operation 15.3.2012). **b–d** Ilizarov montage seen from above, medially and laterally.



Fig 3e, f. e Visible callus formation after removal of the fixator 3 months postoperatively; start of pulsed ultrasound. **f** Callus development after 5 months postoperatively under increasing full weight bearing in a mid-height sports shoe.

were instructed in detail on how to handle it, including pin care. Despite meticulous pin care by the patient, the fixator had to be removed after 3 months at his home hospital due to pin infections. Subsequent pulsed ultrasound treatment started (**Fig. 3e**). After two further months, the callus was firmly established under increasing full load in mid-height sports shoes (**Fig. 3f**).

Conservative interim phase checking further therapy options (2013 to 2014)

Although the patient was able to walk 3 km pain-free in mid-height sports shoes already 6 months after calcaneogenesis and beeing fully able to work as a mechanical engineer since months, the patient asked repeatedly for more plantar force. But a local m. flexor hallucis longus transfer substituting the lost Achilles was impossible because of complete absence. A m. peroneus brevis-transposition into the "neocalcaneus" appeared to make no biomechanical sense because the dorsal part was too short. So the last option for regaining plantarflexion force was just a transplantation of a homologous Achilles tendon bone block.

However, since the severe hindfoot infection had only occurred one and a half years ago, the patient's overall situation was improved by the uncomplicated calcaneogenesis with regaining the ability to walk 3 km in a mid-height sports shoe, since a fivefold increase of the repulsive force was measured (**Fig 6b**), and a recovery of the fatty degenerated triceps surae muscle after 18 months inactivity seemed unlikely, we hesitated to offer the only remaining treatment option as one homologous Achilles tendon-bone transplant. Because of these thoughts we initially advised the patient to continue with the safe conservative treatment, so as not to lose what he had gained so far.

Fresh frozen, homologous Achilles tendon bone block transplant

However, since the young patient repeatedly pushed us to improve his personal freedom of movement with sporting options such as cycling and accepting all the risks of reinfection and even the uncertain success of a homologous transplant, we carried out this procedure in a minimal-invasive manner 3.5 years after his accident (**Fig. 4a**).



Fig 4a. Minimally invasive Achilles tendon bone allograft transplantation 3.5 years after the accident. Op 25.11.2014



Fig 4b, c. Weightbearing x-rays taken a.-p. (**b**) and lateral (**c**) 12 years after talus osteotomy and almost 10 years after homologous Achilles tendon bone block transplantation. Moderate osteoarthritis of the ankle joint on the left.

The Achilles tendon specimen with a bone block from the German Institute for Cell and Tissue Replacement (DIZG), Berlin, freshly frozen, on the day of the operation was thawed. Under sterile conditions and prone position, protecting the medial flap vessels, the large tendon mirror was positioned minimal-invasively from distal to proximal after tunneling the way with blunt forceps. The large tendon mirrow was reduced in size and the bone block was fixed with two 3.5 mm cortical screws to the dorsal neocalcaneus. Keeping the foot in a 30° equinus position the narrowed tendon mirror was stitched onto the original triceps surae mirror with absorbable sutures. The 5 × 4 × 1 cm large homologous heel block had to be reduced in size and rounded medially in situ so that the locally mobilized latissimus dorsi muscle flap covered with the mesh graft could just be sutured over it.

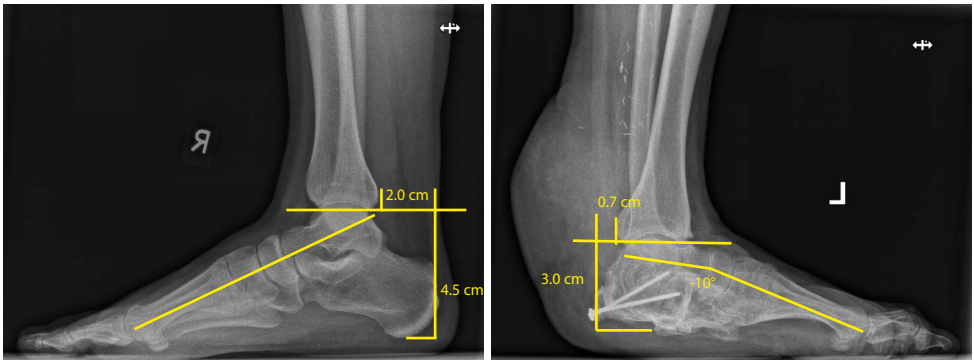


Fig 5. Lateral weightbearing x-rays as shown in Fig. 4c but here with precise measurements (white lines). When comparing sides, the hindfoot height on the left is reduced by a third measuring only 3.0 cm compared to 4.5 cm on the right. The hindfoot leverarm on the left is shortened by almost two third measuring 0.7 cm compared to 2.0 cm on the right. The talometatarsal axis on the left side is inclined by 10°.

RESULT

Clinical

At the 12-year follow-up the gait pattern is normal and fluid in flat sports shoes. The one-legged tiptoe stand is restricted on the left compared to the right, but is possible. The big toe on the left cannot be flexed, the little toes bend moderately. The replaced sole feels firm and dry. With sneakers and cushioning soles, a walking distance of more than 3 km and unlimited cycling are possible. The AOFAS from initially 35 points to now 70 points reflects a significantly improved result. The FFI test shows a mean of 4.5 on the functional scale of 0 to 9. The EQ-5D-5L information on quality of life is documented by the patient on the vertical EQ visual analogue scale with 80 out of 100 points.

Radiological

12 years after calcaneogenesis, the now 37-year-old patient regained a neocalcaneus on the left that was one third less tall than the right (**Figs. 4, 5**). Almost 10 years after homologous Achilles tendon bone block replacement the new hindfoot leverarm was two third shorter than the healthy right one (x-ray measurement 4.5 cm versus 3.0 cm respectively 2.0 cm versus 0.7 cm ; **Fig. 5**). On the left there is moderate osteoarthritis of the ankle joint (**Fig. 4b, c**).

Apparative measurements

The force measurement for plantar flexion with the Isomed 2000 measuring device (**Fig. 6a, b**) shows over the course a fivefold increase in the repulsion force (14 vs. 70 Nm) due to calcaneogenesis alone (**Fig. 6b**), and after additional transplantation of the homologous Achilles tendon bone block, a twenty-fold increase (14 versus 277 Nm; f=19.79)

Isokinetic force measurements right-left-comparison: 11.3.2024

Angular velocity	30°/sek.		120°/sek.	
Side right / left	re	li	re	li
Plantarflexion [Nm]	396	277	150	132
Dorsiflexion [Nm]	78	92	45	50
Muscular relation pl/df	0,20	0,33	0,30	0,38
Muscular dysbalance (op vs non-op) Plantarflexion in %	70%		88%	
Muscular dysbalance (op vs non-op) Dorsiflexion in %	118%		111%	

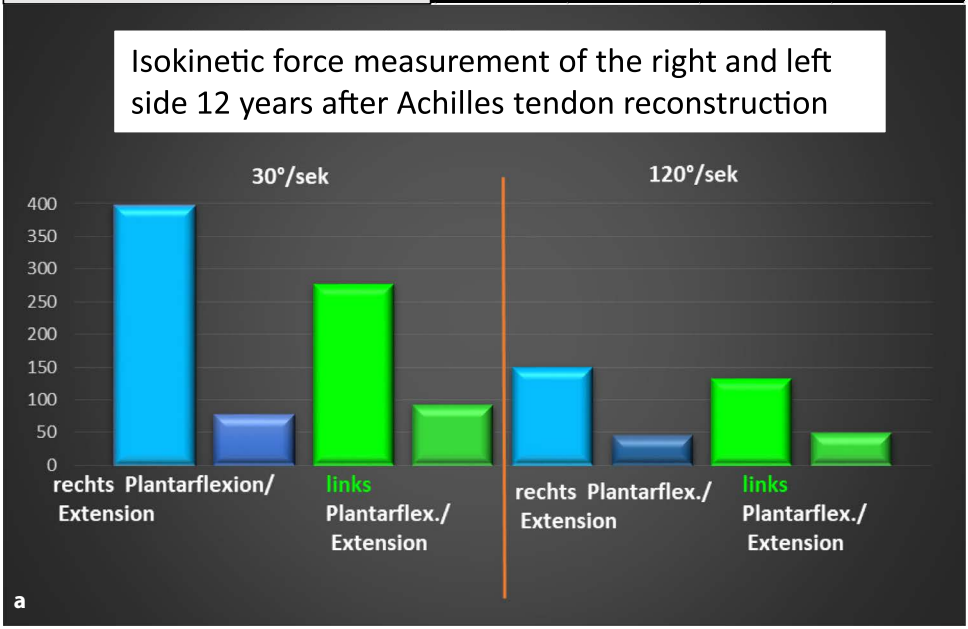


Fig 6. Isokinetic force measurements (Isomed 2000 D. & F. Ferstl GmbH Hernau, Bavaria, Germany) **a**: 12 years post-operatively. Despite the shortened rear foot, the left reconstructed rear foot still achieves 70% of the active plantar flexion force at 30°/s and even 88% of the healthy side at 120°/s. The dorsiflexion force is even greater than on the right because of the shortened leverarm.

Isokinetic measurements of plantarflexion + dorsiflexion: 2012-2015-2024

Dates of measurement	30.11.2012	19.10.2015	11.03.2024
Measured side	left	left	left
Plantarflexion [Nm]	14	70	277
Dorsiflexion [Nm]	23	35	92
muscular relation: plantarflexion/dorsiflexion	1,64	0,50	0,33

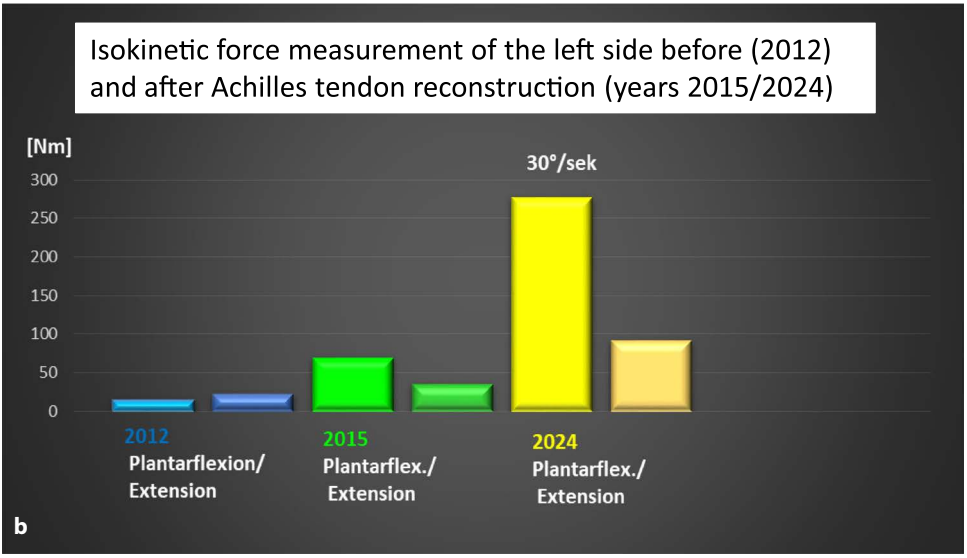


Fig 6. Isokinetic force measurements (Isomed 2000 D. & F. Ferstl GmbH Hernau, Bavaria, Germany) **b**: Isokinetic force measurement over time (years 2012, 2015, 2024) shows a fivefold increase in plantar flexion strength after calcaneogenesis and a twentyfold increase after Achilles tendon replacement. Patient data at the 12 year control: age 37 years, height 179 cm, weight 108.5 kg, BMI 33.9, fat 29%.

Psychosocial

The patient has been fully able to work as an engineer since 2013. He is now married and father of 4 children. For him all operations were valuable. He never wanted an amputation. He was very satisfied with his health. The doctor's recommendation to reduce weight in order to relieve the load on the left ankle joint was accepted.

DISCUSSION

Only a few reports of calcaneogenesis [**3, 4, 7, 8**] are known in the literature. Only Brinker et al. [**3**] reported one case of calcaneogenesis without ankle fusion. The other authors [**4, 7, 8**] did osteotomy of the dorsal joint-forming tibia in combination with a talar osteotomy what principally led to ankle arthrodesis. However, this should be avoided in principle in our own approach. Retrospectively, a more wedge-shaped osteotomy of the talar body (dorsally 2.5 cm instead of 1.5 cm) with a stronger olive K-wire pulling more in the dorsoplantar direction (**Fig. 3a**) instead of just in the plantar direction could have led to a larger leverarm of the neocalcaneus, which on the other hand was deliberately avoided in order to preserve safely the cartilaginous dorsal talus. As an alternative, a vascularized bone reconstruction of the heel bone after calcanectomy with simultaneous soft tissue coverage using a serratus anterior muscle transfer, as previously described [**2**], did not appear to be appropriate because a vascularized latissimus dorsi muscle had been sacrificed initially for saving the limb.

Boorboor et al. [**10**] were able to show in seven cases after resection of an infected Achilles tendon that after plastic coverage without replacement of the Achilles tendon, the plantar force measurement at 120°/s in average was reduced by 46%. Heikkinen et al. [**6**] showed by using MRI even 14 years after acute rupture and suturing the Achilles tendon that volume measurements of the soleus muscle, of the medial and lateral gastrocnemius muscle were with 63 cm^3 high significantly (<0.001) lower than those on the non-operated side. In addition, the measured plantar flexion strength was reduced by an average of 12–18% compared to the healthy side [**6**].

In 2014, at the time of the allogenic Achilles tendon bone block transplantation like in the case presented, there were no figures available on the infection risk of such allografts. Later reports [**5, 9**] showed, for example, that in other conditions such as replacement operations due to resection of chronic ruptures with large defects due to local inflammatory or tumorous processes, there were no postoperative complications like infection observed.

CONCLUSION

Restoring the rare complete loss of the heel bone and Achilles tendon as a prerequisite for free walking is surgically possible, done in specialized centers, but requires a high level of compliance and the cooperation of the patient.

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Author's adress:
Prof. em. Dr. med. Hans Zwipp
e-mail: hans.zwipp@t-online.de

A NOVEL SPLICING VARIANT OF *FGFR3* GENE - A CAUSAL VARIANT OF BONE DYSPLASIA IN TWO PATIENTS WITH OVERLAPPING PHENOTYPES OF ACHONDROPLASIA AND HYPOCHONDROPLASIA

NOVÁ SESTŘIHOVÁ VARIANTA GENU *FGFR3* – KAUZÁLNÍ VARIANTA KOSTNÍ DYSPLAZIE U DVOU PACIENTŮ S PŘEKRÝVAJÍCÍMI SE FENOTYPY ACHONDROPLAZIE A HYPOCHONDROPLAZIE

Krulišová Veronika[1], Zemková Daniela[2], Mařík Ivo[3,4], Paszeková Helena[1], Michalovská Renáta[1], Vlčková Zděnka[1]

[1] GHC Genetics, Prague, Czech Republic

[2] Dept. of Paediatrics, Charles University, University Hospital Motol; Prague, Czech Republic

[3] Centre for Defects of Locomotor Apparatus l.l.c.; Prague, Czech Republic

[4] Faculty of Health Care Studies, West Bohemia University; Pilsen, Czech Republic

SUMMARY

Background

Achondroplasia (ACH) and hypochondroplasia (HCH) are the most common forms of skeletal dysplasia. Both ACH and HCH are associated with pathogenic variants in the fibroblast growth factor receptor 3 (*FGFR3*) gene. The vast majority of cases can be attributed to the hotspot missense variants in a heterozygous state in the *FGFR3* gene: 99% patients with ACH are carrying pathogenic variant c.1138G>A or c.1138G>C located in exon 10. Approximately 70% of individuals with HCH carry a pathogenic variant in exon 13 (involving codon 540) or a pathogenic variant in exon 15 (involving codon 650).

Case reports

Here, we present the phenotype and radiologic features of 2 patients (a Vietnamese boy and a Czech girl) with a novel splicing variant c.1075+95C>G of *FGFR3* that represents a probably recurrent causal variant of bone dysplasia in patients manifesting with overlapping phenotypes of ACH and HCH. In the first case report, we also presented the results of surgical treatment for varus defor-

mity of the distal shank, achieved through permanent drilled epiphysiodesis of the distal fibula and temporary lateral hemi-epiphysiodesis of the distal tibia.

Conclusion

Molecular genetic results are in concordance with previous literature findings that the c.1075+95C>G alteration in *FGFR3* represents a recurrent variant causing ACH, HCH and overlapping forms of ACH/HCH. Recognition of the molecular genetic background enables appropriate surveillance for the patient. Furthermore, intronic variant c.1075+95C>G represents a candidate for clinical trial strategies and subsequent treatment. Based on the trials vosoritide might become the first targeted pharmacological therapy for overlapping forms of ACH/HCH.

Recommendation

We recommend including this variant in routinely used diagnostic tests for HCH and ACH. We also recommend reanalysing data from patients clinically diagnosed with ACH or HCH, who tested negative using methods based on Next-Generation Sequencing technologies.

Keywords: achondroplasia, hypochondroplasia, *FGFR3* gene, splicing variant, clinical exome sequencing, surgery of tibial varus deformity

BACKGROUND

Achondroplasia (ACH) and hypochondroplasia (HCH) are the most common forms of skeletal dysplasias. ACH is estimated to affect approximately 1 in 20,000 to 1 in 30,000 live births (**3**), i.e. 3–5 in 100,000. HCH represents a rarer and milder form of bone dysplasia with less severe medical problems. The estimated incidence of HCH is around 1 in 50,000 live births (**17**), i.e. 2 in 100,000.

Clinically, ACH is characterized by rhizomelic shortening of the limbs, macrocephaly with frontal bossing, midfacial hypoplasia, a characteristic trident configuration of the hands and limitation of elbow extension. Additional features include hypotonia, joint hypermobility, genu varum, as well as thoracolumbar kyphosis in infancy that transitions to lumbar hyperlordosis in childhood. Neurological complications such as cervicomedullary compression due to foramen magnum stenosis, hydrocephalus, and spinal stenosis are well-documented (**6**). Recurrent otitis media and conductive hearing loss are common. Intellectual development is typically normal, though developmental delays may occur in the presence of complications.

Radiographically, ACH is marked by lack of iliac flaring, horizontal superior acetabular margins and narrow sacroschiatic notches (the term „champagne glass" pelvis is now used to describe the pelvis of children with ACH); decreased interpedicular distance from upper to lower lumbar spine (so-called caudal narrowing of lumbar canal), short vertebral laminae, narrowed foramen magnum,

and metaphyseal flaring of the long bones (**7**). Diagnosis is often suspected clinically and confirmed by molecular genetic testing of the *FGFR3* gene.

HCH represents a milder allelic variant of the same gene. The phenotype includes mild to moderate short stature, accompanied by mesomelic or rhizomelic limb shortening, macrocephaly (less pronounced than in ACH), and a stocky body habitus. Facial features are less distinctive, and midfacial hypoplasia is usually absent. Intelligence is generally normal, although some individuals may exhibit learning difficulties. Neurological complications are less common but may include spinal stenosis in adulthood.

Radiological findings in HCH are similar but quantitatively much milder, with less pronounced changes in the spine (vertebral laminae are not so short, interpedicular distance is increased in the lower lumbar spine), hands, and long bones compared to ACH (**9**). Due to phenotypic variability and overlap with other causes of short stature, diagnosis often requires molecular confirmation.

While mutations in the *FGFR3* gene cause both disorders and share some phenotypic overlap, key distinguishing features include the severity and timing of presentation, craniofacial morphology, and the extent of limb shortening. ACH typically presents at birth with more severe manifestations, whereas HCH usually has a later onset with a milder clinical course (**2**). However, some more severe HCH cases are detected prenatally or at birth. The risk of significant neurological and orthopaedic complications is considerably higher in ACH.

Both ACH and HCH result from pathogenic variants in the gene coding for the transmembrane portion of fibroblast growth factor receptor 3 (*FGFR3*). Pathogenic variants represent "gain-of-function mutations" leading to the constant activation of the FGFR3 receptor. This results in the abnormal chondroid production affecting endochondral ossification, leading to impaired bone growth among other functions. This pathologic process generally spares intramembranous ossification, which occures in flat bones such as those in the skull (except of the base of the skull), face, and clavicles. Both ACH and HCH are inherited in an autosomal dominant manner, are fully penetrant, and occur either due to *de novo* pathogenic variant, or are inherited from an affected parent.

The vast majority of cases can be attributed to the hotspot missense variants in a heterozygous state in the *FGFR3* gene (transcript NM_000142.5): 99% patients with ACH are carrying pathogenic variant c.1138G>A or c.1138G>C located in codon 380 of exon 10 (**14**). Approximately 70% of individuals with HCH carry a pathogenic variant in exon 13 (involving codon 540) (**11**) or a pathogenic variant in exon 15 (involving codon 650) (**1**).

Here, we present the clinical and radiological features of 2 patients with a novel splicing variant c.1075+95C>G in intron 9 of *FGFR3*, which probably represents a recurrent causal variant of bone dysplasia in patients with overlapping phenotypes of ACH and HCH (**5**, **10**, **15**).

CLINICAL CASE REPORTS

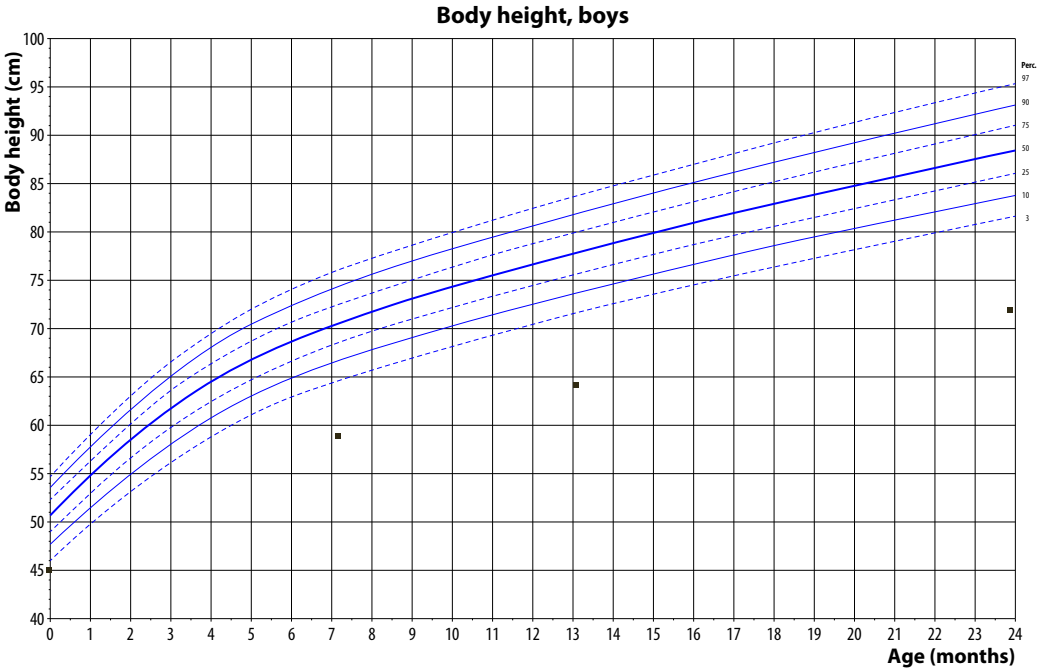
First case report

Here, we report a 16.5-year-old boy of Vietnamese origin with a clinical diagnosis of HCH. The family history of bone dysplasia was negative. He was the first child of healthy, young Vietnamese parents (father's height 159 cm, mother's height 155 cm), born at the 37th week of pregnancy with a birth length of 45 cm and birth weight of 2,780 g. Shortening of the upper and lower limbs was apparent after birth.

At the age of 13 months, his body length was 64.3 cm (-4.3 SD) – see **Graph 1**, crown-rump length 46 cm (-0.9 SD), subischial leg length 18.3 cm (-6.7 SD) and head circumference 48.6 cm (1.2 SD).

The boy was examined at the Centre for Defects of Locomotor Apparatus at the age of 2.5 years, on the recommendation of a clinical anthropologist, in order to clarify the diagnosis of short stature. Clinical findings (**Fig. 1a–c**) and radiographic examination (**Fig. 2a–c**) were suggestive of the diagnosis of HCH. The radiographs were later consulted with Associate Professor Kazimierz Kozlowski,

Text continues on page 176



Graph 1. Growth curve of the proband in infancy and toddlerhood: At the age of 13 months his body length was 64.3 cm (-4.3 SD)



Fig. 1a–c. Phenotype of a boy Vietnamese origin at 2 years and 7 months: height 74.5cm; weight 11.7 kg; Sitting height 52 cm; subischial leg length 22.5 cm; arm span 71.5 cm; head circumference 52.5 cm (macrocephaly); hypertelorism and epicanthal folds – **a**. Short disproportional stature, rhizomelic shortening of upper and lower extremities; elbow contractures 10°; mild varosity of both shanks – **c**.

