WORLD CONGRESS

on Debates & Consensus

in Bone, Muscle & Joint Diseases

CONGRESS PROGRAM

BMJD

World Congress

on Debates & Consensus

Barcelona, Spain

19-22/1/2012

www.congressmed.com/bmjd

TIMETABLE

Thursday, January 19, 2012

18:00-19:30	**OPENING SESSION**
19:30-20:30	Welcome reception - Cocktail

Friday, January 20, 2012

	Hall A	Hall B	Hall C Oral Presentations
08:30-10:00	BONE METASTASIS	WHAT IS THE FUTURE OF PTH AND PTHrp?	MUSCLES/OSTEOARTHRITIS
10:00–10:20	Coffee break		
10:20-11:50	SEX STEROIDS AND BONE HEALTH	DO JOINT BLEEDS LEAD TO JOINT DESTRUCTION IN HEMOPHILIA? *Supported by an unrestricted grant from **Baxter International Inc.***	OSTEOARTHRITIS
11:50-12:10	Poster viewing		
12:10-13:40	LATE POST-MENOPAUSAL OSTEOPOROSIS (OP) *Supported by an unrestricted grant from **Pfizer***	GLUCOSAMINE FOR OSTEOARTHRITIS (OA) *Supported by an unrestricted grant from **Rottapharm/Madaus***	OSTEOPOROSIS
13:40-14:30	Lunch break		
14:30-16:00	SYMPTOM AND STRUCTURE MODIFICATION IN OSTEOARTHRITIS WITH PHARMACEUTICAL-GRADE CHONDROITIN SULFATE: WHAT'S THE EVIDENCE? *Supported by an unrestricted grant from **IBSA Institut Biochimique SA & BIOIBERICA, S.A.***	NEW PLAYERS AND NEW INDICATIONS FOR EXISTING DRUGS *Supported in part by an unrestricted grant from **MSD***	JOINT BIOLOGY
16:00-16:30	Coffee break		
16:30-18:00	EARLY POST-MENOPAUSAL OSTEOPOROSIS (OP)	PREVENTION AND TREATMENT OF OSTEOARTHRITIS (OA)	OSTEOARTHRITIS

Saturday, January 21, 2012

08:30-10:00	CONTROLLING PAIN IN MUSCULOSKELETAL DISEASES	Go to Hall A	OSTEOPOROSIS
10:00–10:20	Coffee break		
10:20-11:50	FRAILTY SYNDROME: THE NEW TARGET POPULATION WHEN LOOKING AT THE BASKET OF BENEFITS OF SELECTED TREATMENT OPTIONS	MONITORING PROGRESSION OR REMISSION – IMPLEMENTATION OF BIOMARKERS	OSTEOARTHRITIS
	SARCOPENIA: THE EFFECT OF MUSCLE ON HEALTHY AGING AND THE QUALITY OF DISEASE		
11:50-12:10	Poster viewing		
12:10-13:40	GLUCOCORTICOIDS AND SMALL MOLECULES FOR THE MANAGEMENT OF RHEUMATOID ARTHRITIS (RA)	METABOLIC SYNDROME AND OSTEOARTHRITIS (OA)	TRANSLATIONAL SCIENCE/ OSTEOARTHRITIS
	CHOOSING THE RIGHT TREATMENT FOR PATIENTS WITH RHEUMATOID ARTHRITIS (RA)		
13:40-14:30	Lunch break		
14:30-16:00	DOES INFLAMMATION CAUSE SYNDESMOPHYTE FORMATION IN ANKYLOSING SPONDYLITIS	MUSCLE PERFORMANCE IN THE PHYSIOPATHOLOGY OF OSTEOARTHRITIS (OA)	RHEUMATOID ARTHRITIS
16:00-16:30	Coffee break		
16:30-18:00	LATE BREAKING NEWS AND HOT TOPICS	Go to Hall A	OSTEOARTHRITIS

Sunday, January 22, 2012

08:30-10:00	BONE BEYOND OSTEOPOROSIS *Organized by the **PORTUGUESE SOCIETY OF OSTEOPOROSIS AND BONE METABOLIC DISEASES (SPODOM)***	*Session Organized by the **JAPANESE OSTEOPOROSIS FOUNDATION/ JAPANESE OSTEOPOROSIS SOCIETY (JOF/ JOS)***
10:00-10:20	Coffee break	
10:20-12:20	BIOTHERAPY IN OA TREATMENT: DREAM OR REALITY?	Go to Hall A
	FOOD SUPPLEMENTATION- ARE THEY OF ANY VALUE?	

WORLD CONGRESS

on Debates & Consensus

in Bone, Muscle & Joint Diseases

CONGRESS PROGRAM

BMJD

World Congress

on Debates & Consensus

GLUCOSAMINE SULFATE

the original in the world

DETAILS MAKE THE DIFFERENCE

DONA®

XICIL®

OSAFLEXAN

viartril®-S

Donacom®

ДОНА

Glucoreumin®

dona

DONA™ The original

GLUSARTEL™

Arthryl®

维固力®

στην οστεοαρθρίτιδα

Donarot™ θεική Γλυκοζαμίνη

ROTTAPHARM | MADAUS

TABLE OF CONTENTS

Welcome Letter

Dear Friends and Colleagues,

It is our honor and pleasure to welcome you to the **World Congress on Debates and Consensus in Bone, Muscle and Joint Diseases (BMJD)** in **Barcelona, Spain.**
Over the years, the field of Bone, Muscle & Joint Diseases has undergone enormous expansion in clinical and basic data, as well as that of field-related technology. With the problem of bone, muscle & joint diseases reaching epidemiological dimensions, treatment possibilities have digressed diversely. This development has created a need for debates on the numerous controversial issues.

The intention of the BMJD Congress is to function as an exclusive forum for international experts to share and compare experiences, in order to outline appropriate treatment.