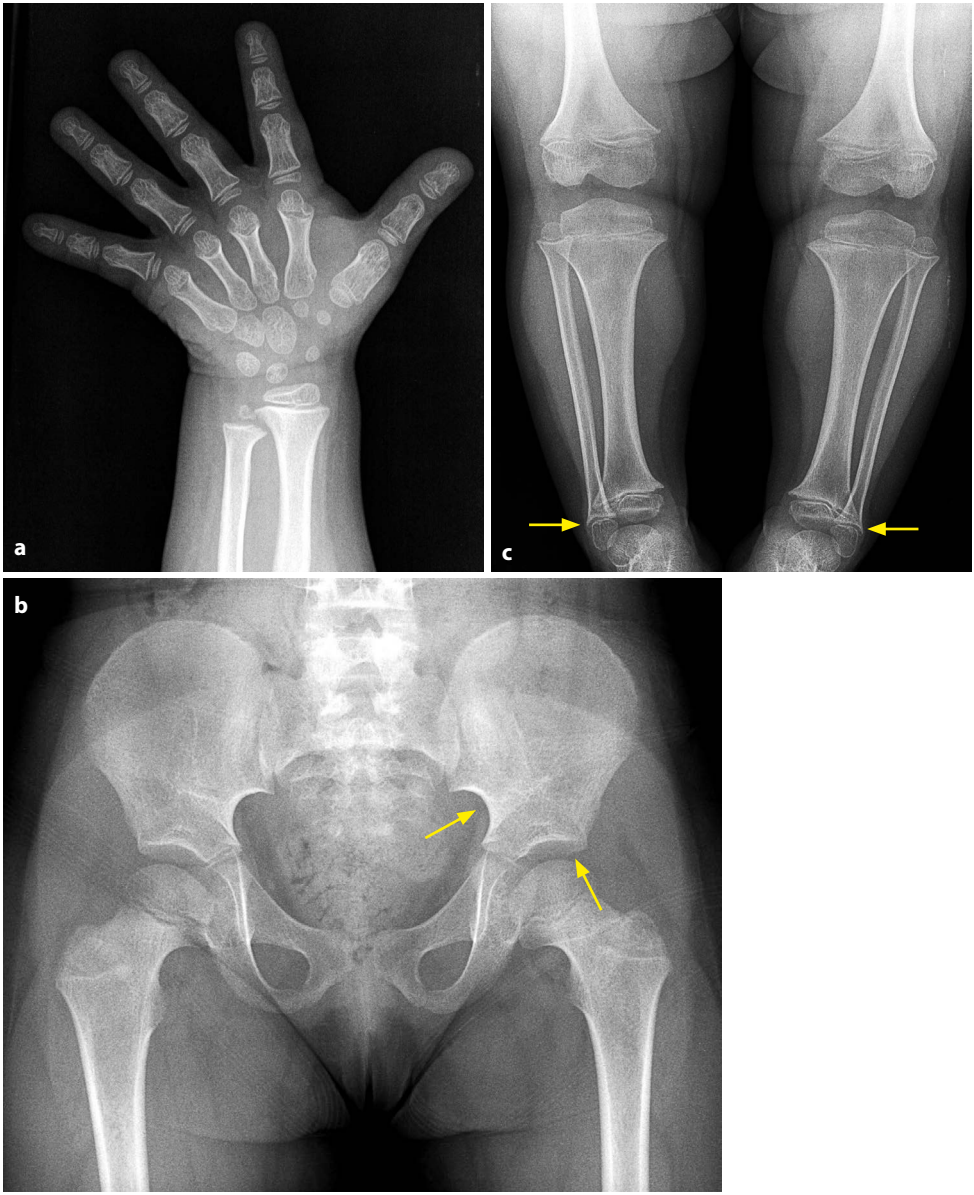


Fig. 2a–c. X-rays – anteroposterior (AP) projection, 4.5 years: **a**. L hand: short metacarpals and phalanges, shortening of distal ulna; **b**. pelvis and hips: rounded ilia, wide sacroiliac (sciatic) notches – *arrow*, the lower protions of the iliac bones are broad, the acetabular roofs are almost horizontal – arrow; femoral necks are short and broad; **c**. knees and shanks: shortened robust long bones with metaphyseal flare, genua et crura vara bilat, overgrowth of fibula – *arrows*.

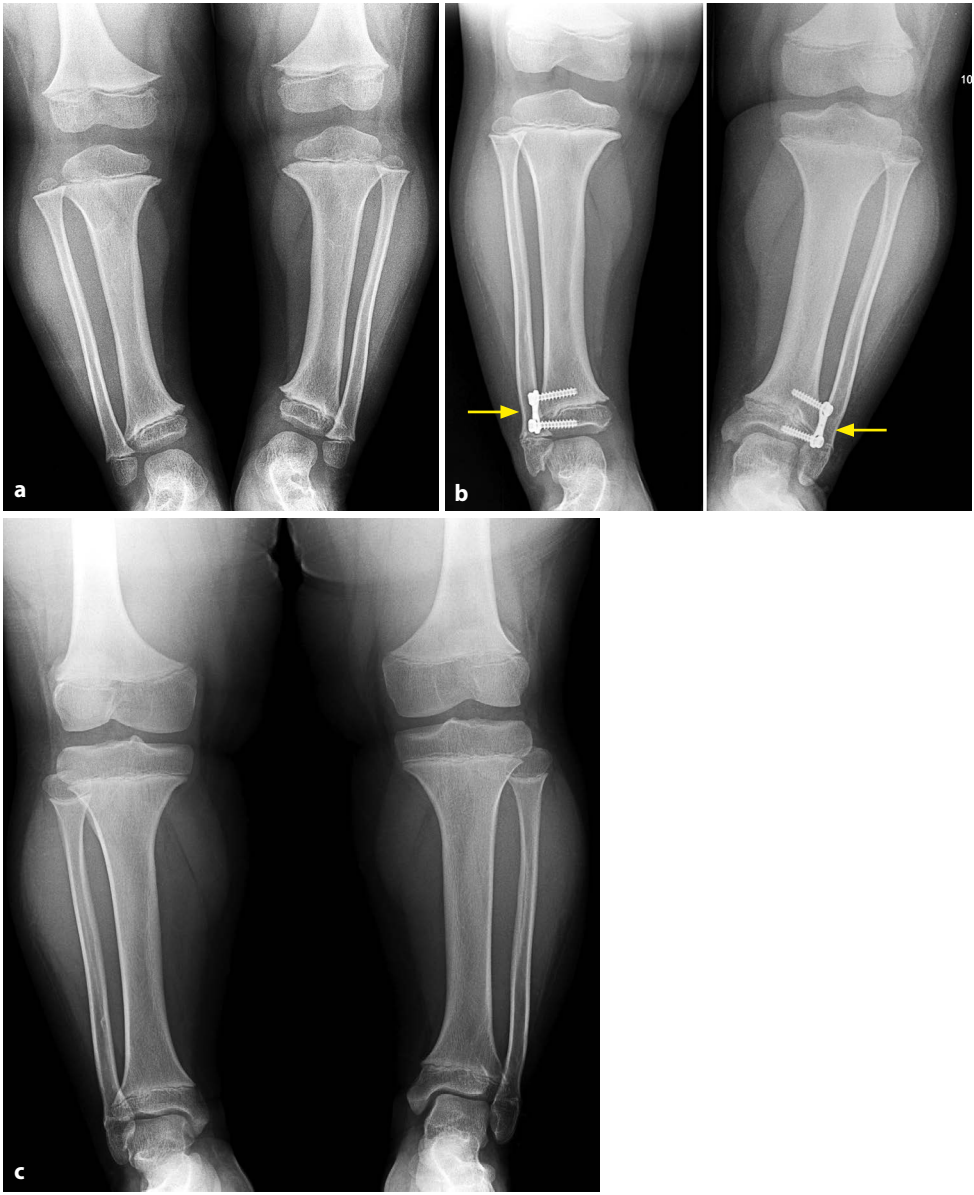


Fig. 3a–c. X-rays of shanks, AP projections: **a**. 7.3 years: overgrowth of the fibula causes varus slope of the talocrural joints and varus position of the heel; **b**. 9.5 years: permanent drilling epiphysiodesis of the distal fibula bilaterally and temporary hemi-epiphysiodesis of the distal tibia – see the eigth plates (arrows) – with the aim to correct varus heel position was carried out; **c**. 13.7 years: result of the surgery.



Fig. 4a–c. Clinical outcome of the operation that was performed at 8 years – see **b** and **c**. 10.7 y and 15 y.



Fig. 5a–c. Phenotype of 15 years boy of Vietnamese origin: a-c. height 130.2 cm (-5.6 SD); Sitting height 84 cm (-0.8 SD), subischial leg length 46.2 cm (- 7.9 SD), arm span 131 cm; macrocephaly (head circumference 61 cm, 3.2 SD), hypertelorism and epicanthal folds – **b**.

M.R.A.C.R., Westmead NSW, Sydney, who concluded the diagnosis as HCH. Genetic analysis excluded typical mutations for both HCH and ACH.

With the growth, the varus position of the heel progressed, which was a consequence of the overgrowth of the fibula. At the age of 8 years, in collaboration with a clinical anthropologist, surgery

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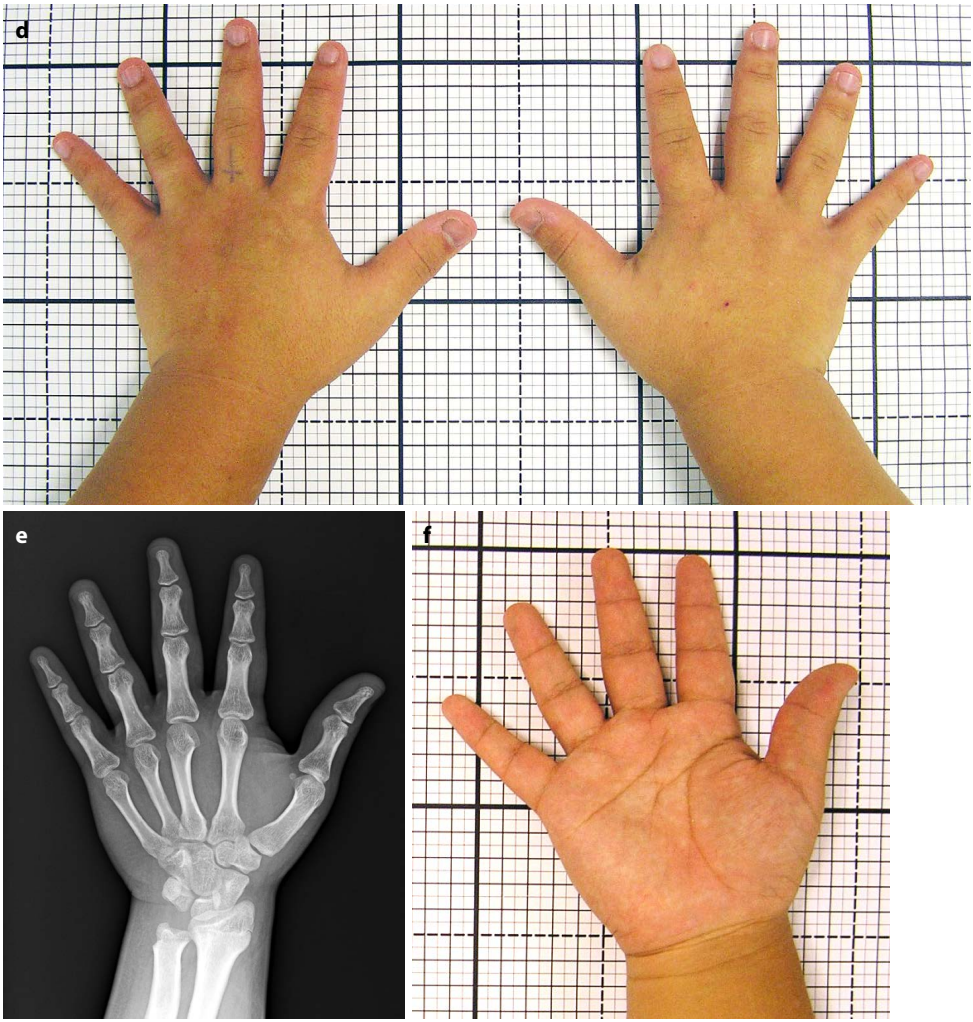


Fig. 5d–f. Mild brachydactyly; normal palmar creases on the right hand – **f**.

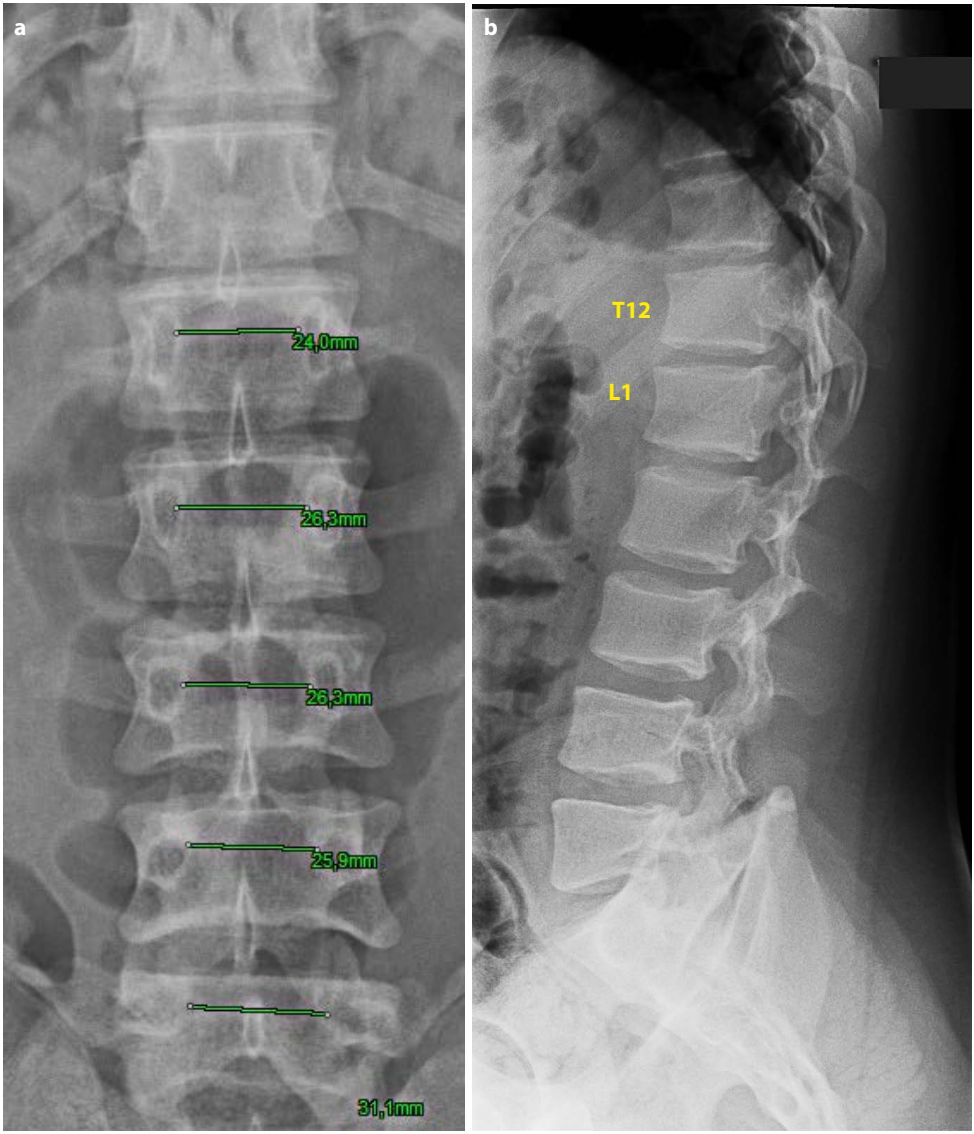
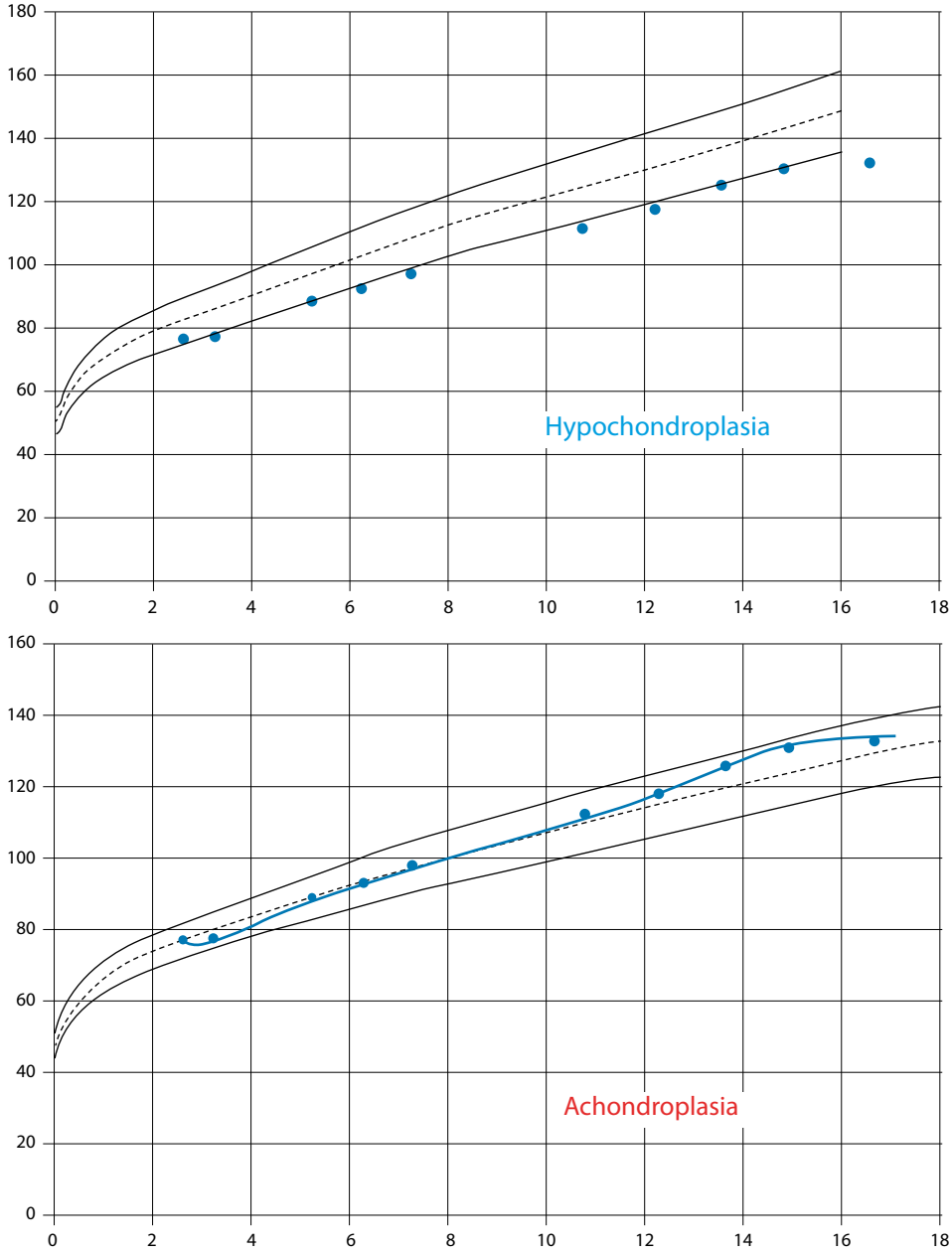


Fig. 6a, b. X-ray images of the lumbar spine, AP projection,16 years: **a**. rectangular shape of the lumbar canal, i.e., unchanged intervertebral distance in the lumbar spine; lateral projection: **b**. dorsolumbar kyphosis and slight anterior wedge-shaped narrowing of T12 and L1, other vertebrae are squared, their laminae are short.



Graph 2a, b. Growth curve and final height is more similar to ACH than HCH; but he had a more pronounced pubertal growth spurt compared to ACH.

was indicated, namely, permanent drilling hemi-epiphysiodesis of the distal fibula and temporary hemi-epiphysiodesis of the distal tibia bilaterally using so-called eight-splints. The deformity of both tibias and the results of the operation are documented on radiographs and photographs (**Fig. 3a–c**) and (**Fig. 4a–c**).

At the age of 15 years, when he underwent genetic counselling, his body hight was 130.2 cm (-5.6 SD) and showed a stocky body habitus with rhizomelic shortening of the limbs. Sitting height was 84 cm (-0.8 SD), subischial leg length 46.2 cm (- 7.9 SD) and arm span 131 cm. Brachydactyly of both hands was evident. Macrocephaly (head circumference 61 cm, i.e. 3.2 SD), hypertelorism and epicanthal folds were present (**Fig. 5a–f**). The face typical of ACH, i.e. prominent forehead, depressed nasal bridge, midface hypoplasia, was absent. He had no congenital defect and no intellectual disability.

Clinical symptoms and radiological findings were more consistent with HCH than ACH. However, at the younger age of 2.7 years, he also showed some X-ray findings typical of ACH: e.g. dorsolumbar kyphosis, slightly wedge-shaped T12 and L1, short laminae and caudal narrowing of interpedicular distance.

At the age of 16 years, we proved rectangular shape of lumbar canal and almost normal length of pedicles (**Fig. 6a, b**). Furthermore, using percentile charts specifically designed for patients with HCH and ACH, we observed, that both the final height and body proportions were more similar to those of ACH than to those of HCH (**16**). On the other hand, his pubertal spurt was more pronounced than in ACH (**Graph 2a, b**).

Since DNA testing for common pathogenic variant in *FGFR3* gene for HCH and ACH had already been performed with negative result, the detailed DNA analysis focused on the whole *FGFR3* gene and other genes associated with bone dysplasias using clinical exome sequencing (CES).

A deep intronic alteration c.1075+95C>G in intron 9 was detected in a heterozygous state in the *FGFR3* gene (NM_000142.5). Since the variant was initially evaluated as a variant of unknown significance, targeted testing of this particular variant in both healthy parents was performed to elucidate the causality. Both parents tested negative for c.1075+95C>G *FGFR3* variant and thus the causality was suspected. In the meantime, the c.1075+95C>G variant in the *FGFR3* gene was described in the literature as pathogenic, causing HCH (**15**) and ACH (**10**). No other pathogenic variant in genes associated with skeletal dysplasias was found using exome sequencing in the patient.

The same pathogenic splicing variant was detected in one additional patient (second case report) among genetically unresolved patients with skeletal dysplasias in our affiliation.

SECOND CASE REPORT

The child was born to healthy parents. The family history of bone dysplasia was negative. The delivery was spontaneous at the 38th week of pregnancy, with a birth weight of 3,600 g and a birth length of 47 cm. Shortening of the upper and lower extremities was apparent after birth.

DNA testing for typical hotspot mutations in *FGFR3* gene for ACH and thanatophoric dysplasia has been performed with negative result prenatally and for HCH in infancy. A normal female karyotype, i.e. 46,XX, was confirmed.

The girl was followed up at the Centre for Defects of Locomotor Apparatus from the age of 20 months, on the recommendation of a geneticist for rhizomelic bone dysplasia in order to clarify the diagnosis. At the age of 20 months she showed short disproportional stature, rhizomelic shortening of upper and lower extremities, body length 67.5 cm (-4.9 SD), crown-rump length 48 cm, subischial leg length 19.5 cm, head circumference 47.6 cm (0.2 SD) with a prominent forehead and slightly depressed nasal bridge (**Fig. 7a, b**). She showed a mild thoracolumbar kyphosis and lumbosacral lordosis. Some radiological features resembled ACH (**Fig. 8a–d**) at the age of 20 months.

X-rays at 4.5 years: The findings on the left hand, pelvis and hips, shanks and spine were somewhat typical of HCH (**Fig. 9a–e**).

Her body height at the age of 7 years was 100.7 cm (-4.3 SD) and showed stocky body habitus with rhizomelic shortening of the upper and lower limbs; sitting height 65.5 cm (0 SD) subischial leg length 35.2 cm (-6.9 SD), arm span 93.4 cm, upper extremities -4.6 SD. Head circumference 51.6 cm (0.1 SD) corresponded to normocephaly. She exhibited elbow flexion contractures 10°; her hands were of regular shape, and her spine showed a mild dorsolumbar kyphosis and lumbosacral lordosis.

The phenotype of the patient at the age of 7 years and 14.5 years summarise particular photos (**Fig. 10a, b, d–g**) and also radiograms at 4.5 years (**Fig. 9a–e**), 9.5 years and 14.5 years (**Fig. 10c and Fig. 11a–d**). From 9.5 years of age, we observed an unchanged interpedicular distance in the caudal direction at lumbar spine (**Fig. 11a–c**). This feature was not described in either ACH or HCH.

In 2020, a 10-year-old girl of Caucasian origin with a phenotype showing predominantly HCH features came for genetic counselling. She had a prominent forehead, slightly depressed nasal bridge and a bulbous nose; however, her face was not typical of those in ACH patients.

DNA testing for typical hotspot mutations in *FGFR3* gene had been performed with negative result before; therefore, DNA analysis focused on the whole *FGFR3* gene and other genes associated with skeletal dysplasias was conducted by CES. No causal variant was identified initially.

After reanalysis, that was performed 3 years apart, the c.1075+95C>G variant in the *FGFR3* gene was identified in heterozygous state. As this variant corresponds to HCH, ACH and overlapping forms (**10,15**), we consider this variant to be causally related to skeletal dysplasia in our patient.

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Fig. 7a, b. Phenotype at 20 months of age.

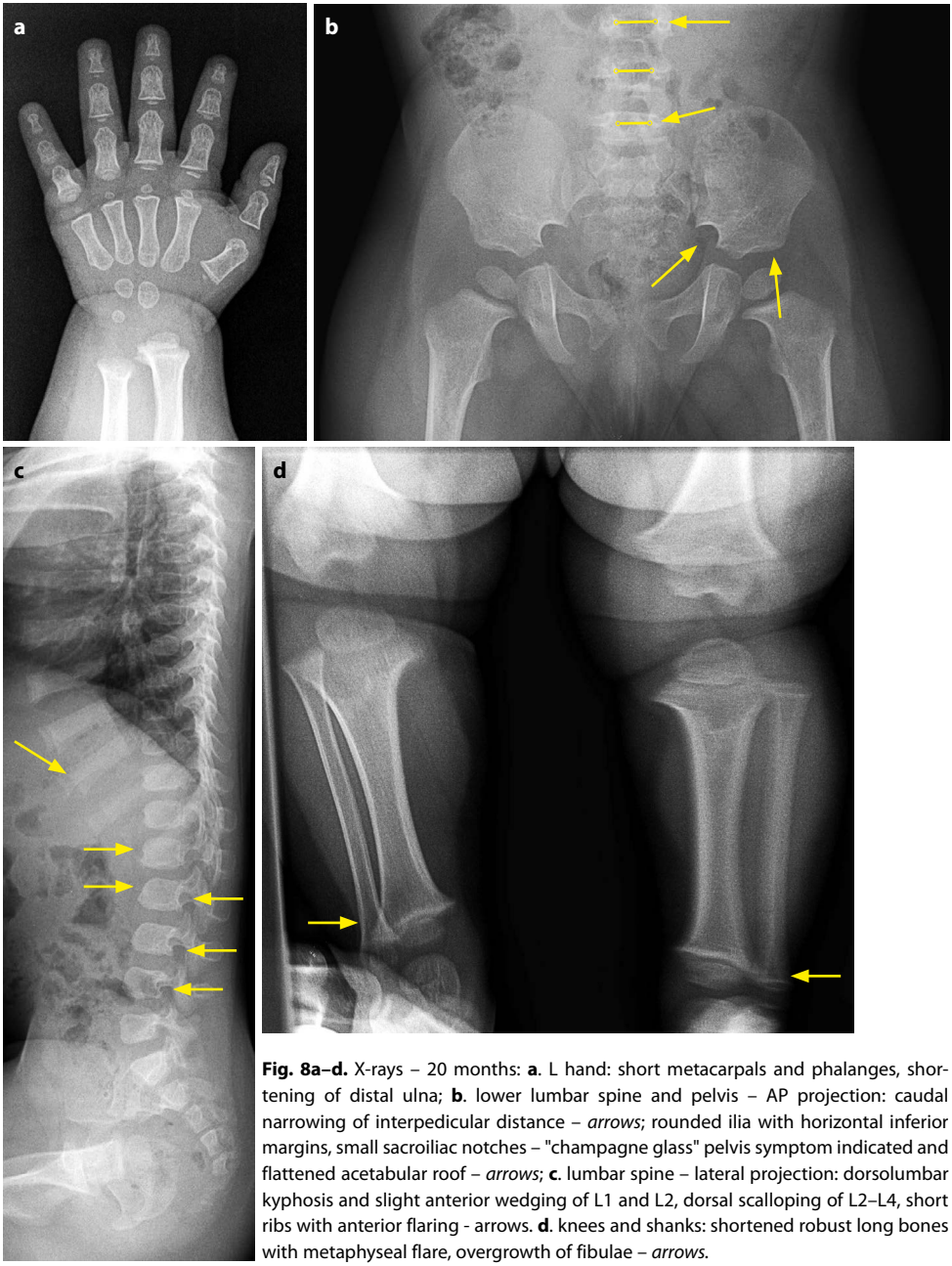


Fig. 8a–d. X-rays – 20 months: **a**. L hand: short metacarpals and phalanges, shortening of distal ulna; **b**. lower lumbar spine and pelvis – AP projection: caudal narrowing of interpedicular distance – *arrows*; rounded ilia with horizontal inferior margins, small sacroiliac notches – "champagne glass" pelvis symptom indicated and flattened acetabular roof – *arrows*; **c**. lumbar spine – lateral projection: dorsolumbar kyphosis and slight anterior wedging of L1 and L2, dorsal scalloping of L2–L4, short ribs with anterior flaring - arrows. **d**. knees and shanks: shortened robust long bones with metaphyseal flare, overgrowth of fibulae – *arrows*.

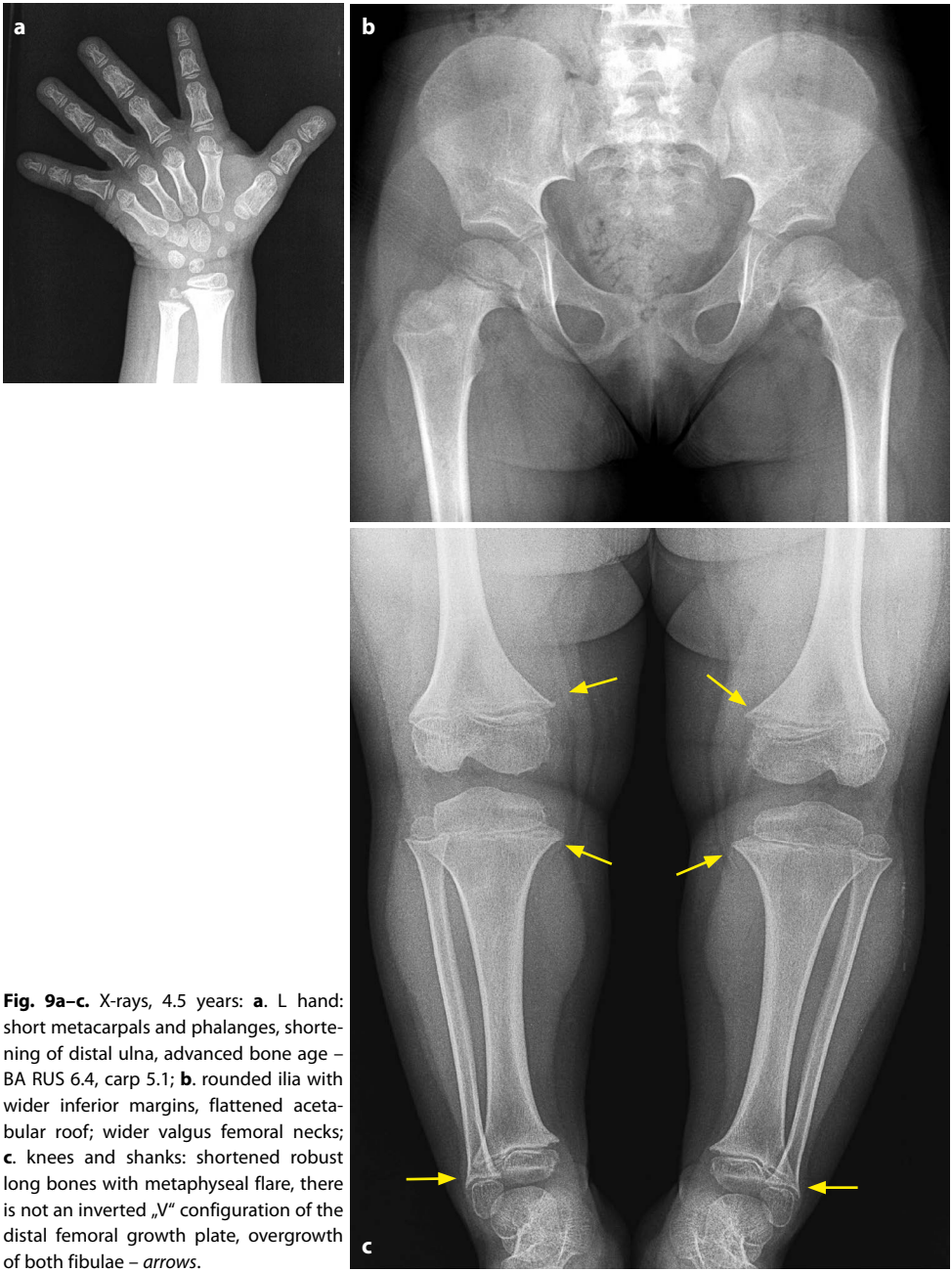


Fig. 9a–c. X-rays, 4.5 years: **a**. L hand: short metacarpals and phalanges, shortening of distal ulna, advanced bone age – BA RUS 6.4, carp 5.1; **b**. rounded ilia with wider inferior margins, flattened acetabular roof; wider valgus femoral necks; **c**. knees and shanks: shortened robust long bones with metaphyseal flare, there is not an inverted „V" configuration of the distal femoral growth plate, overgrowth of both fibulae – *arrows*.

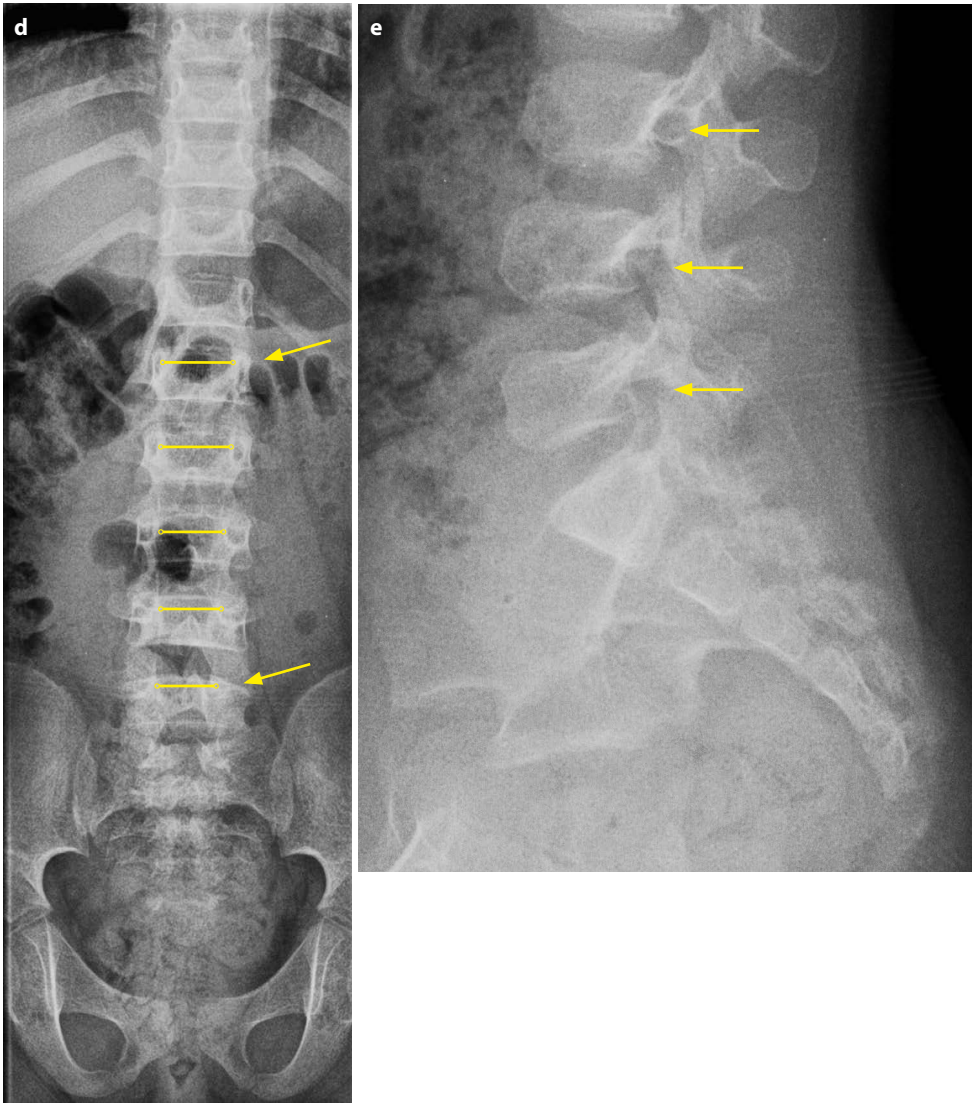


Fig. 9d, e. d. Lumbar spine – AP projection: caudal narrowing of interpedicular distance – *arrows*; **e**. lumbar spine – lateral projection: dorsal scalloping and short laminae i.e. narrowing of spinal canal.

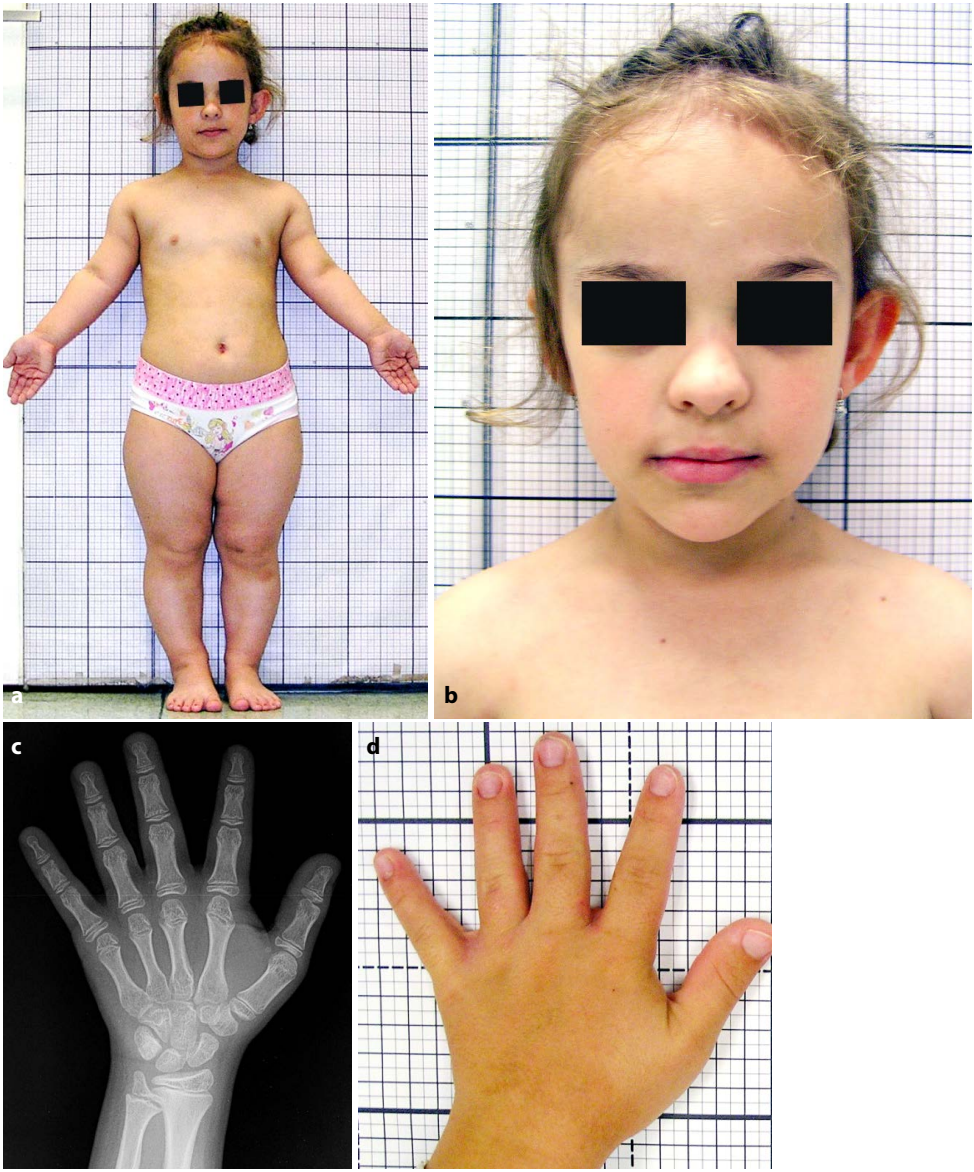


Fig. 10a–d. 7 years: Phenotype – **a**, **b** and X-rayof the left hand – brachydactyly, advanced bone age – RUS 9.5 years; photo and X-ray of the left hand did not show trident hand.

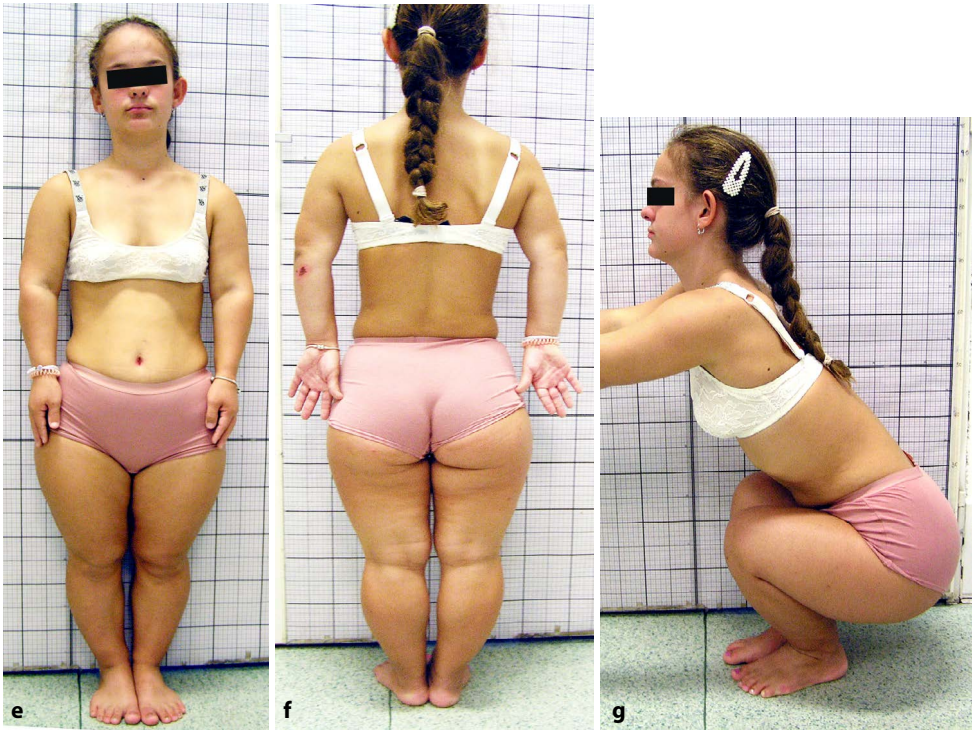


Fig. 10e–g. 14.5 years: Photos document short disproportional stature, rhizomelic shortening of upper and lower extremities, elbow flexion contractures; nearly normal face (slightly depressed nasal bridge and bulbous nose) – **e**.

Growth charts used for patients with HCH and ACH showed that her height was shorter in comparison to those with HCH. Nevertheless, her final height of 132 cm was above the average of ACH (1.7 SD) (**Graph 3a,b**). The girl had a marked early growth spurt because of the early onset and rapid course of puberty (menarche at the age of 11 years and 2 months).

DISCUSSION

Distinguishing between ACH and HCH can be challenging because of their overlapping features. Here we presented two children with clinical and radiographic findings corresponding to features seen in both HCH and ACH, with no common pathogenic variant in the *FGFR* gene. Exome sequencing detected a causal, deep intronic variant c.1075+95C>G in the *FGFR3* gene in heterozygous state in both patients.

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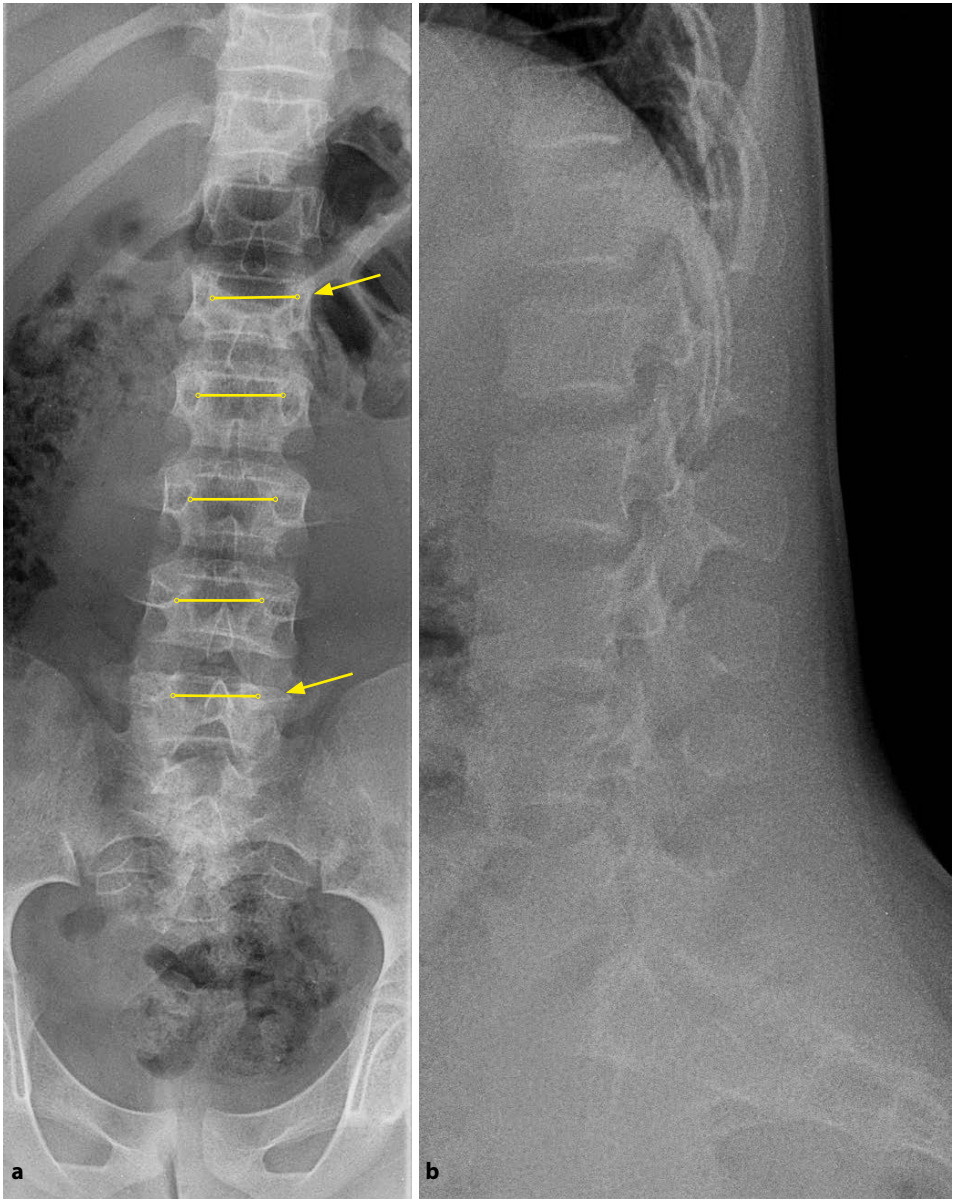


Fig. 11a–d. X-rays of L spine – AP and lateral projection, **a, b**. 9.5 years, **c**, **d**. 14.5 years; **a, c**. Rectangular shape of lumbar canal (L1–L5); **b, d**. squared vertebral bodies and short laminae; **d**. mild dorsal scalloping of vertebral bodies L3–L5.