Ample time will be provided for discussion, and participants will have the advantage of conversing and debating unresolved issues with world authorities in their fields. The Congress aims at reaching the ultimate state-of-the-art solutions, and providing clinicians with conclusive commendations and reliable solutions, all based on current paramount significance.

We look forward to your participation in the 1st World Congress on Debates and Consensus in Bone, Muscle and Joint Diseases (BMJD), which is intended as the first of many future congresses in this field.

The contribution of our sponsors with generous educational grants is very much appreciated

Sincerely,

Prof. Yves Henrotin, Prof. Santiago Palacios
Congress Co-Chairpersons

On behalf of the Organizing Commitee

COMMITTEES

Co-Chairmen

Santiago Palacios

Yves Henrotin

Secretary

Zion Ben-Rafael

International Scientific Committee

Carlina V. Albanese, *Italy*
A. Nasser Alothman, *Kuwait*
M. Anapliotou, *Greece*
Roberto Arinoviche, *Chile*
O. Sahap Atik, *Turkey*
Rafic Baddoura, *Lebanon*
Janusz E. Badurski, *Poland*
Ana Paula Barbosa, *Portugal*
Eduardo Barreira Mercado, *Mexico*
J.W. Bijlsma, *Netherlands*
Horatiu D. Bolosiu, *Romania*
Claudia Campusano, *Chile*
Juliet E. Compston, *UK*
Gaetano Crepaldi, *Italy*
Edward Czerwinski, *Poland*
Tobie de Villiers, *South Africa*
A.B. Dey, *India*
Richard Eastell, *UK*
Samir Elbadawy, *Egypt*
Marco Gambacciani, *Italy*
Andrea Gasparik, *Romania*
Andrea Genazzani, *Italy*
Daniel Grigorie, *Romania*
Bjorn Gudbjornsson, *Iceland*
Peyman Hadji, *Germany*
Alberto Hernandez-Bueno, *Mexico*
Marc C. Hochberg, *USA*
Bari Kaplan, *Israel*
Andreas Kindmark, *Sweden*
Klaus Klaushofer, *Austria*
Khunying Kobchitt Limpaphayom, *Thailand*
Zlatimir Kolarov, *Bulgaria*
Zhonghou Liu, *China*
Roman S. Lorence, *Poland*
Ghassan Maalouf, *Lebanon*
Snezana Markovic Temelkova, *Macedonia*
Carmen Menéndez, *Spain*
Helmut W. Minne, *Germany*
Ambrish Mithal, *India*
Fidencio Cons Molina, *Mexico*
Antonio Moroni, *Italy*
J.C. Netelenbos, *Netherlands*
Moira O'Brien, *Ireland*
Hajime Orimo, *Japan*
Vladmir Palicka, *Czech Republic*
Andreas Patsalides, *Cyprus*
Juraj Payer, *Slovakia*
Serge Rozenberg, *Belgium*
Daniel Salica, *Argentina*
Philip Sambrook, *Australia*
Juan José Scali, *Argentina*
Luis Fernando Somma, *Argentina*
Juan Tamayo y Orozco, *Mexico*
Alan Tyndall, *Switzerland*
Toshiyuki Yoneda, *Japan*

Local Organizing Committee

Santiago Palacios, *Barcelona*
Antonio Cano, *Valencia*
Camil Castelo-Branco, *Barcelona*
Javier del Pino Montes, *Salamanca*
Manuel Diaz Curiel, *Madrid*
Adolfo Diez-Perez, *Barcelona*
Jesus Gonzalez Macias, *Santander*
Esteban Jodar Gimeno, *Madrid*
Manuel Sosa Henriquez, *Las Palmas de Gran Canaria*

Life. Health. Care.

At Baxter, we focus on saving and improving the quality of patients' lives.

Building on our 80 year history of medical firsts, we innovate every day to bring the next generation of therapies, technologies and service to patients and healthcare professionals around the world. Whether in hospitals, clinics or at home, we are there where you need us with our unique combination of expertise in medical devices, pharmaceuticals and biotechnology.

Baxter Healthcare SA
Postfach, 8010 Zürich
+41 (0) 44 878 60 00 +41 (0) 44 878 63 50
www.baxter.com

Baxter

SPONSORS

Gold

ROTTAPHARM | MADAUS

MSD

Pfizer

IBSA

BIOIBERICA

Silver

Supported by AMGEN®

in collaboration with

gsk GlaxoSmithKline

Baxter

Bronze

HOLOGIC™
The Women's Health Company

Lilly

SPONSORS

The Organizing Committee gratefully acknowledges the generous support of the sponsors

Gold

MSD
Today's MSD is a global healthcare leader working to help the world be well. MSD is a tradename of Merck & Co., Inc., with headquarters in Whitehouse Station, N.J., U.S.A. Through our prescription medicines, vaccines, biologic therapies, and consumer care and animal health products, we work with customers and operate in more than 140 countries to deliver innovative health solutions. We also demonstrate our commitment to increasing access to healthcare through far-reaching policies, programs and partnerships. For more information, visit www.msd.com.

Rottapharm I Madaus
Via Valosa di Sopra 9 , 20900 Monza (MB) – Italy
Tel: +39.039.73.90.1
Fax: +39.039.70.90.372
info@rotta.com
www.rotta.com

RottapharmIMadaus has been involved for years in the development of drugs for rheumatic diseases. Important synergies have been achieved in R&D and marketing activities, with leading products such as Dona (glucosamine sulfate - shown to be the first disease-modifying agent in osteoarthritis), Reparil (aescin - analgesic, antiphlogistic) and Go On (hyaluronic acid, visco-supplementation for sinovial joints in osteoarthritis). New developments in the same area will further strengthen the company's relationship with rheumatologists and orthopaedists over the next few years.