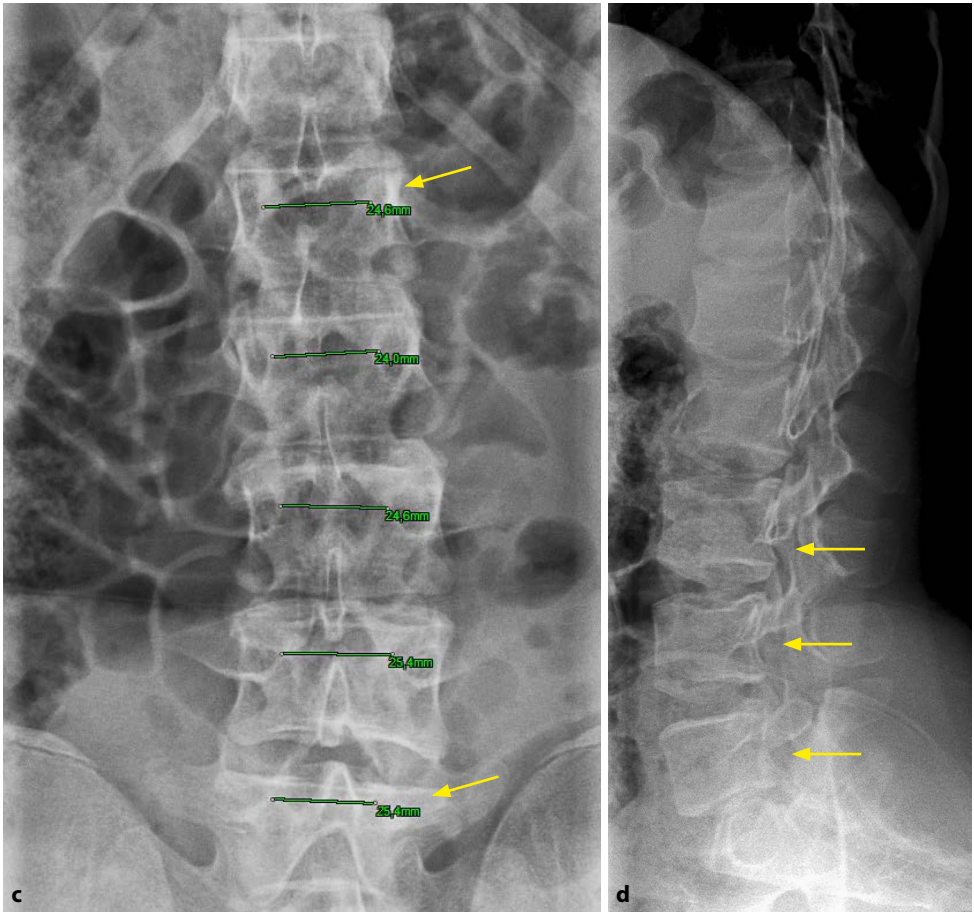
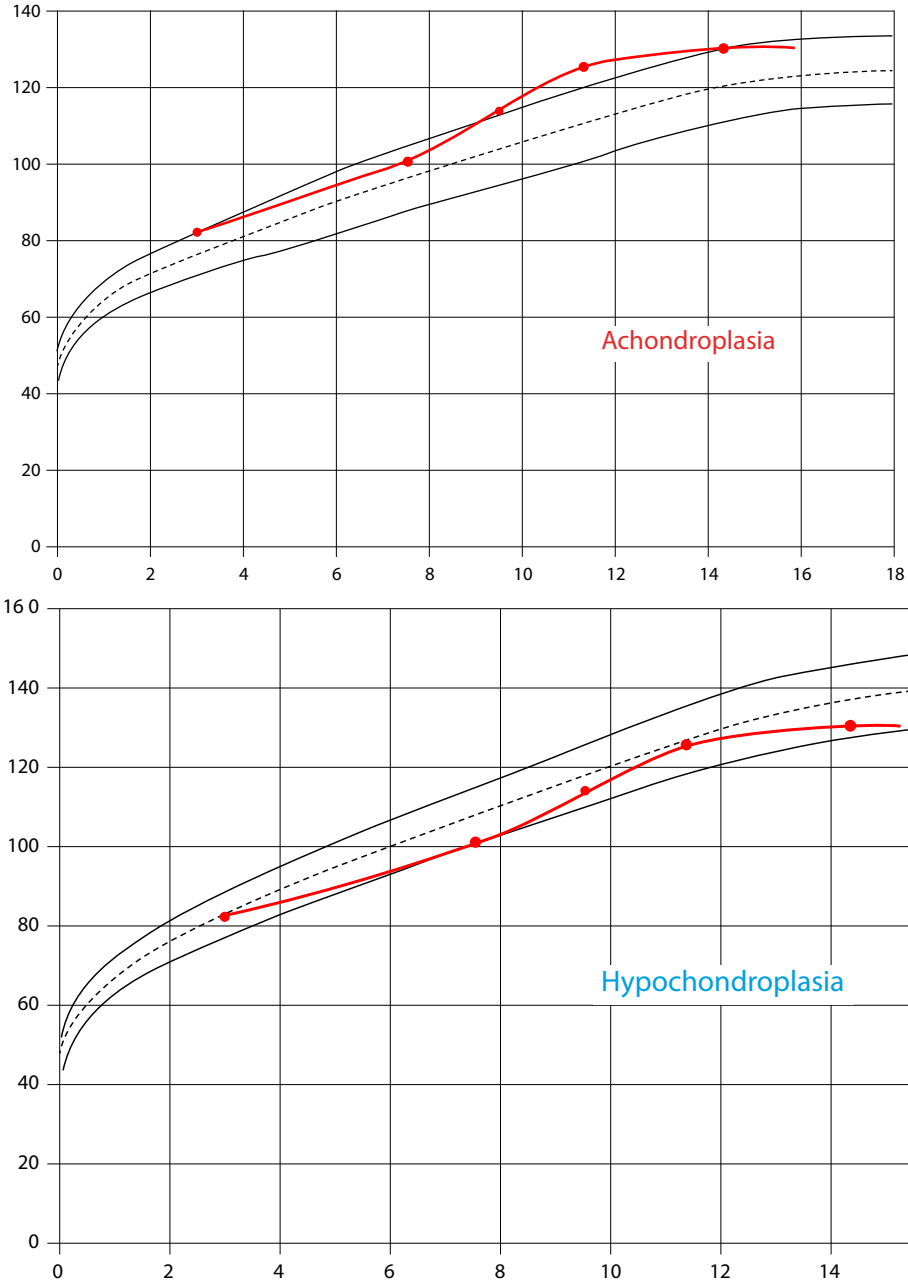


Fig. 11a–d. X-rays of L spine – AP and lateral projection, **a, b**. 9.5 years, c, d. 14.5 years; **a, c**. Rectangular shape of lumbar canal (L1– L5); **b, d**. squared vertebral bodies and short laminae; **d**. mild dorsal scalloping of vertebral bodies L3–L5.

Based on clinical and X-ray findings, we might summarise that the phenotype of both our patients (a Vietnamese boy and a Czech girl) was consistent with a severe form of HCH. Clinical and radiological data are summarized in **Table 1**. Other authors have also described their patients with this particular variant as "severe HCH" or "mild ACH" (**5,10,15**). It is plausible that the c.1075+95C>G variant is associated with phenotypes harbouring traits consistent with HCH/ACH. However, the phenotype–genotype correlation remains inconclusive due to the limited number of subjects.

Text continues on page 190



Graph 3a, b. Comparison of patient's growth data with growth charts of **Achondroplasia** and **Hypochondroplasia**.

Table 1. Comparison of clinical and radiological data for ACH and HCH with case reports 1 and 2.

		achondroplasia	hypochondroplasia	case 1	case 2
Body height (cm)	**M**	M 132 (122–142)	M 143.6 (131–165*)	132 (16 y)	
	F	F 124 (115–134)	F 130.8 (124–138*)		132 (14.5 y)
sitting height		(-2.2 SD)	(-2.1 SD)	(-1.8 SD)	(-0.4 SD)
subischial leg lenght		(-9.6 SD)	(-5.5 SD)	(-8.1 SD)	(-8 SD)
Head circumference		macrocephaly	mild macrocephaly	3.2 SD	0.3
hydrocephalus		occassionally	no	no	no
cervicomedullar compression		occassionally	no	no	no
sleeping apnea		frequent	no	no	no
face		dysmorfic	normal	nearly normal	nearly normal
mental development		normal	norm.-mild retardation	normal	normal
thoracolumbar kyphosis		frequent	no	no	transitory, mild
sacroiliac notches		narrow	short	wide	narrow (20 m), wide (4.5 y)
acetabular roof		horozontal	flattened	almost horizontal (4.5 y)	almost horizontal (20 m and 4.5 y)
lumbar canal		narrowing caudally	rectangular	caudal narrowing (2.3 and 4.5 y), rectangular (16 y)	caudal narrowing (20 m), rectangular (9.5 and 14 y)
wedged shaped vertebrae		yes	no	yes T12, L1 (16 y)	yes L1, L2 (20 m)
vertebral bodies scalloping		yes	yes	no	yes (20 m, 4.5 y, 14 y)
distal femoral growth plate		inverted V	normal	slightly inverted V (5 y), normal (7.5 and later)	normal (20 m and 4.5 y)
overgrowth of fibulae		yes	yes	yes	mild
bowing of shanks		yes	yes	yes	mild
hand		trident, brachydactyly	nearly normal	mild brachydactyly	mild brachydactyly

Abbreviations: ACH – achondroplasia; HCH – hypochondroplasia; M – male; F – female; y – year/years; m – months; SD – standard deviation; T12 – thoracic vertebra 12; L1 – lumbar vertebra 1; L2 – lumbar vertebra 2
* The height of the upper limit is not precisely known; the variability of height in HCH is probably broader, so HCH patients with taller stature might not be diagnosed

Unchanged intervertebral distance in the caudal direction in the lumbar spine, the so-called „rectangular shape" of the lumbar canal, has not been described in ACH, HCH, or other well-defined bone dysplasias. We described this feature in patients with Spondyloepiphyseal dysplasia with short metatarsals, formely known as Czech dysplasia (**8**). This radiological sign can also be considered pathognomonic for the new pathogenic variant associated with the overlapping HCH/ACH phenotype.

In December 2023, the variant c.1075+95C>G was reported in the ClinVar database as a pathogenic variation associated with HCH and ACH. The variant c.1075+95C>G creates a cryptic splice donor site leading to an exonization of part of intron 9 resulting in substitution of Ala359 for a glycine and an insertion of 30 amino acids into a segment adjacent to the receptor transmembrane domain containing the amino acid Gly380, involved in the most recurrent pathogenic variations found in ACH. The minigene in vitro functional analyses confirmed the damaging effect on FGFR3 transcript splicing (**10**). A minor proportion of correctly spliced transcripts remains, but the predominant aberrant product alters receptor structure. The c.1075+95C>G represents a gain-of-function variant

in *FGFR3* resulting in constant activation of the FGFR3 receptor – as well as other *FGFR3* pathogenic variants that cause ACH and HCH.

Recognition of the molecular genetic background enables appropriate surveillance for the patient. Treatment of ACH has shifted from purely supportive care to targeted therapy, particularly with vosoritide as the first approved disease-modifying agent. Vosoritide is a C-type natriuretic peptide (CNP) analog that antagonizes the signalling pathway activated by FGFR3 receptor, thereby promoting endochondral bone growth. Vosoritide has been legally available in the Czech Republic since late August 2021 and is approved for use in children aged 24 months and older with open growth plates, in whom the ACH has been confirmed by genetic testing. Clinical trials demonstrated a mean increase in annualized growth velocity of approximately 1.6 cm per year compared to baseline (**12**, **13**).

Vosoritide has been recently investigated for its therapeutic potential in HCH. Clinical studies have revealed that vosoritide responses in children with HCH are similar to those observed in patients with ACH, suggesting that vosoritide may become the first targeted pharmacological therapy for HCH, offering a novel treatment option beyond supportive and orthopaedic management (**4**).

We can presume, that the novel variant c.1075+95C>G in *FGFR3* might represent a candidate for clinical trials and vosoritide treatment. As both our patients have reached their final height, treatment with vosoritide would not be appropriate, regardless of regulatory approval.

Our findings regarding the c.1075+95C>G alteration align with recent literature, which identifies it as a recurrent variant associated with skeletal dysplasia. We recommend including this variant in routinely used diagnostic tests for HCH and ACH. We also recommend reanalyzing the data of patients clinically diagnosed with HCH or ACH who tested negative using methods based on Next-Generation Sequencing technologies.

CONCLUSIONS

Our results are in concordance with previous literature findings that the c.1075+95C>G alteration in *FGFR3* represents a recurrent variant causing HCH, ACH, and overlapping forms of HCH/ACH. Establishing a molecular genetic diagnosis enables appropriate patient monitoring and management, as well as discussion of potential risks to offspring and reproductive options.

Furthermore, intronic variant c.1075+95C>G represents a candidate for clinical trial strategies and subsequent treatment. Based on the trials vosoritide might become the first targeted pharmacological therapy for overlapping forms of ACH/HCH.

We recommend including this variant in routinely used diagnostic tests for HCH and ACH. We also recommend reanalysing the data of patients clinically diagnosed with HCH or ACH who tested negative using methods based on Next-Generation Sequencing technologies.

At present, drilled epiphysiodesis of the distal fibula and temporary lateral hemi-epiphysiodesis of the distal tibia are the methods of choice for correcting severe varus deformity of the distal tibia (caused by overgrowth of the fibula) in children with HCH and ACH, unless they are indicated for pharmacological therapy with vosoritide or lengthening surgery.

Consent

Written informed consent for the publication of both case reports and accompanying images was obtained from the parents of the children.

Conflict of interest

The authors declare that they have no conflict of interest.

All authors have read and approved the final version of the article.

Acknowledgements

We want to thank the parents for their exceptional cooperation.

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Address for correspondence
Krulišová Veronika, MD, PhD
krulisova@ghcgenetics.cz
GHC Genetics l.l.c.
V Holešovičkách 1156/29, 182 00, Prague 8
Czech Republic

Professor Mařík Ivo, MD, PhD
ambul_centrum@volny.cz
Centre for Defects of Locomotor Apparatus l.l.c.
Olšanská 7, 130 00 Prague 3
Czech Republic

WNT1 OSTEOGENESIS IMPERFECTA: CASE STUDY OF A CZECH GIRL

WNT1 OSTEOGENESIS IMPERFECTA: PŘÍPADOVÁ STUDIE ČESKÉ DÍVKY

Mařík Ivo[1,2], Zemková Daniela[1,3], Maříková Alena[1], Šumník Zdeněk[3], Souček Ondřej[3], Krulišová Veronika[3], Hudáková Olga[1]

[1] Centre for Defects of Locomotor Apparatus l.l.c.; Prague, Czech Republic

[2] Faculty of Health Care Studies, West Bohemia University; Pilsen, Czech Republic

[3] Dept. of Paediatrics, Charles University, University Hospital Motol; Prague, Czech Republic

[4] GHC Genetics, Prague, Czech Republic

SUMMARY

The authors present an interdisciplinary complex care of a patient with congenital bone fragility in whom two variants in the *WNT1* gene were found to cause osteogenesis imperfecta type XV. She suffered her first fracture at birth, the second at 2 years of age. From 2.5 years of age she was treated at the *Dept. of Paediatrics; University Hospital Motol* with cycles of pamidronate, from 5 years of age with zoledronate. From the age of 3 to 17 she was treated at the Centre for Locomotor Defects (CLD) in Prague for long bone fractures, repetitive deformities and pseudoarthroses, which required more than 10 reconstructive surgeries (segmental osteotomies). Now a conservative approach is preferred. The patient moves in a wheelchair, standing only when moving from the wheelchair to the bed. She uses a corset to sit in the wheelchair. The final height of the patient is 129 cm (- 6 SD), both trunk and limbs are shortened, and the limb disability became more pronounced during the growth period. The left lower limb is shortened by 4 cm. These parameters corresponded to type IV osteogenesis imperfecta according to Sillence, but healing after surgery was more complicated and longer. Despite treatment with bisphosphonates, bone density in the lumbar spine was significantly low; according to pQCT, trabecular bone density in the radius metaphysis was normal, but cortical density was reduced. The authors discuss the importance of comprehensive care and discuss surgical treatment options and new pharmacological approaches.

Keywords: osteogenesis imperfecta, OI type XV – *WNT1* gene, bone fractures, intramedullary nailing and plates, bone density, bisphosphonates, teriparatide treatment.

INTRODUCTION

Osteogenesis imperfecta, type XV; OI15 (OMIM # 615220) is caused by a mutation in the wingless MMTV integration site gene, member 1, the *WNT1* gene (**11**). In humans, biallelic mutations in the *WNT1* gene lead to recessive OI, whereas heterozygous *WNT1* mutations can lead to dominant forms of osteoporosis with early onset (**5, 7**).

Keupp et al. (**4**) and Pyott et al. (**9**) described in 2013, osteogenesis imperfecta type XV, an autosomal recessive form of the disorder characterized by early recurrent fractures (multiple limb fractures, vertebral fractures), bone deformities (upper and lower limb curvatures) due to inadequate bone modeling, marked reduction in bone density, impaired calvarial mineralisation, thin ribs and long bones, short stature (shortening of limbs, platyspondyly), blue sclerae in some patients. Tooth development and hearing are normal. In some patients, learning and developmental delays and brain anomalies have been observed, e.g. unilateral cerebellar hypoplasia, congenital absence of vermis, pontine hypoplasia, Chiari malformation type 1, etc.

The authors present the interdisciplinary comprehensive care of a patient with congenital bone fragility who was found to have two variants in the *WNT1* gene, confirming the diagnosis of OI 15 at the DNA level (**7**)

CASE REPORT

The patient was examined for the first time at the *Centre for Locomotor Defects (CLD) in Prague* at the age of 3 years and 1 month on the recommendation of prof. Šumník, MD, Ph.D. with the diagnosis of *susp. osteogenesis imperfecta, type IV A*.

Personal anamnesis

The child was born from the first physiological pregnancy, perinatal period without complications, delivery in the 41st week of pregnancy, spontaneous, head-to-head, unchanged, 2860 g/49 cm, postpartum adaptation was good. Psychomotor development was insignificantly delayed, sitting at 7 months, walking independently at 15 months. Speech normal. Growth retardation was detected at 18 months.

Family anamnesis

Parents healthy.

Present disease

After birth, she was treated at *Pediatric Surgery Department of the Na Bulovce Hospital* due to fracture of the right (R) humerus diaphysis. An X-ray of skull proved caput membranaceum and ossa wormiana – see **Fig. 1a, b**.

The first injuries were sustained in falls on the plane (23 months – epiphysiolysis of the distal right (R) femur; 26 months – fracture of the left (L) femur, 30 months – refracture of the diaphysis of the L femur. She was treated at the Pediatric Surgery Department of Na Bulovce Hospital. For further orthopaedic treatment she was referred to the CLD in Prague. In the last 2 years she was treated at the Department of Pediatric and Adult Orthopaedics and Traumatology at Motol University Hospital.

She was treated at the *Paediatric Clinic of Motol University Hospital in Prague* with cycles of pamidronate from 2.5 years of age. At the age of 5 years she was transferred to infusion treatment with zoledronate. The treatment is continued with regular monitoring of biochemical markers and bone density to this day (currently at the age of 17 years, i.v. zoledronate at a dose of 0.05 mg/kg á 6 months). Daily use of vitamin D and calcium is part of the medical treatment.

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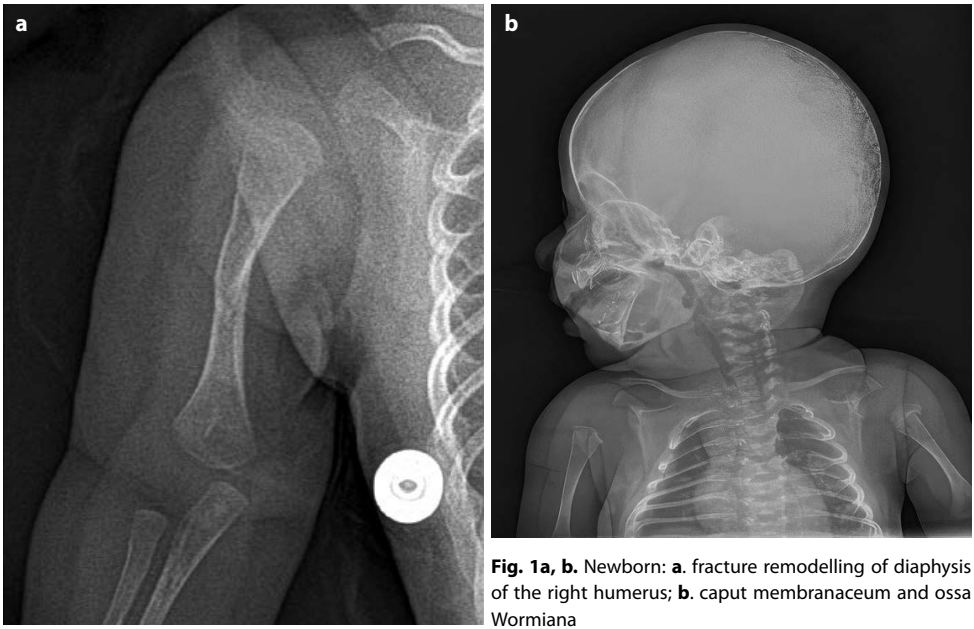
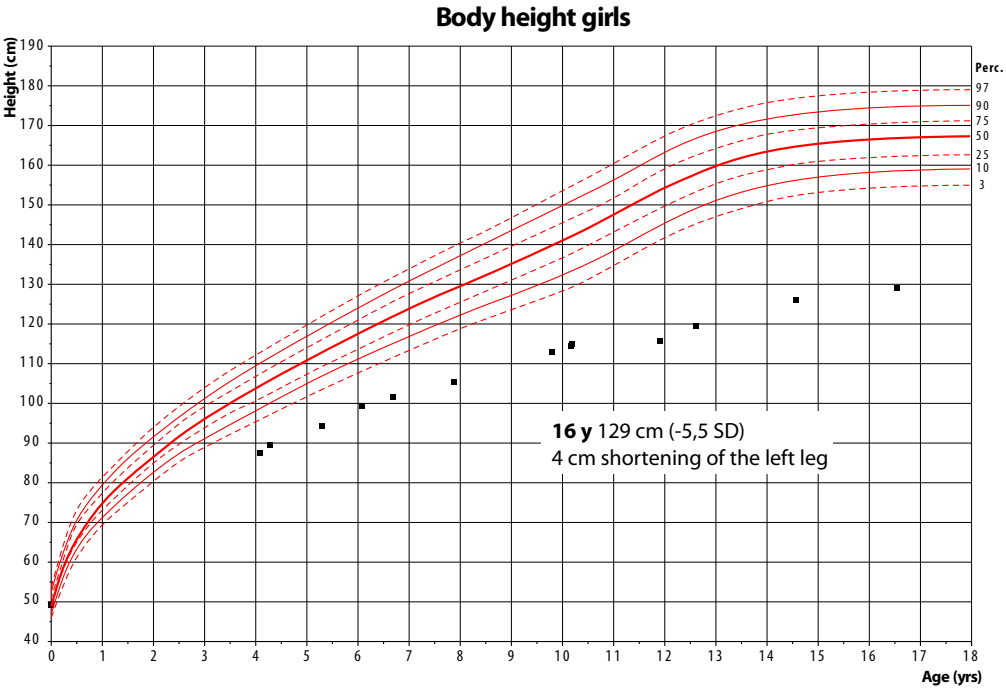
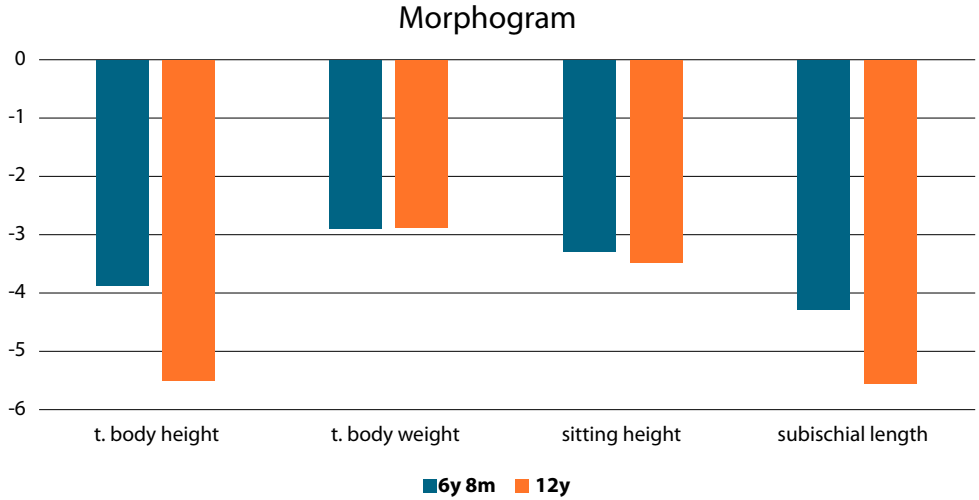


Fig. 1a, b. Newborn: **a**. fracture remodelling of diaphysis of the right humerus; **b**. caput membranaceum and ossa Wormiana



Graph 1. The body height was significantly reduced compared to both the norm and the height of the parents.



Graph 2. Documents progression of growth retardation and shortening of the lower limbs from 6y 8m. to 12y. Compared to the norm, both trunk and limbs were shortened.

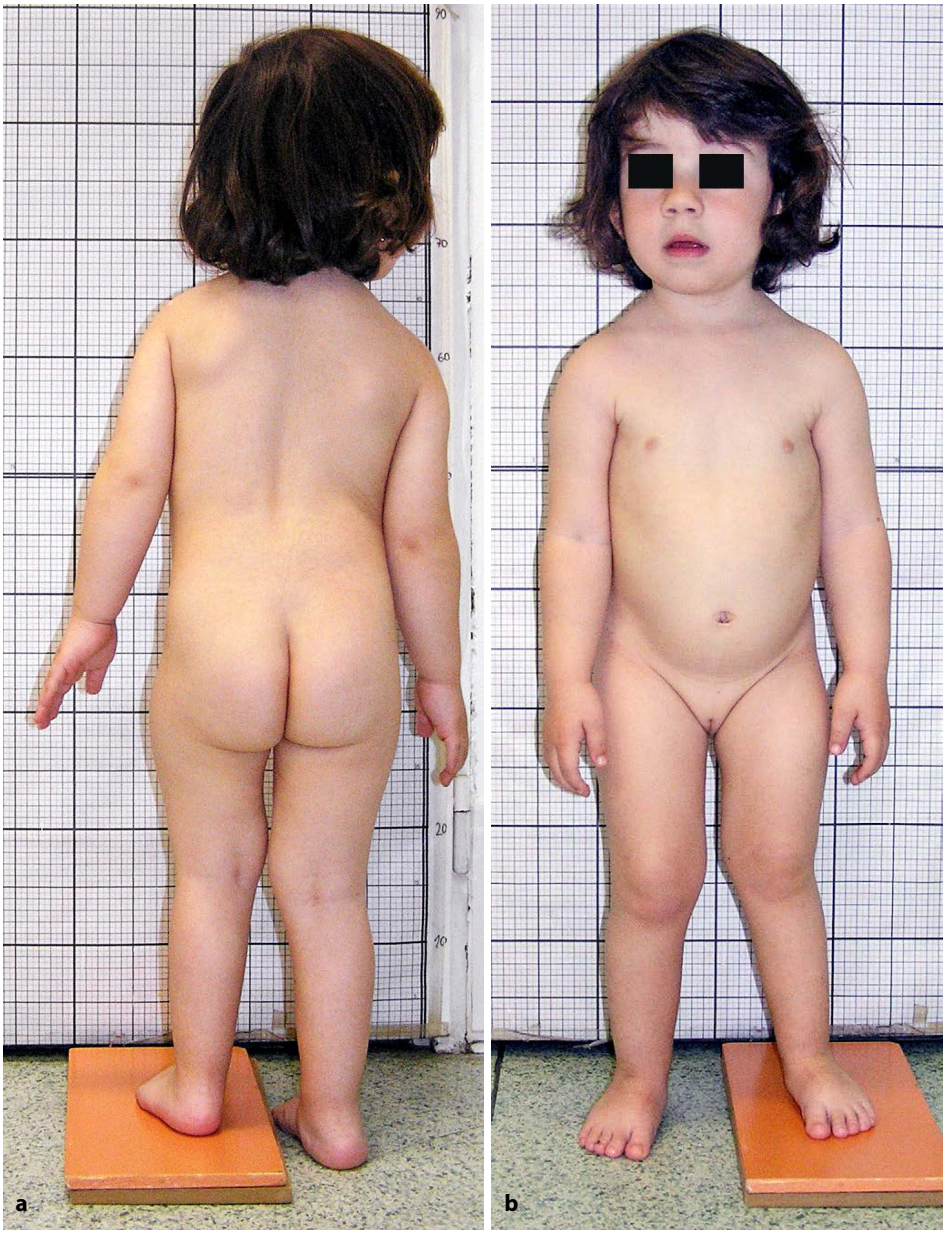


Fig. 2 a–d. Proportionality of stature at **3y** and **8y**. The left lower limb was shortened by 2 cm at **3y**. and by 4 cm at **8y**.

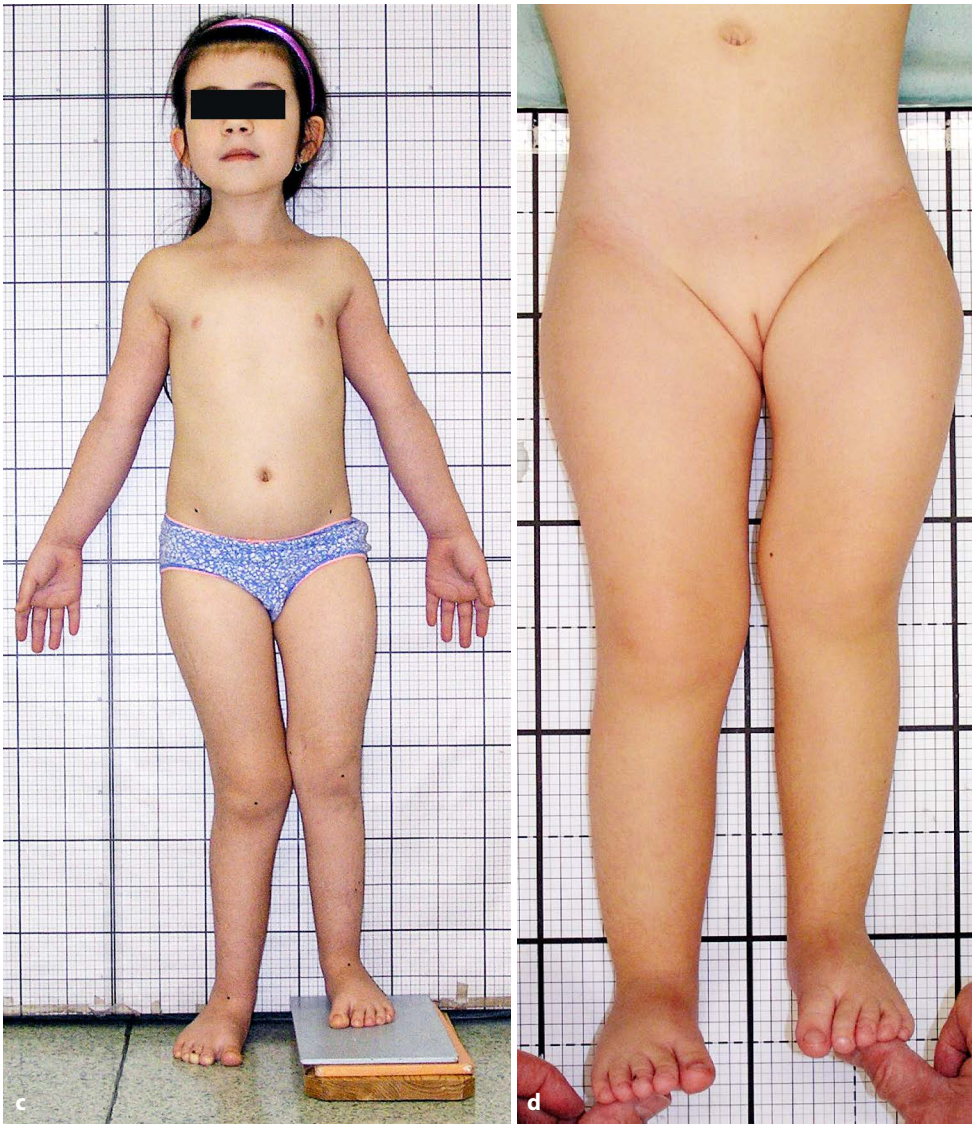


Fig. 2 a–d. Proportionality of stature at 3y and 8y. The left lower limb was shortened by 2 cm at 3y. and by 4 cm at 8y; **d**. anterolateral angulation of the left femur.

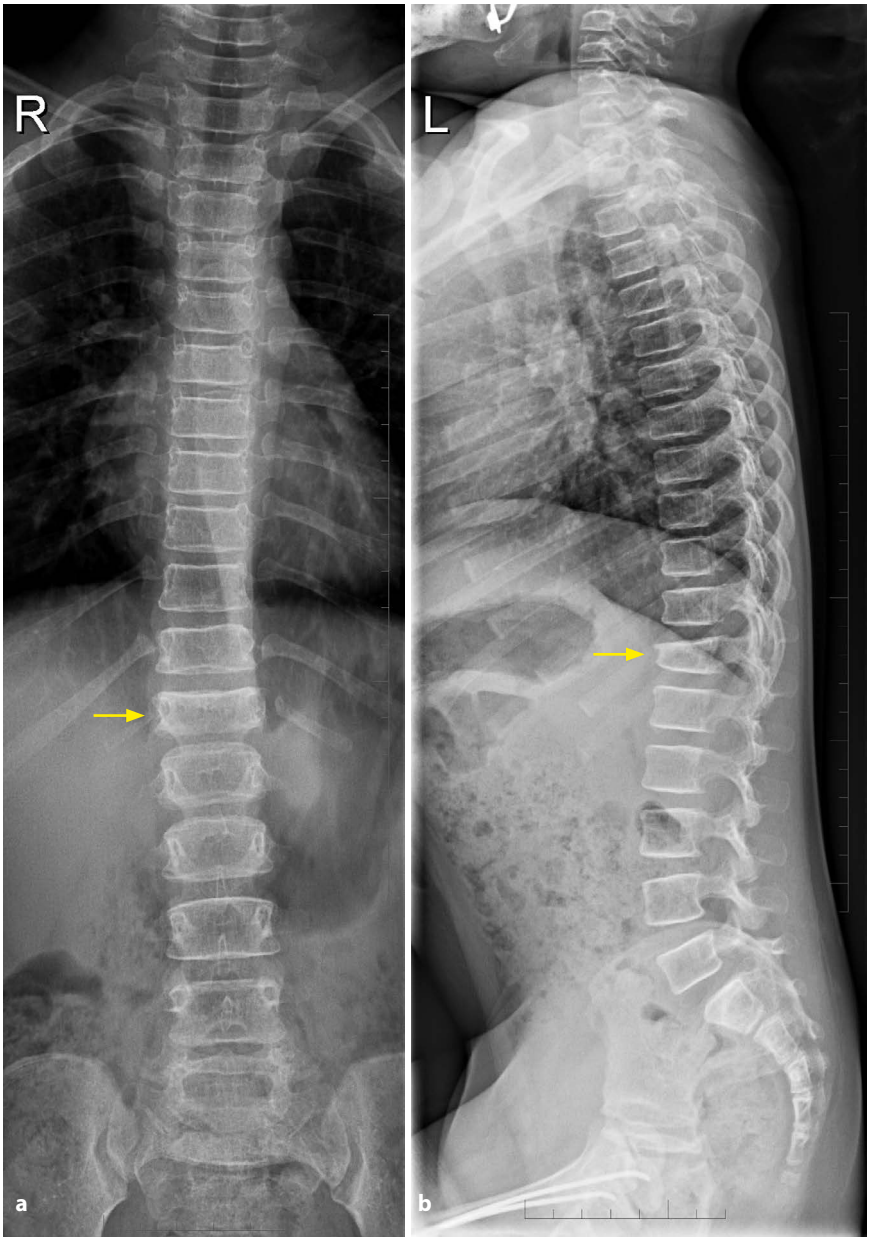


Fig. 3a, b. Spine at 5.5y: compressive fracture of the vertebral body of T 12 with flattening of the vertebral body and its wedge-shaped defiguration – *arrows*.

Anthropometric findings

Anthropometric findings at 4 years of age were consistent with dg. osteogenesis imperfecta, type IV. The body height was already significantly reduced compared to both the norm and the height of the parents. The girl measured 87.5 cm (- 4 SD) at 4 years of age, with further slowing during puberty, the final height being 129 cm (- 6 SD) – see **graphs 1** and **2**. The graphs document the progression of growth retardation and shortening of the lower limbs. Endocrinological examination confirmed that this is not an endocrinopathy but a growth disorder with underlying OI disease. Compared to the norm, both trunk and limbs were shortened, and limb involvement became more pronounced during the growth period. The left lower limb was shortened by 1.5–2 cm at 4 years of age, and by the end of growth this shortening increased to 4 cm.

X-ray of the spine

X-ray of the spine at 5.5 years of age showed a mild dextro-convex protrusion in the thoracolumbar region of the spine and a compressive fracture of the vertebral body of T 12 with flattening of the vertebral body and its wedge-shaped defiguration – **Fig. 3a, b**.

At 10 years of age, a mechanical wheelchair and a corset for sitting in a wheelchair were prescribed. Until then, she used a wheelchair.

Orthopaedic treatment

Orthopaedic treatment of lower and upper limb deformities was repeatedly performed at the *Department of Orthopaedics and Traumatology in Příbram Hopital* until the age of 15.5 years. Minor procedures were performed in the *CLD in Prague*, e.g. shortening or extraction of ESIN nails, extraction of 8-point splint, knee joint mobilization.

The patient suffered repeated fractures of the right and left femur, both tibias and both right and left humerus. The fractures healed with pseudoarthrosis and angulation, requiring more than 10 surgeries from 3 to 16 years. These included corrective and segmental osteotomies of both femurs, tibias and humeri with intramedullary fixation with ESIN nails (Prévot rods) and plaster fixation (for adequate time) converted to CombiCast fixation, which was usually modified into Knee Ankle Foot Orthosis (KAFO) or Ankle Foot Orthosis (AFO) orthoses.

The phenotype of the proband at ages 3 and 16.5 is documented in photographs – see **Figures 2a–d** and **14a–c.** Fractures, pseudoarthrosis, surgical treatment of lower and upper limb deformities, and complications are shown in selected X-ray images – see **Figures1a, b, 3a, b, 4a–g, 5a–c, 6a–c, 7a–d, 8a–h, 9a–c,** and **10a, b.** Figures **10c, d, 11a–d,** and **12a–d** show pseudoarthroses and their successful surgical treatment with intramedullary (IM) fixation and small plates (8-shaped plate, mini Aptus plate). Bone union was achieved.

Note: On X-ray images showing the knee joints, it is possible to identify Harris lines (growth lines) that correspond to cycles of bisphosphonate infusion therapy.



Fig. 4a. X ray of left femur: 2.3y – fracture (*arrow*) treated with simple plaster spica cast.

The patient is in a wheelchair, she only stands up when moving from the wheelchair to the bed. A conservative approach is now preferred.

DXA densitometric examination

DXA densitometric examination (University Hospital Motol; Prague) in 2024 showed a decrease in low bone density in the lumbar spine (Z-score: -4.5 /16 years/) compared to previous examinations, which were repeatedly performed in the child until 2020 at the Central Military Hospital in Střešovice, Prague (Z-score: -4.2 /4 years/ Z-score: -3.0 /12 years/).

Peripheral QCT of the forearm

Peripheral QCT of the forearm showed trabecular bone density at the metaphysis of the radius to be normal for age, whereas cortical bone density at the diaphysis of the radius was significantly reduced. The bone strength index at the diaphysis of the radius is also reduced relative to age. There is a marked decrease in all parameters in the last year.

Biochemical examination

Bone markers repeatedly showed increased bone turnover, low vitamin D levels, mild elevation of PTH.

Molecular genetic

Molecular genetic testing (Assoc. Professor RNDr. Lenka Fajkusová, Ph.D. and Mgr. Lenka Kopečková, Ph.D., Section of Congenital Genetic Disorders, Centre for Molecular Biology and Gene Therapy, Brno): The analysis detected the previously described pathogenic variant c.774C>A (p.Tyr258*) in a heterozygous state in the *WNT1* gene (Lu et al. 2018) and the previously undescribed variant c.526T>C (p.Phe176Leu) in a heterozygous state in the *WNT1* gene. Regarding the variant c.526T>C, most prediction programs agree on the pathogenic impact on the protein. Considering the observed phenotype, we regard the two above-described variants in the *WNT1* gene in the proband as causal.

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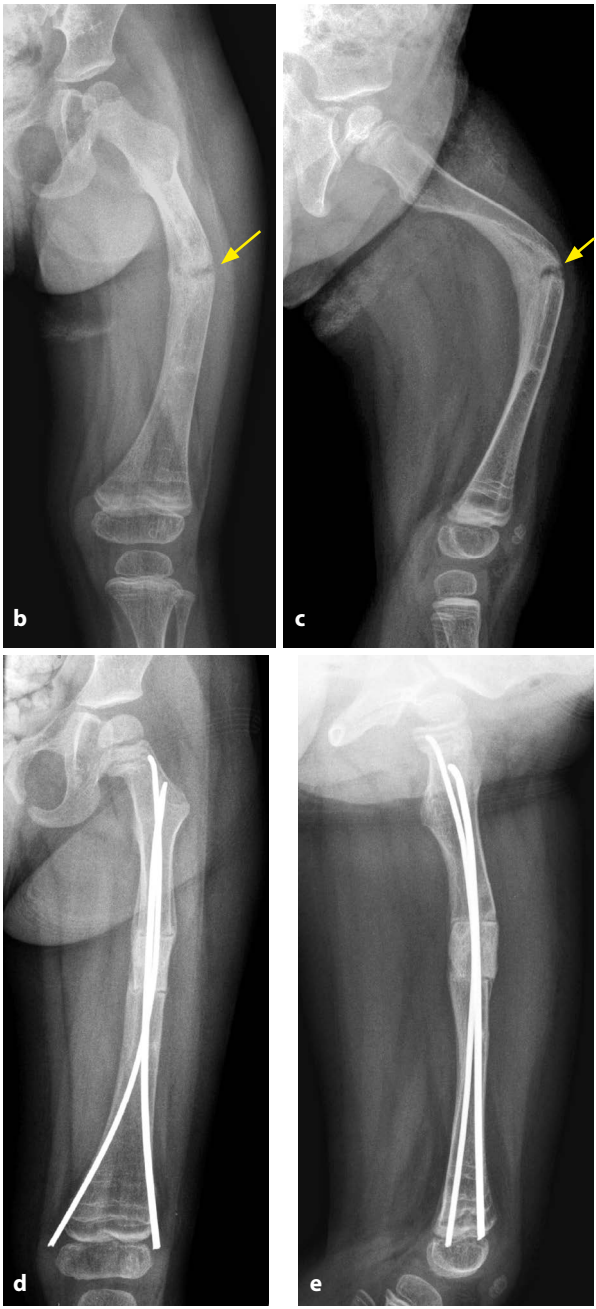


Fig. 4b–e. 3y 3m: remodelling of left femur fracture with pseudoarthrosis – arrows – **b, c**; **3y 9m**: left femur remodelling after surgery with fixation 2 ESIN rods (Prevot´s nails) – **d, e**.

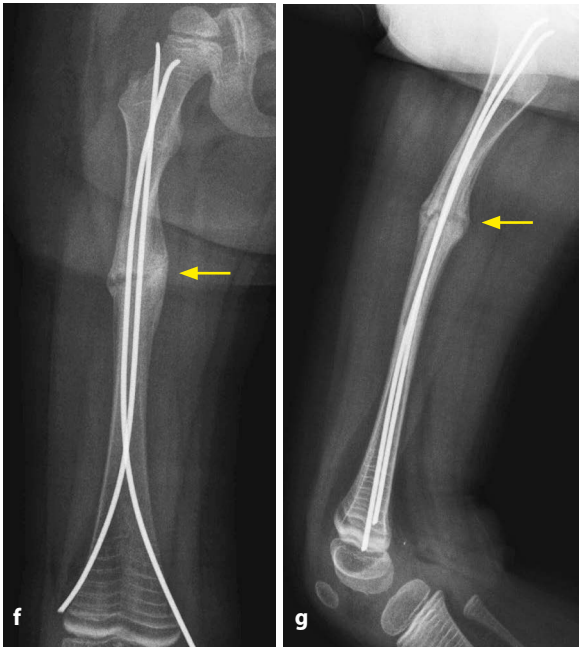


Fig. 4f, g. 4y 10m: Right femur remodelling after the same procedure.

In order to verify that the two variants found are in *trans* position with each other, it was recommended to test the above mentioned variants in both parents of the proband. Unfortunately, examination of the parents has not yet taken place.

DISCUSSION

In the presented case of AR deforming type of OI, the authors document the irreplaceable complex treatment and care of children with OI, which is multidisciplinary and includes mainly pediatric, osteological, rehabilitation and surgical interventions aimed at the treatment of fractures and skeletal deformities Treatment of fractures and correction of limb deformities are common procedures, with intramedullary (IM) fixation of long bones being particularly effective in reducing fractures and revision surgeries (**8**). Revision surgeries are unavoidable in severe (AR) deformity types. To date, there is a need for an international exchange with orthopedic surgeons (adults, pediatrics) to collect more data at longer term, and harmonize procedures (**1**). Regarding small splints that we used in recent years as an adjunct to IM fixation, our experience and recent work in the literature (**6**) have shown good results, although further research is needed to further define their indication and long-term complications.

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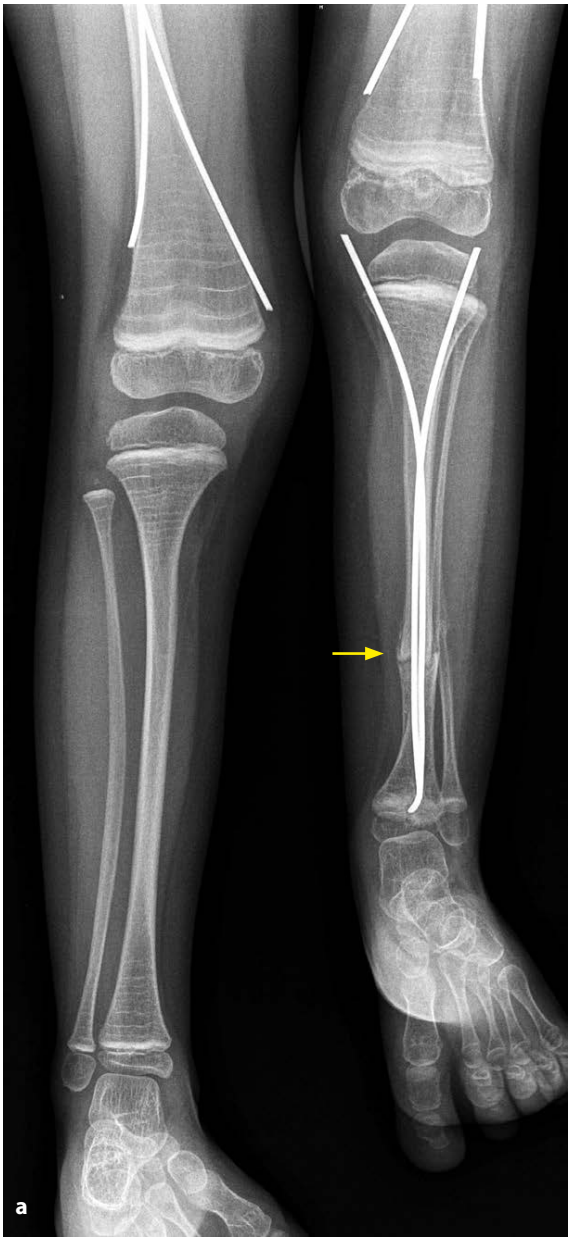


Fig. 5a–c. 6y 7m: Remodelling of the left tibia after wedge OT with resection of the pseudoarthrosis (AP projection), 2 ESIN nails fixation (*arrows*).