IBSA Institut Biochimique SA
Via del Piano 29, P.O. Box 266, 6915 Pambio-Noranco, Lugano, Switzerland
Tel: +41 58 360 10 00
Fax: +41 58 360 16 77
General Email Address: info@ibsa.ch
Web Address: www.ibsa-international.com

IBSA is an international pharmaceutical company based in Lugano, Switzerland, delivering specific and tailored pharmacological solutions in different therapeutic areas.
As a leading company in the field of osteoarthritis and pain/inflammation management, IBSA's portfolio includes a full range of presentations of oral highly purified chondroitin sulphate (Condrosulf®, Chondrosulf®, Condral®), an intra-articular hyaluronic acid (Sinovial®, Yaral®, Intragel®) and an innovative, patented epolamine salt of diclofenac (Flector® EP Tissugel, Flector® Patch).

BIOIBÉRICA, S.A.
Pza. Francesc Macià 7, 08029 Barcelona, Spain
Tel: + 34 93 490 49 08
Fax: +34 490 97 11
www.bioiberica.com

BIOIBERICA is a research-based pharmaceutical company specialized in osteoarthritis (OA) and chondroprotection. Based on a holistic approach of the disease, it has a full range of chondroprotective drugs such as Condrosan® / Cartexan® (Chondroitin Sulfate) and Cartisorb® (Glucosamine Sulfate). Recently, BIOIBERICA's product portfolio has been complemented with Droglican®, the first combination of chondroitin and glucosamine approved as an ethical reimbursed drug Product, which is currently marketed in Spain. BIOIBERICA is also positioned within the OA Personalized Medicine field, currently focused on R&D of genetic tests, biomarkers, tissue engineering and cell therapy.

Silver

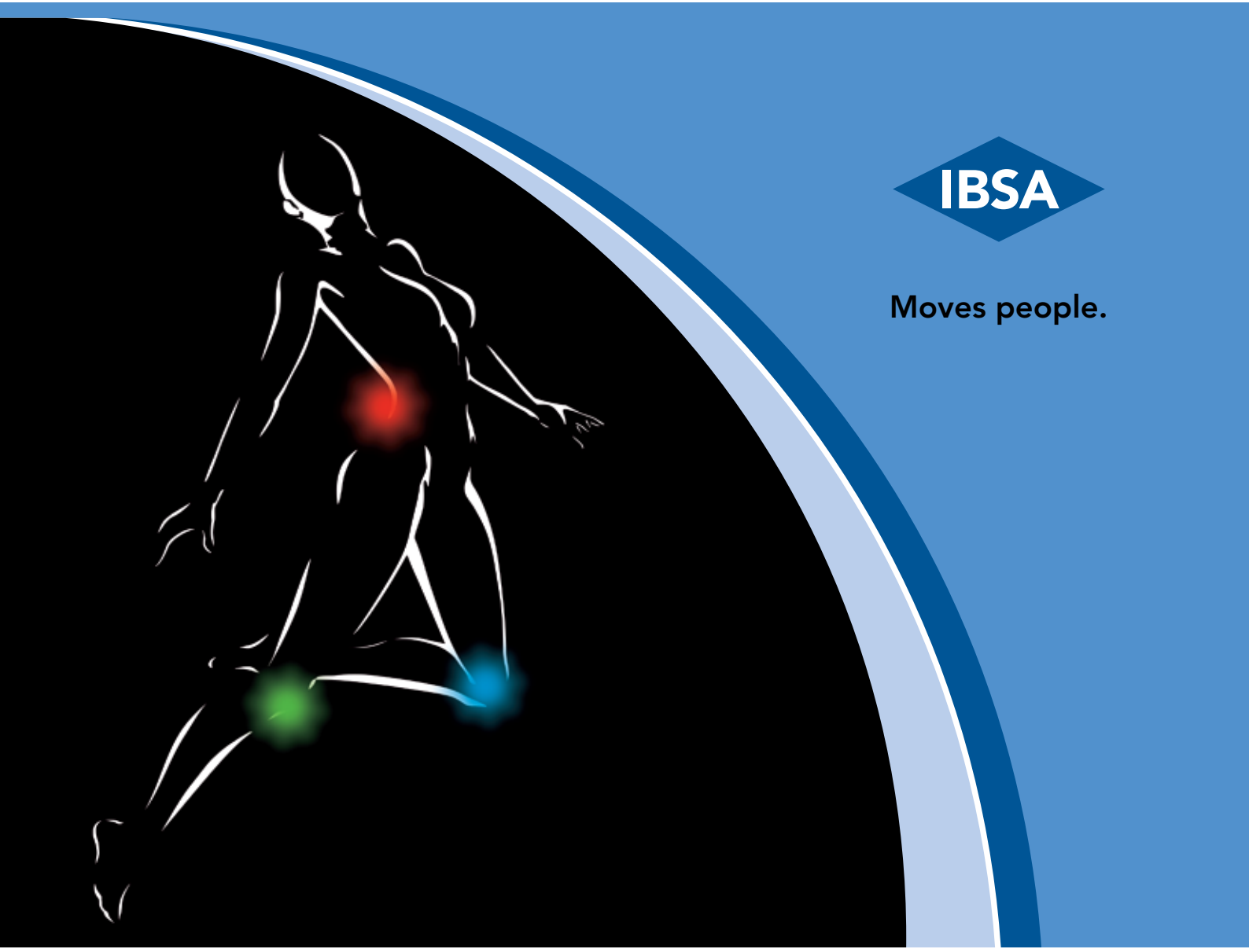
Baxter International Inc.
Baxter International Inc., through its subsidiaries, develops, manufactures and markets products that save and sustain the lives of people with hemophilia, immune disorders, infectious diseases, kidney disease, trauma, and other chronic and acute medical conditions. As a global, diversified healthcare company, Baxter applies a unique combination of expertise in medical devices, pharmaceuticals and biotechnology to create products that advance patient care worldwide.