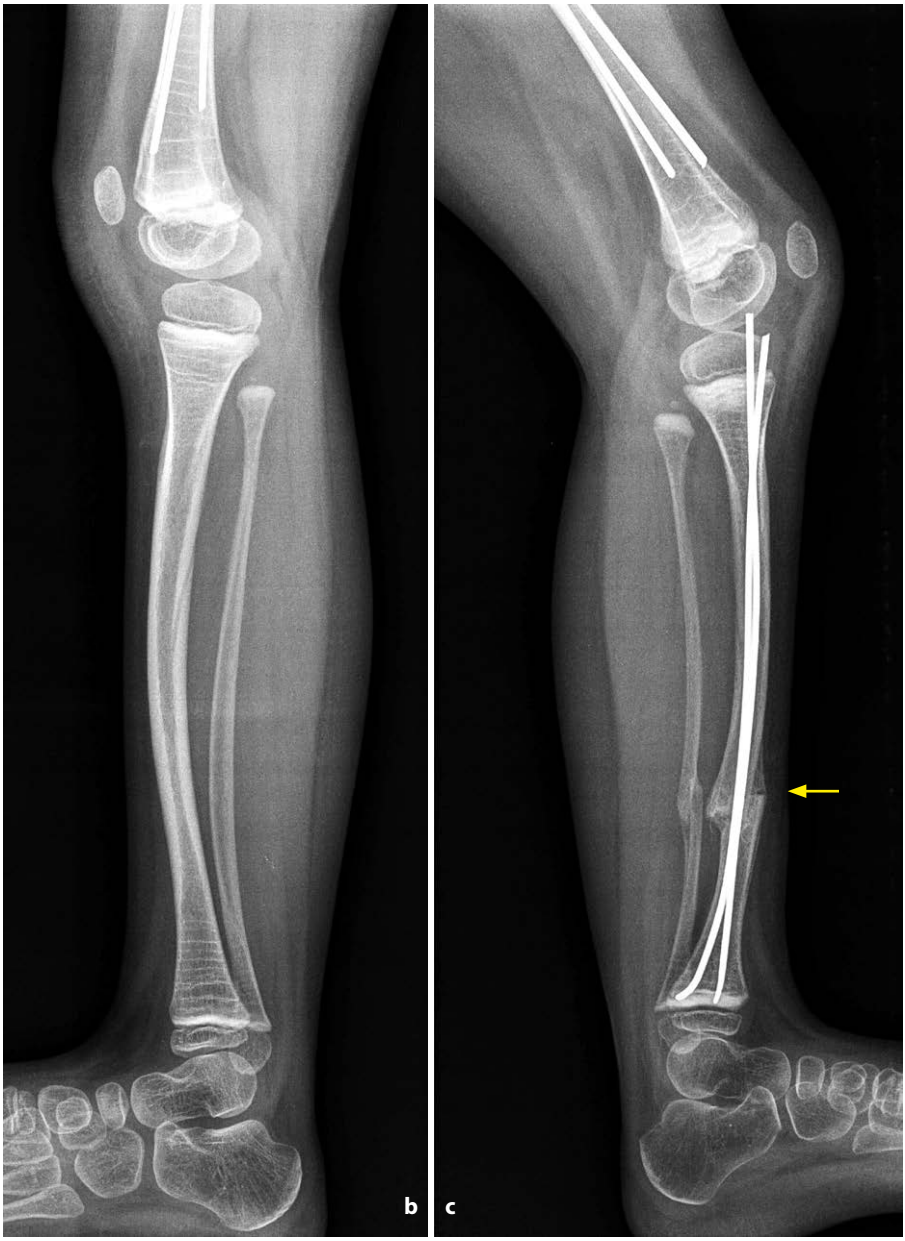


Fig. 5a–c. 6y 7m: Remodelling of the left tibia after wedge OT with resection of the pseudoarthrosis (lateral projection), 2 ESIN nails fixation (*arrows*).

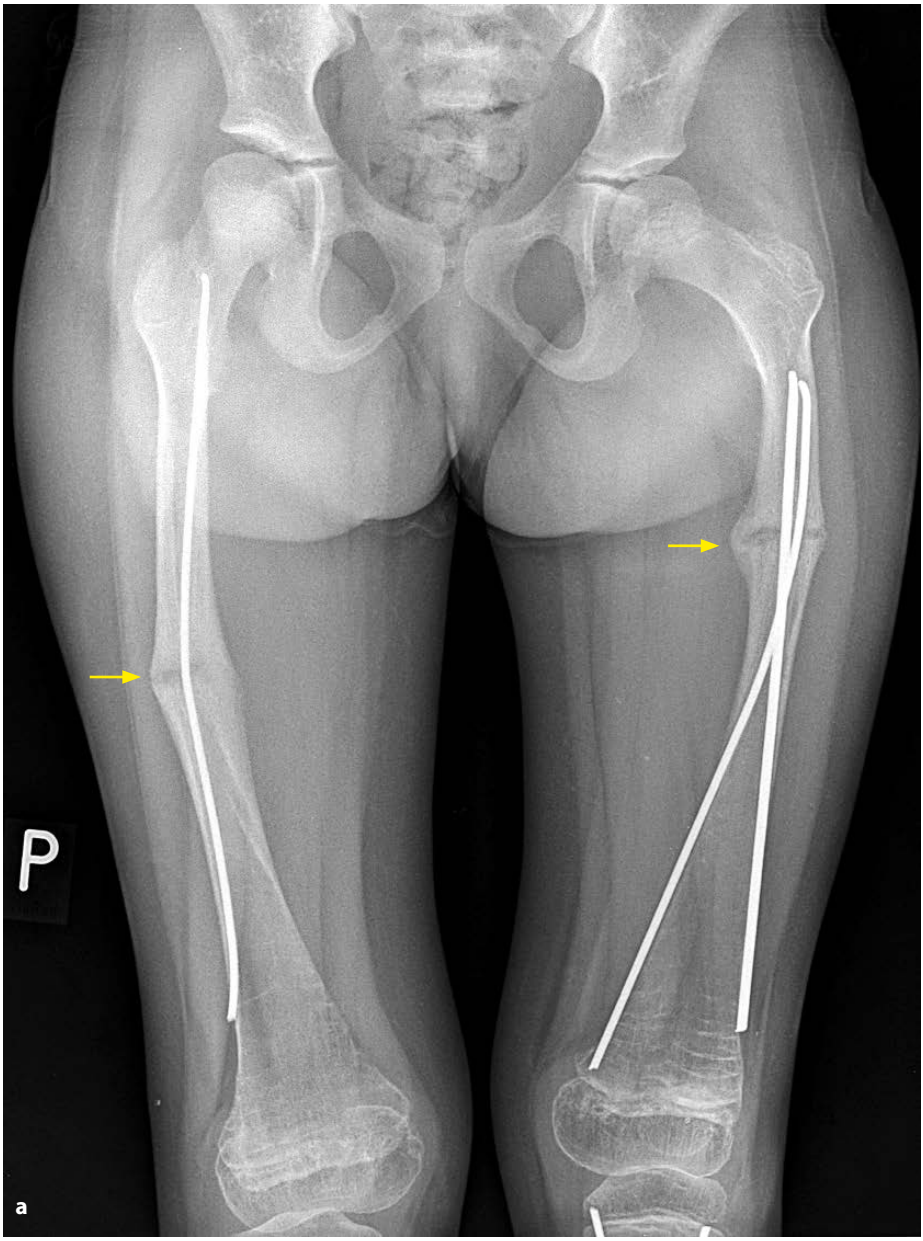


Fig. 6a. 8y 9m: Right and left femur, AP projection: bilateral pseudoarthroses in the diaphyses (*arrows*); on the right desaxation of the distal fragment medially – approximately 25°

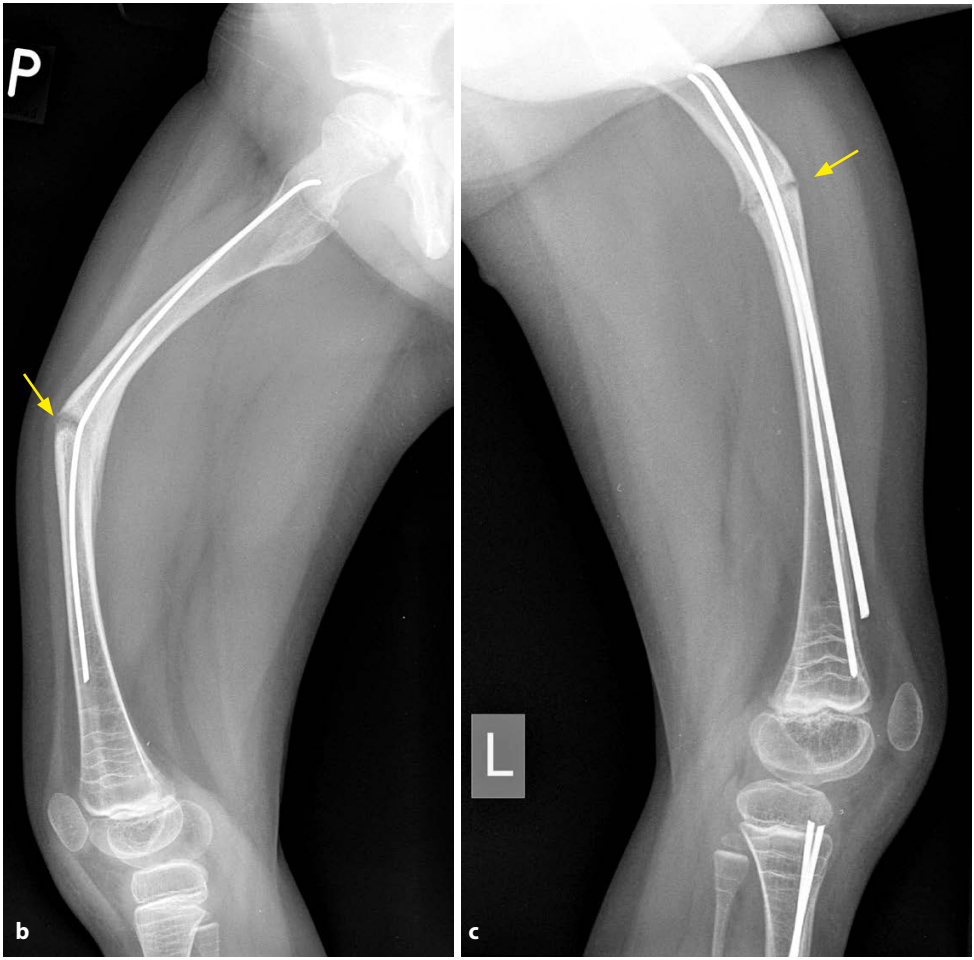
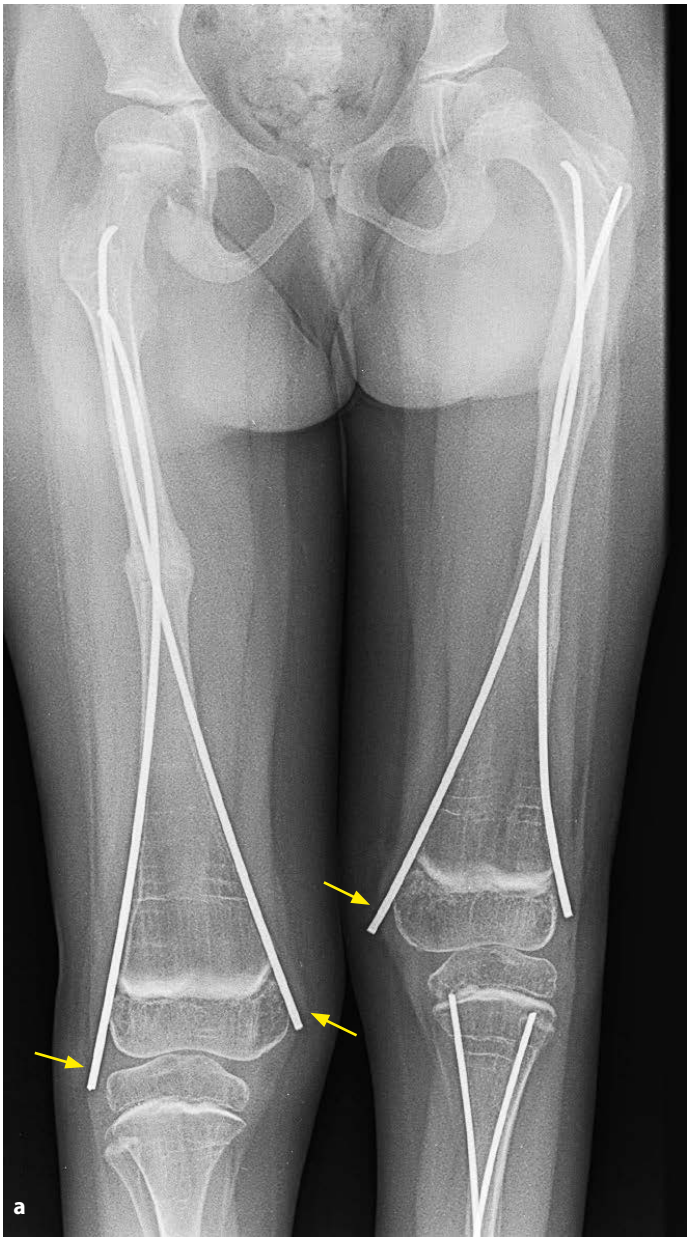
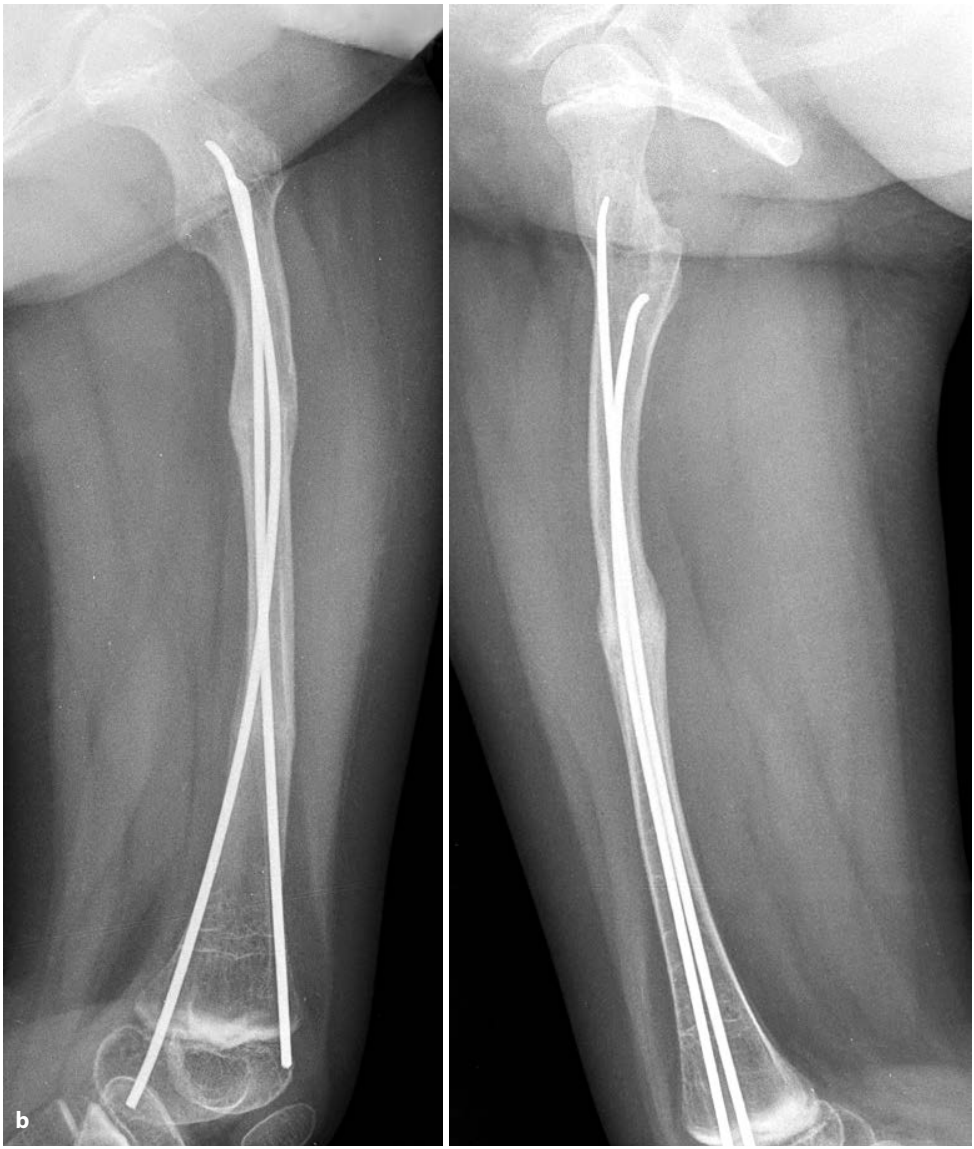


Fig. 6b, c. 8y 9m: Lateral projection: pseudoarthroses (*arrows*), on the right femur dorsal desaxation 53°, on the left 30°.



8y 10m: Corrective OT of the right femur; **9y**: corrective OT of the left femur was carried out.
Fig. 7a. 9.5y: Mild distal migration of ESIN nails from both femurs – AP projection (*arrows*).



8y 10m: Corrective OT of the right femur; **9y**: corrective OT of the left femur was caried out.
Fig. 7b. 9.5y: Mild distal migration of ESIN nails from both femurs – lateral projection;



8y 10m: corrective OT of the right femur; **9y**: corrective OT of the left femur was carried out.
Fig. 7c, d. 14y: Migration of medial nail from L femur and lateral nail from L tibia – **c**. AP and **d**. lateral projection (*arrows*).

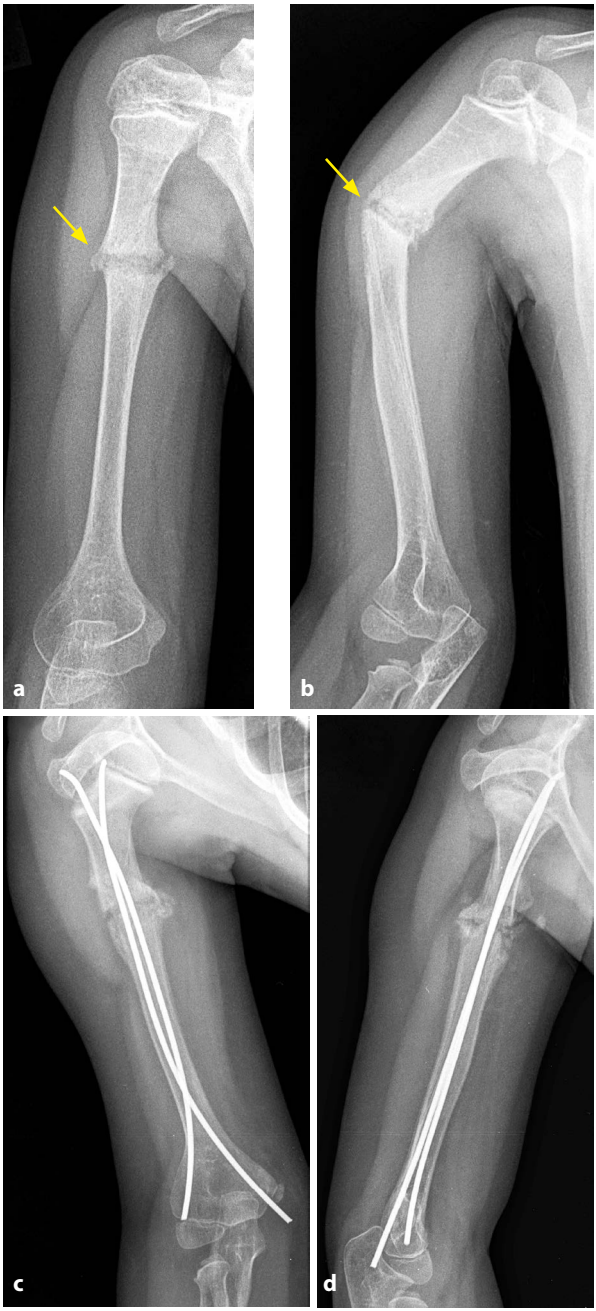


Fig. 8a–d. 9.5y: Wedge-shaped resection of pseudoarthrosis of right humerus (*arrows*), where was 50° anterolateral desaxation, intramedullary fixation with 2 ESIN nails



Fig. 8e–h. 12.5y: Wedge-shaped resection of pseudoarthrosis of left humerus (*arrows*) with correction of 40° desaxation, 2 ESIN nails.

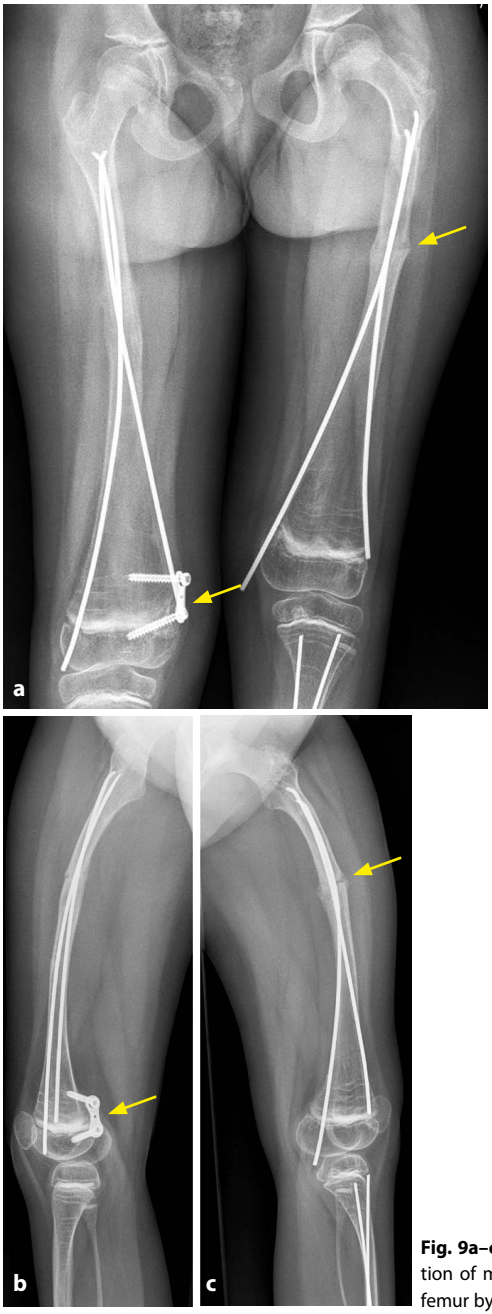


Fig. 9a–c. 11.5y: Stress fracture of left femur (*arrows*); distal migration of medial ESIN nail; **a**, **b**. correction of valgusity of distal right femur by medial hemiepiphysiodesis – 8-point splint (*arrows*)

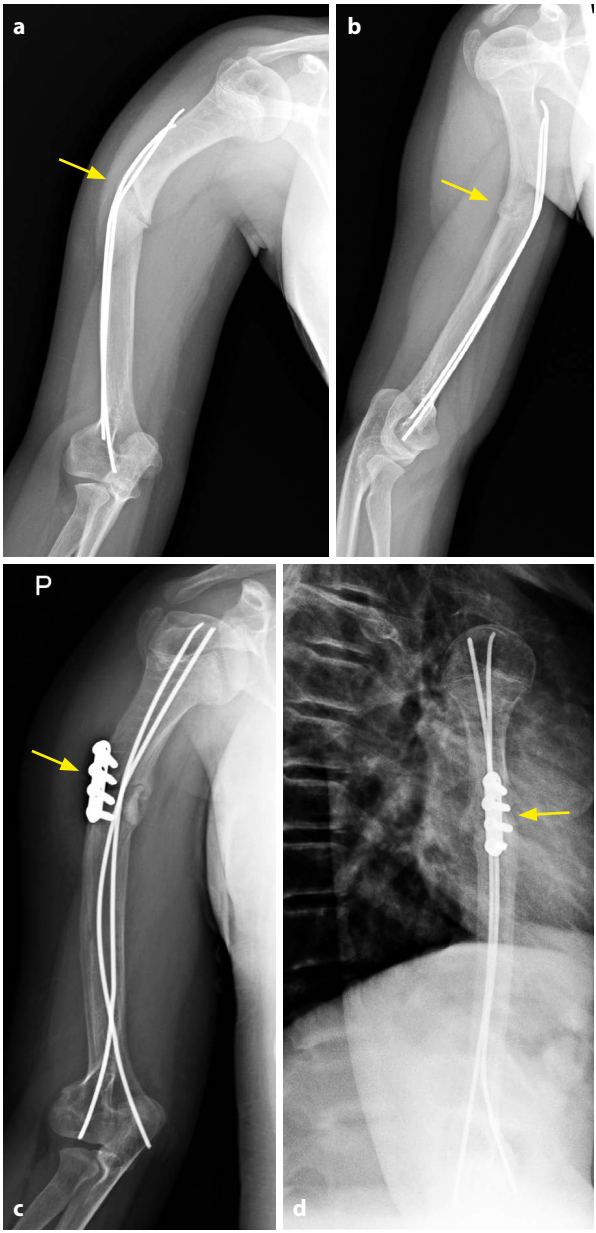


Fig. 10a–d. 14.5y: **a, b:** Recurrence of right humerus angulation and pseudoarthrosis (*arrow*); **c, d**. Result of reoperation – 2 nails + mini splint (*arrows*). Bone union was obtained.



Fig. 11a–d. 14y: **a, b:** Nails migration, varus deformity of the prox. diametaphysis of the left tibia, pseudoarthrosis and angulation in the lower 1/3 of diaphysis (*arrow*); **c, d**. Result of surgery: nail extraction, valgus OT of the prox. diametaphysis of left tibia, osteoclasia of fibula, resection of the tibial pseudoarthrosis, correction of angulation and internal tibial torsion, fixation: 1x ESIN nail (2 mm), 1x 8-plate and 1x mini Aptus plate (2.0) – *arrows*. Bone union was obtained.

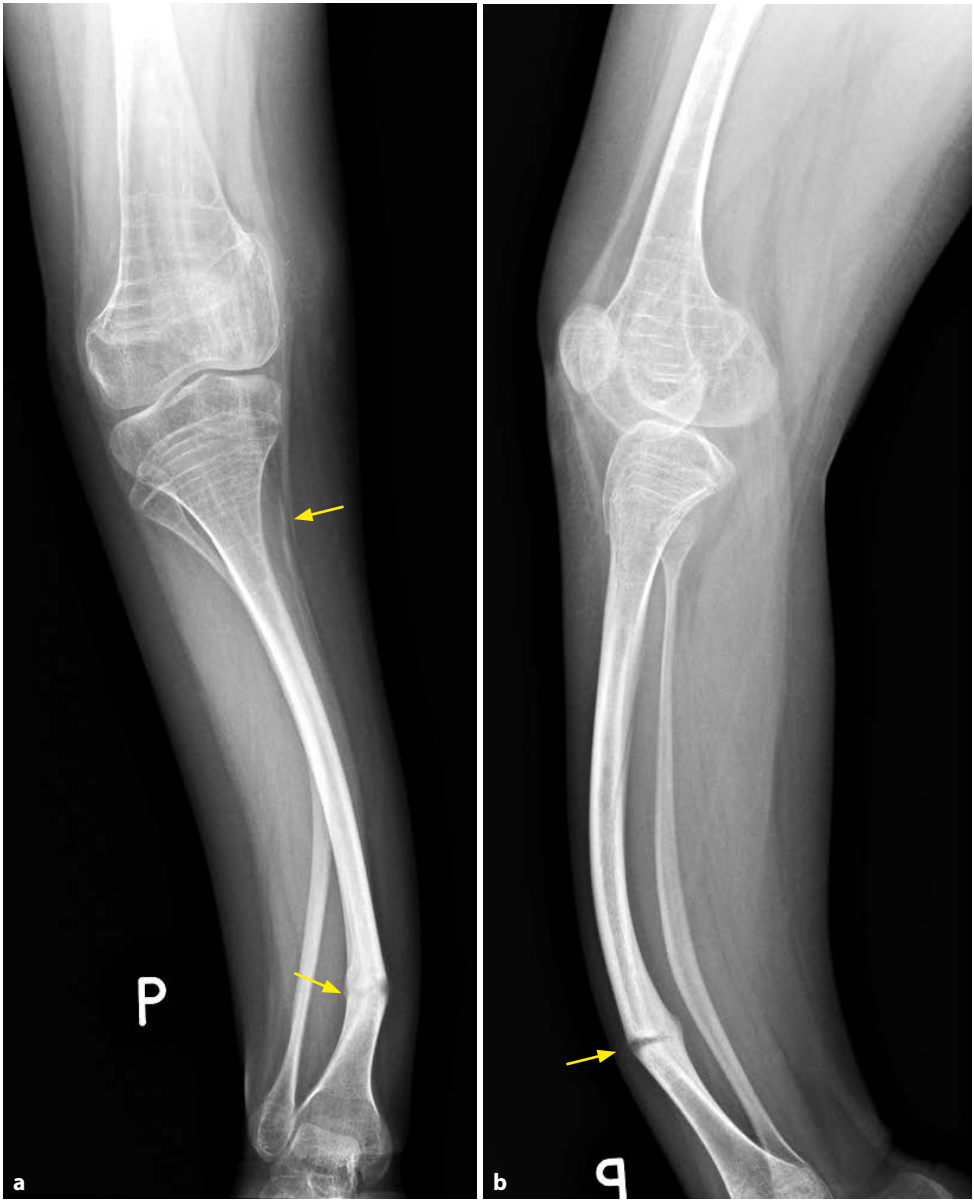


Fig. 12a, b. 14y 9m: **a, b:** Varosity of prox. diametaphysis of right tibia – *arrow;* ventral angulation, valgusity and pseudoarthrosis at distal 1/4 diaphysis – *arrows*.

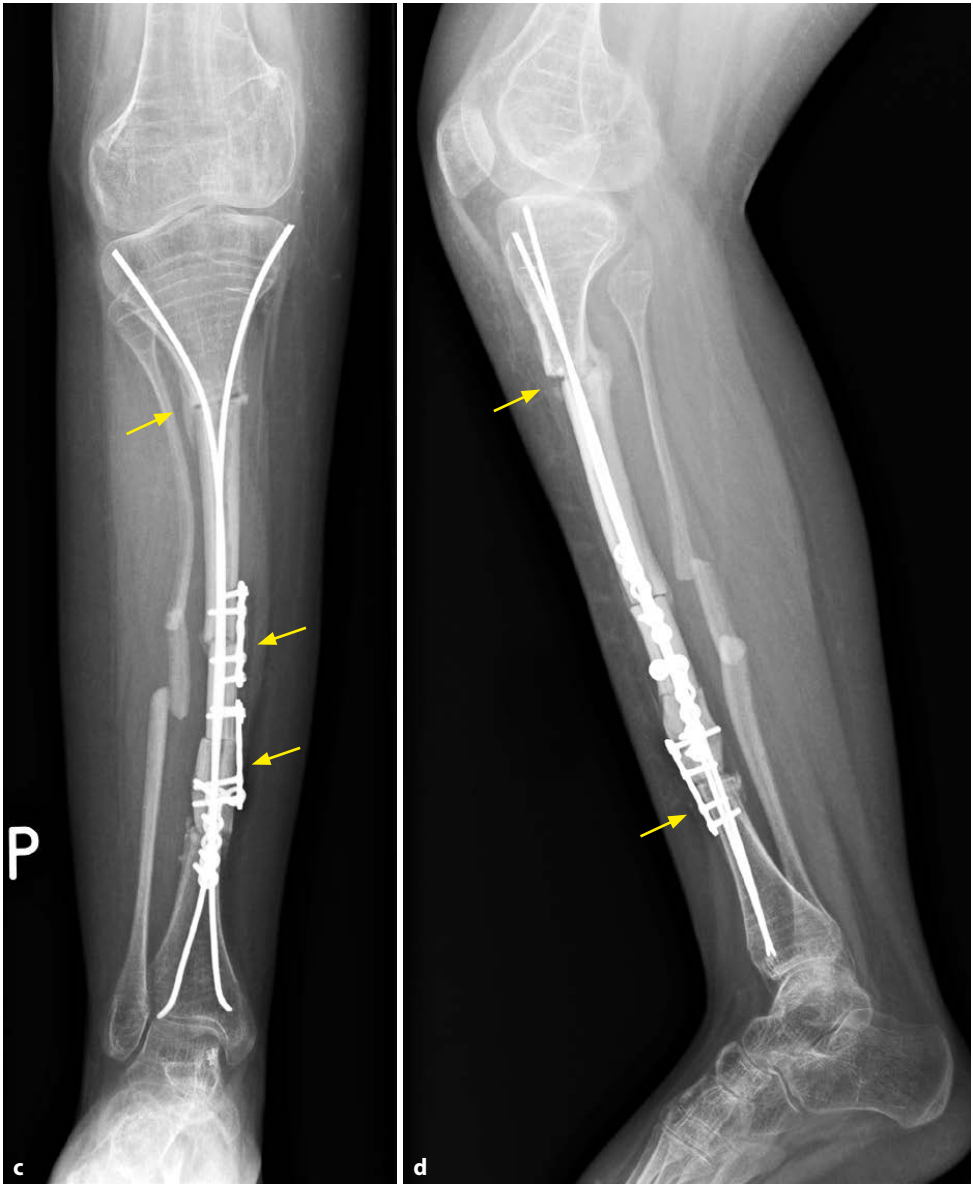


Fig. 12c, d. 15y 4m: Result of surgery: wedge-shaped valgus OT of prox. tibia, osteoclasia of fibula, resection of 3 fragments of diaphysis where the marrow cavity was obliterated, these were appropriately shortened, and cannulated with a drill to a translucency of 4.5 mm, the pseudoarthrosis resected. 2x ESIN nails (2 mm) introduced; fragments fixed with 3x mini Aptus plate (2.5) – *arrows*; bone grafts to osteotomies; periosteal sleeve lined with Gelaspon, suture in layers.



Fig. 13. 15y 4m: Fracture of R femur (*arrrow*), surgery in Motol – ESIN nail; **15y 6m**: removal of plaster spica, shortening of the curved distal end of the nail (*arrow*) and Combicast fixation according to Sarmiento on right tight.

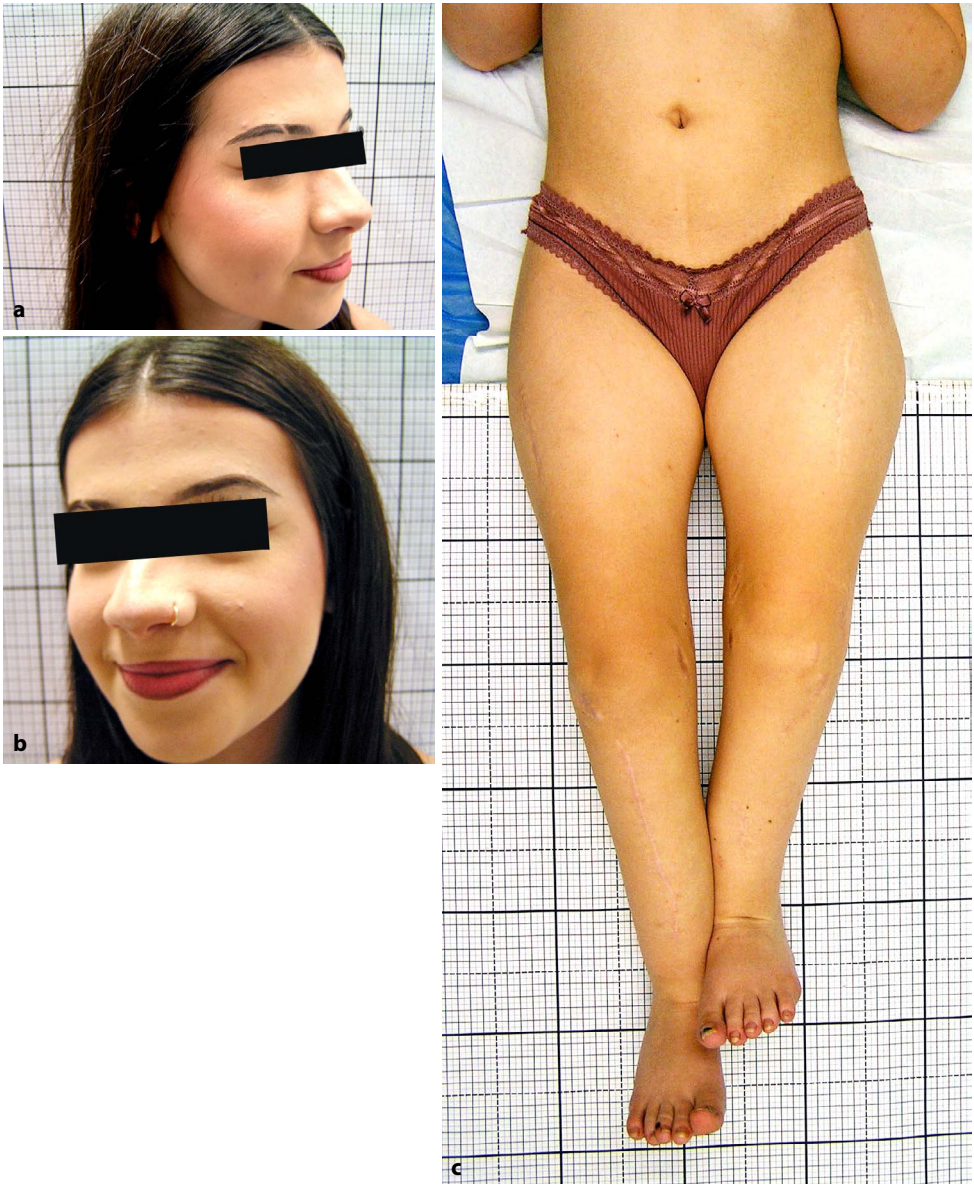


Fig. 14a–c. 16y 6m: Body height 129 cm (- 5.5 SD); shortening of left lower limb 4 cm.

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Bisphosphonate therapy remains the gold standard of medical treatment, although new pharmacological approaches are being explored (**3**). Screening of drugs in a cellular model (**2, 10**) showed that teriparatide exhibited high osteogenic potential in *WNT1* MSCs (mesenchymal stem cells), while denosumab showed promising results in *SERPINF1* MSCs, suggesting their therapeutic potential for the treatment of OI in children and adults.

CONCLUSION

In the first case of molecularly genetically diagnosed OI type 15 in the Czech Republic, the authors highlight the progression of significantly low bone density with persistently increased bone turnover with i.v. bisphosphonate treatment (pamidronate from 2.5 to 5 years, when conversion to zoledronate) and the recurrences of pseudofractures and deformities of both humerus, femur and tibia that required repeated adjustments and replacements of intramedullary rods (Prevot´s nails). They point to their own good experience with plates used as an adjunct to IM fixation. Bone union was achieved.

Based on the results of teriparatide screening in a cellular model presented in the literature, which demonstrated high osteogenic potential in WNT1 MSC (mesenchymal stem cells), it is considered to switch a 17-year-old female patient to teriparatide in order to favorably influence peak bone mass in adulthood.

Early molecular genetic diagnosis of pathogenic variants in a heterozygous state in the *WNT1* gene in children at an early age is crucial for early comprehensive treatment provided by a team of interested experienced professionals.

Acknowledgements

We thank to Assoc. Professor RNDr. Lenka Fajkusová, Ph.D. and Mgr. Lena Kopečková, Ph.D. (Centre for Molecular Biology and Gene Therapy, Brno) for the results of New Generation sequencing analysis of the gene panel. We would like to thank the colleagues of the Pediatric Surgery Department of the Na Bulovce Hospital who treated the patient in the first years of her life, the colleagues of the Orthopaedics and Traumatology Department of the Příbram Hospital who assisted the first author during the reconstructive operations, and the colleagues of the Department of Pediatric and Adult Orthopaedics and Traumatology of the University Hospital in Motol for their indispensable cooperation in the orthopaedic treatment of the presented patient.

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Professor Mařík Ivo, MD, PhD
ambul_centrum@volny.cz
Centre for Defects of Locomotor Apparatus l.l.c.
Olšanská 7, 130 00 Prague 3
Czech Republic

SUBKATEDRA ORTOPEDICKÉ PROTETIKY A PODIATRIE NA IPVZ

SUBDEPARTMENT OF ORTHOPAEDIC PROSTHETICS AND PODIATRY AT THE INSTITUTE OF POSTGRADUATE MEDICAL EDUCATION (IPME)

MUDr. Petr Krawczyk, Ph.D.
Předseda Ortopedicko-protetické společnosti ČLS JEP
Vedoucí Subkatedry ortopedické protetiky a podiatrie na IPVZ
E-mail: krawczyk@proteorcz.cz

Od října 2022, kdy byla obnovena činnost Subkatedry ortopedické protetiky a podiatrie na IPVZ, zorganizovali pedagogičtí pracovníci subkatedry již tři ucelené ročníky vzdělávání v ortopedické protetice, které vždy zahrnovaly celkem 7 víkendových kurzů zakončených testem. Kurzy svým obsahem a náplní nahrazují vzdělávací program dřívější nástavbové atestace z Ortopedické protetiky.

V rámci činnosti subkatedry bylo navázáno na úspěšnou práci paní primářky MUDr. Marie Součkové, která jako prezidentka České podiatrické společnosti organizovala první certifikované podiatrické kurzy pro lékaře již od roku 2015. I díky jejím zkušenostem byl připraven v roce 2023 úvodní kurz Základy kalceotiky, který opakovaně vedla a vede i v následujících letech. Následoval kurz PC pedobarografie, který byl organizováván MUDr. Petrem Krawczykem, Ph.D. Kurz věnovaný Syndromu diabetické nohy byl zajištěn MUDr. Miroslavem Kolibou, Ph.D., MBA, LL.M, MHA, prezidentem České podiatrické společnosti. V současnosti tento kurz organizuje paní doc. MUDr. Vladimíra Fejfarová, Ph.D. předsedkyně podiatrické sekce české diabetologické společnosti ČLS JEP. Prof. MUDr. Ivo Mařík, CSc. garantuje kurz věnovaný vrozeným vývojovým vadám, ortopediii a ortopedické protetice v dětském věku. Další kurzy jsou zaměřené na ortotiku trupu a končetin, protetiku horních a dolních končetin. Opakovaně je rovněž organizován kurz zaměřený na správnou preskripci adjuvatik, mechanických a elektrických invalidních vozíků a opěrných prostředků, který je realizován za účasti předních odborníků v ČR.

Od roku 2024 rozšířila Subkatedra ortopedické protetiky a podiatrie IPVZ nabídku vzdělávacích akcí také o kurzy určené pro protetické techniky a ortotiky-protetiky.

Pro letní semestr roku 2026 připravila subkatedra tyto odborné akce:

KURZY PRO LÉKAŘE

PC pedobarografie, vrozené a získané vady nohy u dětí a dospělých
6. 2.–8. 2. 2026

Komplexní léčba pacientů s amputací dolních a horních končetin
20. 2.–22. 2. 2026

Ortopedická protetika pro revizní lékaře a krajské revizní techniky zdravotních pojišťoven
6. 3. 2026

Ortotika trupu a končetin
10. 4.–12. 4. 2026

Adjuvatika – preskripce mechanických a elektrických vozíků, pomůcky pro lokomoci a sebeobsluhu
24. 4.–25. 4. 2026

Syndrom diabetické nohy, hojení ran, nelékařské služby v podiatrii
15. 5.–17. 5. 2026

Ortopedická protetika a ortopedie u dětí
12.6.–14. 6. 2026

KURZY PRO NELÉKAŘSKÉ PRACOVNÍKY

Kalceotika 1 pro ortoticko-protetické pracovníky – ortopedické vložky
9.1.–11. 1. 2026

Kalceotika 2 pro ortoticko-protetické pracovníky – ortopedická obuv
17.4.–19. 4. 2026

Aktuální informace a možnost přihlásit se na výše uvedené kurzy je možné získat prostřednictvím tohoto odkazu:

https://www.ipvz.cz/o-ipvz/kontakty/pedagogicka-pracoviste/ortopedicka-protetika-a-podiatrie/kontakty-pracoviste

Ortopedicko-protetická společnost ČLS JEP jako garant oboru Ortopedická protetika si plně uvědomuje, že indikace a preskripce složitějších ortéz i protéz je v současné době zatížena řadou nepřesností vyplývajících z rychle se rozvíjejícího medicínsko-technického oboru Ortopedická protetika a nedostatečných znalostí lékařů, kteří pomůcky předepisují. Od 1. 1. 2019, kdy začala platit nová pravidla pro preskripci a úhradovou regulaci zdravotnických prostředků, se zvýšily požadavky zdravotních pojišťoven na přesné medicínské zdůvodnění indikovaných zdravotnických prostředků. Dle zákona o zdravotnických prostředcích č.48/1997 Sb. mohou ortopedicko-protetické prostředky předepisovat kromě odbornosti Ortopedická protetika i další odbornosti, jejichž vzdělávací programy problematiku ortopedické protetiky obsahuji buď velmi okrajově nebo vůbec.

Dle „Nařízení Evropského parlamentu a Rady (EU) 2017/745 – MDR, příloha XIII" musí indikující lékař přesně technicky specifikovat individuálně zhotovenou ortopedicko-protetickou pomůcku. Dle vyhlášky 377/2022 Sb.: „Přesný rozsah a struktura údajů uváděných na listinném poukazu" musí indikující lékař vypracovat při předpisu individuální pomůcky návrh charakteristik příslušného zdravotnického prostředku. Vzhledem k výše uvedeným faktům a požadavkům na předepisující lékaře se projevil nedostatek dostatečně erudovaných a zkušených lékařů v ortopedické protetice.

Nástavbová atestace z Ortopedické protetiky byla v roce 2018 zrušena. V současné době působí v tomto oboru 8 atestovaných lékařů z toho je většina v důchodovém věku.

Vzhledem k zajištění adekvátní léčebné lékařské péče s využitím stále více sofistikovaných ortoticko-protetických pomůcek je nevyhnutelné zajistit pro další generaci výchovu adekvátního počtu erudovaných lékařů schopných v rámci mezioborové péče ve všech souvislostech indikovat a garantovat správnost a účelnost zhotovené ortopedicko-protetické pomůcky u tělesně postižených pacientů.

Za poslední 3 roky se nám podařilo rozšířit řady lékařů, kteří mají díky kurzům z Ortopedické protetiky dostatek teoretických znalostí a mnozí z těchto lékařů tyto znalosti využívá již v praxi. Tímto způsobem se nám alespoň částečně daří zachránit dostupnost ortopedicko-protetické péče našim pacientům.

Seznam lékařů, kteří mají absolvován celý vzdělávací program z Ortopedické protetiky bude pravidelně aktualizován na stránkách Ortopedicko-protetické společnosti ČLS JEP.

http://www.ortoprotetika.cz/

Od roku 2026 budou moci absolventi výše uvedených kurzů po splnění dalších podmínek vykazovat některé kódy zdravotních výkonů odbornosti 607 (ortopedická protetika). Věříme, že se nám tímto způsobem podaří zachránit náš obor i personálně.

Zájemcům o vzdělávání v našem oboru doporučujeme pravidelně sledovat výše uvedený link na IPVZ.

INFORMACE O SPOLEČNOSTI PRO POJIVOVÉ TKÁNĚ ČLS J. E. PURKYNĚ (SPT)

Vážená paní kolegyně, vážený pane kolego,

dovolujeme si Vás informovat o možnosti stát se členem **Společnosti pro pojivové tkáně** (SPT), která v roce 2004 navázala na plodnou desetiletou činnost Společnosti pro výzkum a využití pojivových tkání vedenou panem prof. MUDr. M. Adamem, DrSc. Posláním SPT je podpora rozvoje výzkumu pojivových tkání, šíření nových poznatků týkajících se všestranných analýz tkání z obecného pohledu, moderních klinických přístupů k diagnostice a léčbě. Dalším posláním SPT je usnadnění styků mezi jednotlivými odborníky navázáním spolupráce s různými vědeckými, odbornými, výrobními a farmaceutickými společnostmi.

Vědecké poznání a aplikace nejnovějších poznatků v klinické praxi nabyly v posledních letech nebývalého zrychlení, a to nejenom v zahraničí, ale i u nás. Tato skutečnost bezprostředně souvisí s kvalitativním rozvojem poznání i v nebiologických vědách a v moderních inženýrských přístupech. Stále více se prokazuje, že vše se vším souvisí – není náhodou, že nové poznatky a objevy vznikají na rozhraní oborů a různých vědních disciplín. Lidská společnost v posledních desetiletích dosáhla nové civilizační kvality – ve vědě a v jejich aplikacích zcela jistě, avšak v morálce a etice ne tak příliš. Biomedicína je v současné době rozsáhlou interdisciplinární vědou, která bez kooperace s jinými vědními obory by byla odsouzena ke stagnaci. Proto cílem SPT je nejenom integrovat odborníky v biomedicíně, ale i v technických sférách.

Prioritní snahou SPT je presentovat odborné veřejnosti a specialistům v klinické praxi nejnovější poznatky v oblasti pojivových tkání. SPT je i společenskou organizací klinických pracovníků, vědců, pedagogů, která si klade za cíl společensky sblížit nejenom pracovníky v aktivní službě, ale i kolegyně a kolegy v důchodovém věku a v neposlední řadě i studenty a mladé doktorandy z vysokých škol, universit a akademických ústavů.

SPT organizuje během každého roku alespoň dvě odborná a společenská setkání, kde vedle odborných přínosů je kladen důraz také na společenské – přátelské diskuse všech vás, kteří nechtějí stagnovat a kteří nechtějí přemýšlet o nových poznatcích izolovaně a osamoceně.

Pro uhrazení nejzákladnějších nákladů na korespondenci se členy společnosti, jejich informovanost a pořádání odborných kolokvií, symposií a společenských odborných setkání byl stanoven **roční členský příspěvek pro aktivní kolegyně a kolegy 200 Kč** a **pro studenty a důchodce 100 Kč.**
SPT vydává časopis Pohybové ústrojí – pokroky ve výzkumu, diagnostice a terapii, do kterého se i vy můžete aktivně zapojit odbornými články a vašimi zkušenostmi. **Pro současné odběratele časopisu PU a další zájemce doporučujeme přihlásit se na http://www.pojivo.cz/en/newsletter/, zadat jméno a e-mailovou adresu, na kterou bude časopis posílán. Na webové doméně SPT ČLS JEP http://www.pojivo.cz/cz/pohybove-ustroji/ naleznete ve formátu PDF všechna jednotlivá čísla a dvojčísla časopisu (včetně Suplement) vydaná od roku 1997 (bezplatný přístup).**
Milí kolegové, nestůjte opodál a připojte se k české inteligenci – v oblasti pojivových tkání, ke které i Vy zcela jistě patříte. V naší krásné české zemi je třeba, aby prameny poznání byly stále živé a permanentně udržované. Poslání každého z nás není náhodné. Jsme velice zavázáni našim předkům, kteří rozvíjeli kvalitu odbornosti v naší zemi. Nepřipusťme útlum vědy u nás. Nenechme se zmanipulovat programovanou lhostejností, vyrůstající z neodbornosti, závisti a z patologického prosazování ekonomicko-mocenských zájmů.