Pfizer Inc.: Working together for a healthier world™
At Pfizer we strive to set the standard for quality, safety and value in the discovery, development and manufacturing of medicines for people and animals. Our health care portfolio includes human and animal biologic and small molecule medicines and vaccines, as well as nutritional products and many consumer products. Pfizer colleagues advance wellness, prevention, treatments and cures that challenge the most feared diseases. Consistent with our responsibility as the world's leading biopharmaceutical company, we collaborate with health care providers, governments and local communities to support and expand access to reliable and affordable health care.

Exhibitors

Wisepress Medical Bookshop
25 High Path, Merton Abbey
London, SW19 2JL, UK
Contact: Michelle Coogan, Bookshop Manager
Phone: +44 20 8715 1812
Fax: +44 20 8715 1722
bookshop@wisepress.com
www.wisepress.com

Wisepress.com, Europe's leading conference bookseller, has a complete range of books and journals relevant to the themes of the meeting. Books can be purchased at the stand or, if you would rather not carry them, posted to you – Wisepress will deliver worldwide. In addition to attending 200 conferences per year, Wisepress has a comprehensive medical and scientific bookshop online with great offers.



IBSA

Moves people.

www.ibsa-international.com

Our products in OA & Inflammation

Diclofenac epolamine

(Flector EP Tissugel®, Flector® patch, Dicloplast®, Dicloreum® Tissugel)

For a controlled delivery in the topical treatment of inflammatory pain (OA, strains, sprains, contusions)

Chondroitin 4&6 sulfate

(Chondrosulf®, Condrosulf®, Condral®)

For an algo-functional and structure modifying effect in OA

Hyaluronic acid

(Sinovial®, Yaral®, Intragel®)

For an effective and well tolerated intra-articular viscosupplementation

GENERAL INFORMATION

Congress Venue
Centre Convencions International Barcelona (CCIB)
Rambla Prim 1
17 08019 Barcelona

Language
English is the official language of the Congress

Registration Desk
The registration desk at the CCIB will operate during the following hours:

Thursday, January 19	15:00-20:00
Friday, January 20	07:30-18:00
Saturday, January 21	08:00-18:00
Sunday, January 22	08:00-12:30

Congress Kit and Nametag
The congress kit you have received contains your nametag. Please wear your nametag to all sessions and events.

Certificate of Attendance
The Certificate of Attendance has been inserted in your registration kit. If you wish to make changes please apply to the Registration Desk.

Refreshments
Coffee will be served in the exhibition area during the coffee breaks. Lunch will be available for participants of the Congress on Friday, January 20 and Saturday, January 21. Entrance will be with nametags.

Exhibition Opening Hours

Friday, January 20	08:30-18:00
Saturday, January 21	08:30-18:00
Sunday, January 22	08:30-12:30

Speakers' Preview Room
Speakers are invited to visit the Speakers' Preview Room to upload their presentations at the following times:

Thursday, January 19	15:00 to 19:00
Friday, January 20	07:30 to 18:00
Saturday, January 21	08:00 to 18:00
Sunday, January 22	08:00 to 10:30

Posters Display
The posters will be displayed at the Exhibition Area.

Posters should be mounted from 07:30 on Friday, January 20 and removed by the end of the sessions on Saturday January 21.

The dedicated poster viewing times are on Friday, January 20 and Saturday January 21 from 11:50-12:10.

Poster Presenters should plan to be next to their poster board during these times and during coffee breaks.

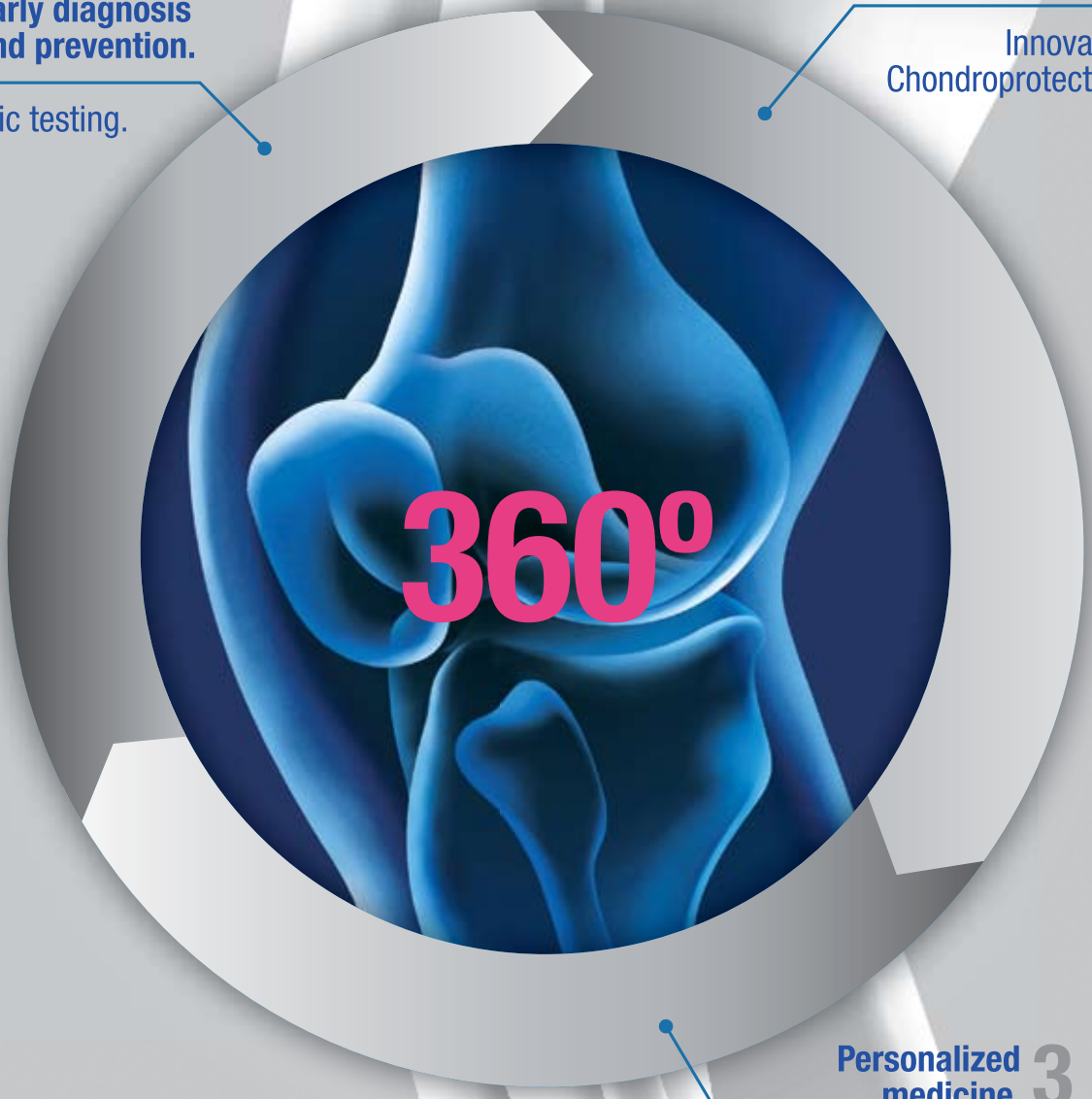
Dismantling of posters is the responsibility of the presenter. The Organizing Committee is not responsible for posters that are not removed on time.

Safety and Security
Please do not leave any bags or suitcases unattended at any time, whether inside or outside session halls.

Liability
The Congress Secretariat and Organizers cannot accept liability for personal accidents or loss or damage to private property of participants either during or directly arising from The World Congress on Controversies in Obstetrics, Gynecology and Infertility. Participants should make their own arrangements with respect to health and travel insurance.

A UNIQUE HOLISTIC APPROACH TO OSTEOARTHRITIS

Bioibérica is the only company researching, developing and providing a wide range of therapeutic solutions for Osteoarthritis. From a 360º, integrated and holistic perspective.



1 Early diagnosis and prevention.

Genetic testing.

Pharmacological treatment. 2

Innovative Chondroprotectors.

Personalized medicine. 3

Pharmacogenomics and cell therapy.

BIOIBERICA

Bioibérica S.A. Pza Francesc Macià 7, 08029, Barcelona, SPAIN
www.bioibérica.com / +34 93 490 49 08

CME ACCREDITATION

SeronoSymposia International Foundation SSIF (http://www.seronosymposia.org) has submitted the main congress program of the "**World Congress on Debates and Consensus in Bone, Muscle and Joint Diseases (BMJD)" (Barcelona, Spain, January 19-22, 2012)** for accreditation by the European Accreditation Council for Continuing Medical Education (EACCME).

The **"World Congress on Debates and Consensus in Bone, Muscle and Joint Diseases (BMJD)" (Barcelona, Spain, January 19-22, 2012)** is designated for a maximum of

15 (fifteen) hours

of European external CME credits. Each medical specialist should claim only those credits that he/she actually spent in the educational activity. EACCME credits are recognized by the American Medical Association towards the Physician's Recognition Award (PRA). To convert EACCME credit to AMA PRA category 1 credit, please contact the AMA

Italian Accreditation

SSIF has submitted, in compliance with the procedures indicated by the Italian Ministry of Health, the main congress program of this event entitled *"World Congress on Debates and Consensus in Bone, Muscle and Joint Diseases (BMJD)" (Barcelona, Spain, January 19-22, 2012)*

The CME accreditation is valid for the main congress program only and does not cover the company-sponsored symposia.

ISO 9001 Certification:

Serono Symposia International Foundation has received the ISO 9001 Certification of Quality Management Systems. This Quality certification requires all participants to fill in a scientific questionnaire and to evaluate the overall quality of the event. Questionnaires will be distributed onsite during the congress.

ACCOMPANYING PERSON'S PROGRAM

The accompanying person's program includes the following:

Thursday, January 19, 2012

Welcome Reception - Cocktail

All registered accompanying persons are invited to the Welcome Reception at 19:30 in the Centre Convencions International Barcelona (CCIB)

Friday, January 20, 2012

Half Day Tour

All registered accompanying persons are invited to join the half day bus tour from 10:00-14:00. The tour will include the following attractions:

- *Basílica de la Sagrada Família*
- *La Pedrera - a building designed by Antoni Gaudí*
- *Diagonal & Pg. Gracia - The modernist facades*
- *Casa Batlló - the modernist building designed by Antoni Gaudí*
- *The Gothic Quarter - the center of the old city*
- *The Cathedral of Barcelona - The Cathedral of the Holy Cross and Saint Eulalia*

Pick-up at the CCIB at 10:00am

Saturday, January 21, 2012

Lunch

All registered accompanying persons are invited to join the Congress lunch at 13:40-14:30 at the CCIB

****Please wear your nametag to all occasions.**

WORLD CONGRESS

on Debates & Consensus

in Bone, Muscle & Joint Diseases

SCIENTIFIC PROGRAM

BMJD

World Congress

on Debates & Consensus

Thursday, January 19, 2012

18:00-19:30 **OPENING SESSION**
Keynote Lecture

Chairpersons **Y. Henrotin**, Belgium
S. Palacios, Spain

Inhibition of sclerostin in the treatment of osteoporosis: Will it solve the problem of anabolic therapy?
S. Papapoulos, Netherlands

19:30-20:30 **Welcome Reception Cocktail**

Friday, January 20, 2012

08:30-10:00 BONE METASTASIS — Hall A

Capsule *Bone metastasis is a common problem with poor specific treatments. However, can symptoms be alleviated to provide a better quality of life?*

Chairpersons **R.T. Chlebowski**, USA
E. Jódar Gimeno, Spain

08:30-09:00 Can bisphosphonates act as anti-cancer drugs?
R.E. Coleman, UK

09:00-09:30 Treatment induced bone loss in women with breast cancer
P. Hadji, Germany