Těšíme se na Vás a na Vaše zkušenosti – přijďte mezi nás!

Za výbor společnosti:

Prof. MUDr. Ivo Mařík, CSc. – předseda
Prof. MUDr. Josef Hyánek, DrSc. – čestný předseda
Prof. Ing. Miroslav Petrtýl, DrSc. – místopředseda
RNDr. Martin Braun, PhD – vědecký sekretář
Ing. Jana Zelenková – pokladník

Přihlášku do Společnosti pro pojivové tkáně ČLS JEP, z.s. najdete na adrese:
http://www.pojivo.cz/cz/wp-content/uploads/2020/02/PrihlaskaCLS_JEP_SPT_form.pdf

Přihlášku do Ortopedicko-protetické společnosti ČLS JEP, z.s. najdete na adrese:
http://www.pojivo.cz/cz/wp-content/uploads/2020/02/PrihlaskaCLS_JEP_OPS_form.pdf

INFORMATION ABOUT SOCIETY FOR CONNECTIVE TISSUES CMA J. E. PURKYNĚ (SCT)

Dear Sir/Madam, dear Colleagues,

We have great pleasure to inform you about the possibility of joining the **Society for Connective Tissues** (SCT) that was established in 2004 in order to continue the ten-year fruitful activities of the Society for Research and Use of Connective Tissue headed by Professor M. Adam, MD, DSc. The activities of the SCT are aimed at supporting the research development in the field of connective tissues, the dissemination of knowledge related to the all-purpose analyses of the tissues in general, and the application of the up-to-date approaches to the diagnostics and clinical practice. Further, the SCT is determined to facilitate contacts between the respective specialists by means of collaboration with various research, professional, production and pharmaceutical companies.

In the last few years, the scientific knowledge and the application of the latest findings in the clinical practice have accelerated on an unprecedented scale, not only abroad, but also in this country. This fact is closely connected with the qualitative development of the knowledge in the non-biological sciences and in the up-to-date engineering approaches. The fact that all things are mutually connected is becoming more and more evident. It is fairly obvious that the new knowledge and discoveries arise on the dividing line between the different fields and disciplines of science. In the last few decades, the human society has reached the new qualities of civilization. This applies, in particular, for the disciplines of science and their applications; however, this statement can hardly be used with reference to the moral and ethical aspects of the human lives. At present, the biomedical science is a wide-ranging interdisciplinary science which, in case of lack of cooperation with other scientific disciplines, would be condemned to stagnation. That is the reason why the SCT is aimed at integrating the specialists both within the biomedical science and within the engineering fields.

The priority objective of the SCT is to present the professional public and specialists involved in the clinical practice with the latest knowledge in the field of connective tissues. The SCT is also a civic society whose aim is to bring people close together by joining members of the clinical staff, researchers and teachers including the retired ex-colleagues and, last but not least, the undergraduates and PhD students from universities and academic establishments.

The SCT is planning to organize at least two professional and social meetings each year. Beside the professional contribution of these meetings, emphasis will be laid on social activities – informal

discussions of all those who do not want to stagnate and who do not want to acquire the new knowledge in solitary confinement.

The annual membership fee is 200 Czech crowns for full workers, and 100 Czech crowns for students and pensioners. This membership fee shall be used to cover the basic costs on correspondence with the members of the Society in order to inform them about organizing colloquiums, symposiums and social meetings.

The SCT is also engaged in publishing of the interdisciplinary journal entitled **Locomotor System – Advances in Research, Diagnostics and Therapy**. You are invited to contribute to the journal writing professional articles, exchanging experience or, simply sharing your opinions. You can find the volumes of Locomotor System journal at http://www.pojivo.cz/cz/pohybove-ustroji/ since 1997 (free of charge). Since 2013 only electronic edition of the journal is available. That is why we recommend to all subscribers and those interested apply at http://www.pojivo.cz/en/newsletter, enter personal data, titles and e-mail address where the journal will be mailed.

Dear Colleagues, do not stand aside (suffering from terrible lack of time) and join the professional people in the field of connective tissues to whom you undoubtedly belong. In this beautiful country, the sources of knowledge should be kept alive and maintained permanently. Our role in this process is not accidental. We are much obliged to our ancestors who had developed the qualities of proficiency in this country. Do not allow the decline of science. Do not let the programmed indifference arising from lack of professionalism, enviousness, and pathological promotion of economic and power interests manipulate us.

We are looking forward to meeting you. We will be pleased if you join us and share your experience with us.

On behalf of the committee of the Society for connective tissues:

Professor Ivo Marik, MD, PhD – chairman
Professor Josef Hyánek, MD, DSc – honorary chairman
Professor Miroslav Petrtýl, MSc, DSc – vice-chairman
Braun Martin, Dr, PhD – research secretary
Zelenková Jana, Eng – treasurer

Membership application form of the Society for Connective Tissues, Czech Medical Association J.E. Purkynje, Prague you can find on the following link:
http://www.pojivo.cz/cz/wp-content/uploads/2020/02/PrihlaskaCLS_JEP_SPT_form.pdf

Membership application form of the Orthopaedic-Prosthetic Society, Czech Medical Association J.E. Purkynje, Prague you can find on the following link:
http://www.pojivo.cz/cz/wp-content/uploads/2020/02/PrihlaskaCLS_JEP_OPS_form.pdf

TÉMATIKA PŘÍSPĚVKŮ

K uveřejnění v časopise Pohybové ústrojí se přijímají rukopisy prací z oblasti pohybového ústrojí člověka, které se týkají především funkce, fyziologického i patologického stavu kosterního a svalového systému na všech úrovních poznání, diagnostických metod, ortopedických a traumatologických problémů, příslušné rehabilitace a léčebné i preventivní péče. Předmětem zájmu jsou týmové práce z oboru dětské ortopedie a osteologie, dále problémy z oboru biomechaniky, patobiomechaniky a bioreologie, biochemie a genetiky. Redakce časopisu má zájem publikovat články kvalitní, vysoké odborné úrovně, které přinášejí nové poznatky, jsou zajímavé z hlediska aplikací a nebyly doposud nikde uveřejněny s výjimkou publikace ve zkrácené formě.

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Rukopisy zasílejte na adresu:

Prof. MUDr. Ivo Mařík, CSc.
Ambulantní centrum pro vady pohybového aparátu s.r.o., Olšanská 7, 130 00 Praha 3
Tel.: (+420) 222 582 214, e-mail: ambul_centrum@volny.cz

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Professor Ivo Mařík, M.D., Ph.D.
Ambulant Centre for Defects of Locomotor Apparatus
Olšanská 7
130 00 Prague 3
Czech Republic
Phone: (+420) 222 582 214
e-mail: ambul_centrum@volny.cz

OBSAH ROČNÍKU 2023

SLOVO ČTENÁŘŮM – EDITORIAL ..... 1/23, s. 11
..... 2/23, s. 167

OBRÁZEK NA TITULNÍ STRANĚ A POPIS

Paszeková Helena, Krulišová Veronika
Analýza vzorků DNA masivním paralelním sekvenováním ..... 1/23, s. 15
Analýza vzorků DNA masivním paralelním sekvenováním ..... 2/23, s. 171

DOPIS EDITOROVI

Povýšil Ctibor
Toxicita rtuti může vysvětlit ztrátu sluchu u Bedřicha Smetany. ..... 2/23, s. 175

PŘEHLEDOVÉ PRÁCE

Daniš Robert, Vážná Anna, Novák Jan, Sedlak Petr
Aktuální trendy v růstu českých dětí v kontextu sekulárních změn ..... 1/23, s. 19

Mařík Ivo, Myslivec Radek, Zemková Daniela, Maříkova Alena, Kapišinski Peter, Hudáková Olga
Makrodaktylie ruky a koincidence s mírnou formou Polandova syndromu:
Přehled a kazuistika českého chlapce ..... 1/23, s. 37

Kraus Josef
Neurofibromatosis von Recklinghausem typu 1 z pohledu neurologa ..... 2/23, s. 180

PŮVODNÍ PRÁCE

Všetička Jan (překlad)
Nozologie genetických poruch skeletu: Revize 2023 ..... 1/23, s. 60

Smrčka Václav, Musilová Zdenka, Gábor Olivér
Paleopatologická analýza na panonském avarském pohřebišti
Terehegy-Márfa z 9. století ..... 1/23, s. 109

Němec Ivo, Smrčka Václav, Mihaljevič M., Hill M. Pokorný J.
Změny stopových prvků (Mn, Co, Ni, Cu, Rb, Mo a Ba) v molárech dolní čelisti potkana po přerušení nervus alveolaris inferior ..... 2/23, s. 195

KASUISTIKY

Mařík Ivo, Zemková Daniela, Krulišová Veronika, Smrčka Václav, Myslivec Radek, Maříková Alena, Paszeková Helena, Michalovská Renáta, Vlčková Zděnka
Molecular genetic diagnosis of congenital contracture arachnodactyly and complex treatment of a Czech girl: a case study ..... 1/23, s. 123

Mařík Ivo, Zemková Daniela, Maříková Alena, Krulišová Veronika, Myslivec Radek, Povýšil Ctibor
Neurofibromatóza, typ 1: ortopedické léčení pseudoartrózy fibuly u české dívky... 2/23, s. 223

ZPRÁVY

Mařík Ivo
Recenzní posudek na knižní novinku: Ctibor Povýšil: Patologické mikroskopické nálezy v kosterních pozůstatcích významných osobností české historie. GRADA Publishing, a.s., 2024 ..... 2/23, s. 246

Jubilea

Mařík I.
Prof. MUDr. Tomasz Karski, CSc. – 85 let .....2/23, s. 252

Informace o Společnosti pro pojivové tkáně ČLS JEP ..... 1/23, s. 146
..... 2/23, s. 258

Přihláška řádného člena Společnosti pro pojivové tkáně ČLS JEP ..... 1/23, s. 147
..... 2/23, s. 259

Přihláška řádného člena Ortopedicko-protetické společnosti ČLS JEP ..... 1/23, s. 147
..... 2/23, s. 259

Oznámení úmrtí

Mařík I.
Vzpomínka na prof. Ing. Jana Čulíka, DrSc. .....2/23, s. 262

SMĚRNICE AUTORŮM ..... 1/23, s. 150
..... 2/23, s. 265

OBSAH ROČNÍKU 2022 ..... 2/23, s. 270

OBSAH ROČNÍKU 2023 ..... 2/23, s. 276

CONTENTS OF VOLUME 2023

A WORD TO READERS – EDITORIAL ..... 1/23, p. 13
..... 2/23, p. 169

TITLE PICTURE and DESCRIPTION

Paszeková Helena, Krulišová Veronika

Next-generation sequencing (NGS) analysis ..... 1/23, p. 17
Next-generation sequencing (NGS) analysis ..... 2/23, p. 173

LETTER TO EDITOR

Povýšil Ctibor

..... 2/23, s. 175

REVIEW ARTICLES

Danis Robert, Vazna Anna, Novak Jan, Sedlak Petr

Current trends in the growth of Czech children in the context of secular changes .. 1/23, p. 19

Marik Ivo, Zemkova Daniela, Krawczyk Petr, Smrcka Vaclav, Povysil Ctibor

Macrodactyly of hand and coincidence with a mild form of Poland syndrome:
A review and case report of a Czech boy ..... 1/23, p. 37

Kraus Josef

A neurologist's view of Neurofibromatosis von Recklinghausen type 1..... 2/23, p. 180

ORIGINAL PAPERS

Všetička Jan (translation)

Nosology of genetic skeletal disorders: 2023 revision ..... 1/23, p. 60

Smrcka Vaclav, Musilova Zdenka, Gabor Oliver

Paleopathological Analysis at the Terehegy-Márfa Pannonian Avar Burial Site
from the 9th Century ..... 1/23, p. 109

Němec Ivo, Smrčka Václav, Mihaljevič M., Hill M. Pokorný J.

Changes of trace elements (Mn, Co, Ni, Cu, Rb, Mo, Ba) in the molars of a rat mandible
after inferior alveolar nerve transection..... 2/23, p. 209

CASE REPORTS

Marik Ivo, Zemkova Daniela, Krulisova Veronika, Smrcka Vaclav, Myslivec Radek, Marikova Alena, Paszekova Helena, Michalovska Renáta, Vlckova Zdenka

Molecular genetic diagnosis of congenital contracture arachnodactyly and complex treatment of a Czech girl: a case study ..... 1/23, p. 123

Mařík Ivo, Zemková Daniela, Maříková Alena, Krulišová Veronika, Myslivec Radek, Povýšil Ctibor

Neurofibromatosis, type 1: orthopaedic treatment of fibular pseudoarthrosis in a Czech girl ..... 2/23, p. 223

NEWS

Mařík Ivo

Review of the book: Ctibor Povýšil: Pathological Microscopic Findings in Skeletal Remains of Important Personalities of Czech History. GRADA Publishing, a.s., 2024 ..... 2/23, p. 246

Jubilee

Professor Tomasz Karski, MD, Ph.D. – 85 years ..... 2/23, p. 252

Information on the Society for Connective Tissues, Czech Medical Association J.E. Purkynje, Prague, CZ ..... 1/23, p. 148
..... 2/23, p. 260

Membership application of The Society for Connective Tissues, Czech Medical Association J.E. Purkynje, Prague, CZ ..... 1/23, p. 149
..... 2/23, p. 261

Membership application of The Orthopaedic and Prosthetic Society, Czech Medical Association J.E. Purkynje, Prague, CZ ..... 1/23, p. 149
..... 2/23, p. 261

In Memoriam

Mařík I.

Remembrance of Prof. Ing. Jan Čulík, DrSc. ..... 2/23, p. 262

INSTRUCTIONS FOR AUTHORS ..... 1/23, s. 153
..... 2/23, s. 268

CONTENTS OF VOLUME 2022 ..... 2/23, s. 273

CONTENTS OF VOLUME 2023 ..... 2/23, s. 279

OBSAH ROČNÍKU 2024

SLOVO ČTENÁŘŮM – EDITORIAL ..... 1/24, s. 11
..... 2/24, s. 121

OBRÁZEK NA TITULNÍ STRANĚ A POPIS

Píchová Renata

Scintigrafie skeletu pomocí techneciem značených fosfátových komplexů (osteotropní radioaktivní látka) ..... 1/24, s. 18
Scintigrafie skeletu pomocí techneciem značených fosfátových komplexů (osteotropní radioaktivní látka) ..... 2/24, s. 127

DOPIS EDITOROVI

Dudin Mihail

Adolescentní idiopatická skolióza (ESEJ) ..... 1/24, s. 22

Karski Tomasz, Karski Jacek

Ortopedická zkušenost s DMSO terapií (krátký popis) ..... 2/24, s. 131

Všetička Jan

Vlastní zkušenost s DMSO a co nám říká AI ..... 2/24, s. 133

PŘEHLEDOVÉ PRÁCE

Krulišová Veronika, Michalovská Renáta, Vlčková Zděnka, Mařík Ivo

Neurofibromatóza typu 1: komplexní multisystémové onemocnění z pohledu klinického genetika ..... 1/24, s. 41

Luňáčková Jitka, Tesař Karel

Hořčíkové vstřebatelné implantáty nejen pro fixaci kostí: možnosti a limitace ..... 1/24, s. 48

van Loon P.J.M., Soeterbroek A.M., Grotenhuis J.A. Smit T.H.

Zdravotní problémy způsobné hypokinezií, sezením a životem v digitálním světě dětí „přecivilizovaných společností. Nebo jak nám kulturní evoluce způsobila „idiopatickou“ skoliózu (Esej) ..... 2/24, s. 137

PŘEHLEDOVÉ PRÁCE A KAZUISTIKA

Mařík Ivo, Myslivec Radek, Krulišová Veronika, Maříková Alena, Hudáková Olga, Vážná Anna, Zemková Daniela

Komplexní léčba hypofosfatemické křivice. Kazuistika ..... 1/24, s. 61

PŮVODNÍ PRÁCE

KAZUISTIKY

Mařík Ivo, Píchová Renata, Tesner Pavel, Maříková Alena, Zemková Daniela

Genochondromatóza typu II: kazuistika mladé české ženy ..... 1/24, s. 86

Zwipp Hans

Calcaneogenese se sekundárním alograftem „Achilles tendon-bone" pro náhradu ztracené funkce. Kasuistika – výsledek po 12 letech ..... 2/24, s. 152

Krulišová Veronika, Zemková Daniela, Mařík Ivo, Paszeková Helena, Michalovská Renáta, Vlčková Zděnka

Nová sestřihová varianta genu *FGFR3* – kauzální varianta kostní dysplazie u dvou pacientů s překrývajícími se fenotypy achondroplazie a hypochondroplazie ..... 2/24, s. 167

Mařík Ivo, Zemková Daniela, Maříková Alena, Šumník Zdeněk, Souček Ondřej, Krulišová Veronika, Hudáková Olga

WNT1 osteogenesis imperfecta: Případová studie české dívky ..... 2/24, s. 194

ZPRÁVY

Zemková Daniela

Recenzní posudek na knižní novinku: Smrčka Václav, Musilová Zdeňka: Tisíc let nemocí a válek z kostnic Čech a Moravy, GRADA Publishing, a.s., 2024 ..... 1/24, s. 96

Krawczyk Petr

Subkatedra ortopedické protetiky a podiatrie na IPVZ..... 2/24, s. 223

Informace o Společnosti pro pojivové tkáně ČLS JEP ..... 1/24, s. 99
..... 2/24, s. 226

Přihláška řádného člena Společnosti pro pojivové tkáně ČLS JEP ..... 1/24, s. 100
..... 2/24, s. 227

Přihláška řádného člena Ortopedicko-protetické společnosti ČLS JEP ..... 1/24, s. 100
..... 2/24, s. 227

SMĚRNICE AUTORŮM ..... 1/24, s. 103
..... 2/24, s. 230

OBSAH ROČNÍKU 2023 ..... 2/24, s. 235

OBSAH ROČNÍKU 2024 ..... 2/24, s. 241

CONTENTS OF VOLUME 2024

A WORD TO READERS – EDITORIAL ..... 1/24, p. 15
..... 2/24, p. 124

TITLE PICTURE and DESCRIPTION

Píchová Renata

Scintigraphy Using Technetium-labeled Phosphate Complexes (Osteotropic Radiotracer) ..... 1/24, p. 17
Scintigraphy Using Technetium-labeled Phosphate Complexes (Osteotropic Radiotracer) ..... 2/24, p. 129

LETTER TO EDITOR

Dudin Mihail

Adolescent idiopathic scoliosis (ASSAY) ..... 1/24, s. 22

Karski Tomasz, Karski Jacek

Personal experience with DMSO and what AI tells us ..... 2/24, s. 131

Všetička Jan

Personal experience with DMSO and what AI tells us ..... 2/24, s. 133

REVIEW ARTICLES

Krulišová Veronika, Michalovská Renáta, Vlčková Zdeňka, Mařík Ivo

Neurofibromatosis type 1: A complex multi-system disorder from the perspective of a clinical geneticist ..... 1/24, p. 41

Luňáčková Jitka, Tesař Karel

Magnesium resorbable implants not only for bone fixation: possibilities and limitations ..... 1/24, p. 48

van Loon P.J.M., Soeterbroek A.M., Grotenhuis J.A. Smit T.H.

Health issues by hypokinesia, sitting and living in a digital world of children in "overcivilized" societies. Or how cultural evolution brought us „idiopathic" scoliosis (ASSAY) ..... 2/24, p. 137

ORIGINAL PAPERS AND CASE REPORT

Mařík Ivo, Myslivec Radek, Krulišová Veronika, Maříková Alena, Hudáková Olga, Vážná Anna, Zemková Daniela

Comprehensive treatment of hypophosphatemic rickets. Case report ..... 1/24, p. 61

ORIGINAL PAPERS

CASE REPORTS

Mařík Ivo, Píchová Renata, Tesner Pavel, Maříková Alena, Zemková Daniela

Genochondromatosis, type II: a case report of a Czech young woman ..... 1/24, p. 86

Zwipp Hans

Calcaneogenesis with secondary Achilles tendon-bone-allograft for repair of the loss of hindfoot function. A 12 years case report..... 1/24, p. 152

Krulišová Veronika, Zemková Daniela, Mařík Ivo, Paszeková Helena, Michalovská Renáta, Vlčková Zděnka

A novel splicing variant of *FGFR3* gene - a causal variant of bone dysplasia in two patients with overlapping phenotypes of achondroplasia and hypochondroplasia ..... 2/24, p. 167

Mařík Ivo, Zemková Daniela, Maříková Alena, Šumník Zdeněk, Souček Ondřej, Krulišová Veronika, Hudáková Olga

WNT1 osteogenesis imperfecta: Case study of a Czech girl ..... 2/24, p. 194

NEWS

Zemková Daniela

Review of the book: Smrčka Václav, Musilová Zdeňka: A thousand years of diseases and wars from the ossuaries of Bohemia and Moravia, GRADA Publishing, a.s., 2024 ..... 1/24, p. 96

Krawczyk Petr

Subdepartment of Orthopaedic Prosthetics and Podiatry at the Institute of Postgraduate Medical Education (IPME) ..... 2/24, p. 223

Information on the Society for Connective Tissues, Czech Medical Association J.E. Purkynje, Prague, CZ ..... 1/24, p. 101
..... 2/24, p. 228

Membership application of The Society for Connective Tissues,
Czech Medical Association J.E. Purkynje, Prague, CZ ..... 1/24, p. 102
..... 2/24, p. 229

Membership application of The Orthopaedic and Prosthetic Society,
Czech Medical Association J.E. Purkynje, Prague, CZ ..... 1/24, p. 102
..... 2/24, p. 229

INSTRUCTIONS FOR AUTHORS ..... 1/24, s. 106
..... 2/24, s. 233

CONTENTS OF VOLUME 2023 ..... 2/24, s. 238

CONTENTS OF VOLUME 2024 ..... 2/24, s. 244



Právní služby poskytovatelům zdravotních služeb:

- obchodní právo - založení společnosti, transformace soukromé ordinace na společnost, registrace poskytovatele zdravotních služeb,
- konzultace v oblasti medicínského práva – školení personálu ve věcech vedení a nakládání se zdravotnickou dokumentací, informovaný souhlas pacienta,
- smluvní agenda – nájemní smlouvy, kupní a úvěrové smlouvy, smlouvy o službách,
- smlouvy se zdravotními pojišťovnami – úprava smluvních dokumentů, korekce plateb,
- otázky náhrady škody na zdraví a z titulu zásahu do osobnostních práv – konzultace vznesených nároků, jednání s pacienty, zastupování v soudním řízení,
- a všechny další otázky, s nimiž se poskytovatelé zdravotních služeb v praxi setkávají

V případě zájmu o nezávaznou konzultaci a poskytnutí bližších informací nás neváhejte kontaktovat.

SVOBODA & KUČERA | ADVOKÁTI

AK Kučera s.r.o. | Stavitelská 1099/6, 160 00 Praha 6 | T +420 222 965 861 | M +420 731 510 675 | E kucera@sk-advokati.cz | W www.sk-advokati.cz

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Ostrava | U Parku 2/2720 | 702 00 Ostrava | tel.: 596 139 259, 596 139 295

Provozovna Olomouc | Mošnerová 7/1184 | 779 00 Olomouc | tel.: 585 414 776, 585 414 823

Provozovna Brno | Milady Horákové 50 | 602 00 Brno | tel. 733 184 083

E | ostrava@proteorcz.cz | olomouc@proteorcz.cz | brno@proteorcz.cz | **www.proteorcz.cz**

lékařská péče v oborech ortopedie a ortopedická protetika ● zdravotní péče v ortotice a protetice ● konsilia pro zdravotnická zařízení ● výjezdová pracoviště v kraji ● zakázková činnost pro zdravotnická zařízení ● skoliotická poradna pro léčbu skolióz páteře mladistvých ● aplikace a výroba individuálních ortopedických vložek pro sport ● výroba individuálních zdravotnických prostředků – protéz končetin, ortéz, ortopedických vložek ● podologická poradna pro pacienty s problémy nohou (syndrom diabetické nohy, bolesti nohou) ● specializované centrum pro aplikaci a výrobu myoelektrických protéz horních končetin