09:30-10:00 Selected presentations

Changes in markers of bone resorption and impact on bone mineral density over the first 6 months after pediatric hematopoietic cell transplantation
A. Petryk, USA

Pharmacological characterization of the potent, selective and orally active Cathepsin K inhibitor MIV-711
U. Grabowska, UK

08:30-10:00 WHAT IS THE FUTURE OF PTH AND PTHrp? — Hall B

Capsule *Bone turnover is mediated by many systemic hormones regulating the calcium balance. PTH is well known to be a catabolic hormone recruiting calcium from bone, even when successfully administered as an anabolic treatment*

Chairpersons **C.M. Kessler**, USA
A.R. Genazzani, Italy
J.B. Cannata-Andia, Spain

08:30-09:30 **Do we really understand the PTH mode of action? Is there any difference between PTH and PTHrp? How may we understand the failure of some calcilytics (calcium receptor antagonists) programs?**

We do understand the PTH mode of action
A. Maeda, Japan/USA

There is a difference between PTH and PTHrp
P. Esbrit, Spain

Discussion

09:30-10:00 Selected presentations

Inverse relationship between 25-hydroxy vitamin D and parathyroid hormone observed in the general population, but not among rheumatoid arthritis patients
A. Broder, A. Skversky, M. Melamed, J.N. Tobin, C. Putterman, USA

Diagnostic criteria for the patients with primary hyperparathyroidism
I. Boulytcheva, Russian Federation

Objectives

Upon completion of this session, the audience will have learned of:
- *The differences in small molecule stimulators of endogenous PTH*
- *The failure of some calcium mimetic programs*
- *The rationale for different PTH programs*
- *The failure of some calcilytics (calcium receptor antagonists) programs*

10:00-10:20 **Coffee break**

10:20-11:50 SEX STEROIDS AND BONE HEALTH — Hall A

Capsule

Studies indicate that a critical age window for treatment with HT might exist. Starting treatment early might prevent CVD and OP. On the other hand, there is the WHO statement that estrogens might be carcinogenic. Do the benefits outweigh the risks?

Chairpersons

J.B. Cannata-Andia, Spain
S. Palacios, Spain

10:20-11:20

Debate: Estrogen and estrogen-like molecules: Do the benefits outweigh the risks?
Yes: **R. Farmer**, UK
No: **R.T. Chlebowski**, USA
Discussion

11:20-11:50

Sex steroids and bone health
A.R. Genazzani, Italy

Objectives

Upon completion of this session, the audience will have found answers to the following questions:
- *What did we learn from the WHO study?*
- *Are all selective estrogen receptor modulators (SERM's) the same?*
- *The estrogen window hypothesis*
- *What is the metabolic representation of a candidate for estrogen-like intervention? Is there an optimal patient?*
- *Effect of sex steroids on bone health*

10:20-11:50 DO JOINT BLEEDS LEAD TO JOINT DESTRUCTION IN HEMOPHILIA? — Hall B

*Supported by an unrestricted grant from **Baxter International Inc.***

Capsule

A range of processes lead to joint damage, loss of joint function and eventually joint replacement. Some of the pathophysiological processes bear similarities in RA and hemophilic patients. Does this allow for a better understanding of thesediseases?

Chairpersons

L. Yamamoto, USA
P.E. Monahan, USA

10:20-10:50

A focused approach for a broader understanding: Joint health in hemophilia patients
L. Yamamoto, USA

10:50-11:20

A clinical overview of hemophilia joint disease
C.M. Kessler, USA

11:20-11:50

Pre-clinical modeling of joint bleeding, inflammation and wound healing in hemophilia mice
P.E. Monahan, USA

Objective

Upon completion of this session, the audience will understand the similarities and differences between hemophilic joint damage and RA

11:50-12:10 **Poster viewing**

12:10-13:40 LATE POST MENOPAUSAL OSTEOPOROSIS (OP) — Hall A

*Supported by an unrestricted grant from **Pfizer, S.A.***

Capsule

The usual patients with low bone mineral density and fracture risk that are seen by gynecologists are often younger than 70 years, while research on drugs is undertaken on women over this age

Chairpersons

Z. Ben-Rafael, Israel
R. Sánchez Borrego, Spain
A.P. Barbosa, Portugal

Friday, January 20, 2012

12:10-13:10 **Debate: Should we treat women with low bone mineral density who are younger than 70 years, and how?**
Proposition: Evidence for the effectiveness of drugs at this age is lacking and treatment is not cost-effective
R.T. Chlebowski, USA
Opposition: There is enough experience to manage these patients, but therapy should be individualized
P. Hadji, Germany
Discussion

13:10-13:40 Recommendations on the management of fragility risk fracture women that are younger than 70 Years
S. Palacios, Spain

Objectives
To acquire knowledge of the following:
- *Risk factors and prevalence of osteoporotic fractures in women over 70 years*
- *FRAX index in this age group, DEXA indication*
- *Older and newer therapies to prevent fracture*

12:10-13:40 GLUCOSAMINE FOR OSTEOARTHRITIS (OA) — Hall B

*Supported by an unrestricted grant from **Rottapharm I Madaus***

Capsule
Every new study tends to fuel the controversy again. Are glucosamines better than placebos for osteoarthritis? Is the source important? Does it decrease NSAIDs consumption and delay prothesis surgery?

Chairperson **Y. Henrotin**, Belgium

12:10-13:10 **Debate: Does glucosamine play any role in OA?**
Yes: **M.C. Hochberg**, USA
No: **R.D. Altman**, USA
Discussion

13:10-13:40 Selected presentations

Obesity and outcome of lower limb arthroplasty patients enrolled in an enhanced recovery programme: A 1000 patient study
P. Buddhdev, N. Davies, T. Waters, UK

Early OA cohort of hip and knee: The check study
J. Wesseling, J. Bijlsma, Netherlands

How widespread are outcomes measures and instruments for osteoarthritis and how valid are they?
B. Hanson, M. Suk, D. Helfet, **D. De Faoite**, Switzerland/USA

Objectives
Upon completion of this session, the audience will have learned of:
- *Conflicting results of the new studies*
- *The source of different glucosamines*
- *Joints that are more positively affected*

13:40-14:30 Lunch break

14:30-16:00 SYMPTOM AND STRUCTURE MODIFICATION IN OSTEOARTHRITIS WITH PHARMACEUTICAL - GRADE CHONDROITIN SULFATE: WHAT'S THE EVIDENCE? — Hall A

*Supported by an unrestricted grant from **IBSA Institut Biochimique SA** and **BIOIBERICA, S.A.***

Capsule
Pharmaceutical-grade chondroitin sulfate (CS) belongs to the groups of drugs with a symptomatic effect on OA (the so-called SySADOA effect), with evidence also of a protective role on knee cartilage (SMOAD effect). How effective is CS on the other joint tissues (e.g. synovial membrane, subchondral bone)? How important is the purity and the quality of CS? Can the prescription of CS have a beneficial effect on NSAID intake?

Chairpersons **Y. Henrotin**, Belgium
M.C. Hochberg, USA

14:30-14:35 Introduction
Y. Henrotin, Belgium

14:35-14:50 Osteoarthritis: A disease of the whole joint
D. Hunter, Australia

14:50-15:05 Mechanisms of action of chondroitin sulfate in the 3 main joint tissues
X. Chevalier, France

15:05-15:20 Chondroitin sulfate: Review of therapeutic efficacy
D. Uebelhart, Switzerland

15:20-15:35 Structure disease modification in osteoarthritis: Evidence from chondroitin sulfate
M.C. Hochberg, USA

15:35-15:50 Interactive debate with the audience

15:50-16:00 Concluding remarks
Y. Henrotin, Belgium
M.C. Hochberg, USA

Objectives ***To acquire knowledge of the following:***
- *Pathophysiology of OA*
- *Mechanism of action efficacy and side effects of Chondroitin sulfate*

14:30-16:00 NEW PLAYERS AND NEW INDICATIONS FOR EXISTING DRUGS — Hall B

*Supported in part by an unrestricted grant from **MSD***

Capsule *With the similarities in the inflammatory components of joint degenerative diseases - RA and OA - the question is: Does an intervention for RA fit the appropriate selected OA population? Will some treatments have additional benefits to muscles?*

Chairpersons **S.B. Abramson**, USA
J.W. Bijlsma, Netherlands

14:30-15:00 Odanacatib: An emerging osteoporosis therapy
B.L. Langdahl, Denmark

15:00-15:30 Can an effective treatment for OP or RA also be effective in a selected patient population with OA?
B.L. Langdahl, Denmark

15:30-16:00 Round Table Discussion

Discussants
B.L. Langdahl, Denmark
C.M. Kessler, USA

Tricks of the trade: Clashing views or consensus? What type of effect can we expect from the use of the following treatments in other fields?

Osteoporosis Drugs
- SERM's
- Estrogen
- Bisphosphonates
- Cathepsin K
- Calcitonin

Rheumatoid Arthritis Drugs
- Anti-TNF-alpha
- Anti-IL-1

16:00-16:30 Coffee break

16:30-18:00 EARLY POST MENOPAUSAL OSTEOPOROSIS (OP) — Hall A

Capsule *With a plethora of anti-osteoporosis, anti-catabolic and anabolic treatments, the questions are as follows: Do all patients need to be treated in a similar manner? What influences the different responses? Do biomarkers of bone turnover identify low/high bone turnover patients, and do they benefit equally from the same intervention? Does a short treatment have a long lasting effect?*

Chairperson **S. Papapoulos**, Netherlands

16:30-17:30 **Keynote Lecture**
Evidence based intervention strategy for postmenopausal OP
J. Calaf-Alsina, Spain

Friday, January 20, 2012

17:30-18:00 Selected presentations

The influence of concomitant administration of prednisolone with alendronate on the incidence of osteonecrosis of the jaws: Observations from a case controlled study from the southeast of Scotland
N. Malden, V. Lopes, UK

2 year treatment effects of the Cathepsin K inhibitor and ONO-5334 on BMD as measured by 3D QCT in the hip and the spine
K. Engelke, S. Nagase, T. Fuerst, M. Small, T. Kuwayama, S. Deacon, R. Eastell, **H.K. Genant**, USA/Germany/UK

Objectives

Upon completion of this session, the audience will have learned:
- *What role do biomarkers play in patient selection of the optimal intervention?*
- *What are the risk factors for osteoporosis?*
- *What are the cost/benefit scenarios and quality of life?*
- *Does the same treatment fit all?*
- *Is there an optimal intervention option for a given patient?*

16:30-18:00 PREVENTION AND TREATMENT OF OSTEOARTHRITIS (OA) — Hall B

Capsule

OA is a disease of the whole joint, including bone, cartilage, muscles and synovial inflammation. With so many structures affected, can one agent be efficacious for the treatment of this multi-factorial disease? Furthermore, with so many different etiologies, all leading to joint failure, does one size fit all?

Chairpersons

D. Hunter, Australia
B.L. Langdahl, Denmark

16:30-17:30

Debate: Do we have an effective mode of treatment or prevention of OA?
No: **R.D. Altman**, USA
Yes: **M.C. Hochberg**, USA
Discussion

17:30-18:00 Round Table Discussion

Discussants
M.C. Hochberg, USA
R.D. Altman, USA

Experts' opinion on:
1. The place of MRI in the treatment scheme
2. Inflammation: An initiator or a driving force of the disease?

Objectives

Upon completion of this session, the audience will have learned:
- *The initiation and progression of OA*
- *Current approaches to OA treatment*
- *Identification of patients' diseases by biochemical markers*
- *Identification of patients with the greatest need of treatment by a combination of markers*
- *The role of synovial inflammation in joint damage and pain*
- *OA before and after synovial inflammation*
- *The role of inflammatory cells in OA*

ORAL PRESENTATIONS

Hall C

08:30-10:00 MUSCLES/OSTEOARTHRITIS

Chairperson **H.K. Genant**, USA

08:30-08:39 Osteopathic treatment method according to the fascial distortion model (FDM) in the management of 'frozen' shoulder
M. Fink, *Germany*

08:39-08:48 The effects of a physical therapy intervention on functional outcome measures in frail patients on hemodialysis
J. Nussbaum, R.K. Garcia, *USA*

08:48-08:57 Myofascial trigger point and plantar heel pain: Overly common but undr-treated
B. Nguyen, *Australia*

08:57-09:06 SEMG activity of masticatory, neck, and trunk muscles during the treatment of scoliosis with functional braces
S. Tecco, S. Mummolo, E. Marchetti, R. Gatto, L. Tettamenti, **G. Marzo**, *Italy*

09:06-09:15 Relation between facial morphology and SEMG activity of head, neck, and trunk muscles in caucasian adult females
S. Tecco, L. Tettamanti, S. Mummolo, E. Marchetti, G. Gallusi, G. Marzo, *Italy*

09:15-09:24 Extensor mechanism rupture following TKA: Should we fix it?
L. Delasotta, A. Rangavajjula, M. Porat, F. Orozco, **A. Ong**, *USA*

09:24-09:33 Intraoperative periprosthetic fractures during total knee arthroplasty: The box cut
L. Delasotta, A. Rangavajjula, **F. Orozco**, A. Ong, *USA*

09:33-09:42 Statin use is associated with reduced incidence and progression
S. Clockaerts, G. van Osch, Y. Bastiaansen-Jenniskens, J. Verhaar, F. Van Glabbeek, J. Van Meurs, H. Kerkhof, A. Hofman, B. Stricker, S. Bierma-Zeinstra, *Netherlands/Belgium*

09:42-09:51 Time-dependent effect of bisphosphonate on osteoporotic rat spine fusion
C.K. Chug, S.B. Park, *Republic of Korea*

09:51-10:00 Intra-articular giant cell tumor of the tendon sheath (GCT-TS) of the knee, a report of seven cases and review of the literature
D. Schrander, M. Schotanus, N. Kort, P. Theunissen, E. van de Bogert, I. Heyligers, *Netherlands*

10:20-11:50 OSTEOARTHRITIS

Chairperson **D. Uebelhart**, Switzerland

10:20-10:29 Transforming growth factor beta signalling and osteoarthritis: Regulation and role of transforming growth factor beta receptor type II in articular chondrocytes
C. Bauge, E. Duval, S. Leclercq, P. Galera, K. Boumediene, *France*

10:29-10:38 Increased periprosthetic stress shielding with an I-beam compared with a finned tibial component stem design. a 2-year DXA and RSA RCT
M. Stilling, A. Odgaard, F. Madsen, L. Rømer, O. Rahbek, N. Trolle Andersen, K. Soballe, *Denmark*

10:38-10:47 High tibial open-wedge osteotomy: New techniques and early results
W. Kolb, *Germany*

10:47-10:56 The activity of Cathepsin d and alpha-1-antitrypsin in synovial fluid and blood serum of patients with osteoarthritis
D. Olszewska-Słonina, D. Mątewski, K. Olszewski, A. Woźniak, B. Kowaliszyn, *Poland*

10:56-11:05 Large-scale assessment of biochemical markers for osteoarthritis: An analysis in check
E. van Spil, J. Wesseling, F. Lafeber, *Netherlands*

11:05-11:14 Cytokine production by infrapatellar fat pad can be stimulated by interleukin 1β and inhibited by peroxisome proliferator activated receptor α agonist
S. Clockaerts, **Y. Bastiaansen-Jenniskens**, C. Feijt, L. De Clerck, J. Verhaar, A-M. Zuurmond, V. Stojanovic-Susulic, J. Somville, M. Kloppenburg, G. Van Osch, *Netherlands/Belgium*

11:14-11:23 Hypoxia induces chondrocyte phenotype: Molecular mechanism and application in Cartilage tissue engineering
E. Duval, C. Bauge, R. Andriamanalijaona, H. Bénateau, S. Leclercq, S. Dutoit, L. Poulain, P. Galera, **K. Boumediene**, *France*

Friday, January 20, 2012

ORAL PRESENTATIONS

Hall C

11:23-11:32 Hyaluronic acid in the treatment of knee osteoarthritis, the current evidence with a special emphasis on the difference between products
S. Colen, M. Van den Bekerom , M. Mulier, D. Haverkamp, *Belgium/Netherlands*

12:10-13:40 OSTEOPOROSIS

Chairperson: **A.M. Malfait**, USA

12:10-12:19 Two unusual cases of male idiopathic osteoporosis
I. Jamall, M.C. Ullrey, M. Rocchietti, V. Rochira, E. Pignetti, *USA/Italy*

12:19-12:28 The effects of the obstructive sleep Apnoe syndrome (OSAS) on bone metabolic parameters
B. Acs, *Hungary*

12:28-12:37 **Evaluation of oxidative status in osteopenic and osteoporotic postmenopausal women**
R. De Giuseppe, F. de Liso, C. Novembrino, P. Bonara, F. Bamonti, *Italy*

12:37-12:46 Does lead exposure contribute to the uncoupling of bone resorption and bone formation?
J. Brito, L. Gonçalves, I. Costa, A. Maia e Silva, I. Cavaleiro, J. Marques, *Portugal*

12:46-12:55 Does lead exposure impact on bone calcium concentration?
J. Pereira, T. Fernandes, J. Brito, *Portugal*

12:55-13:04 Anti-osteoporotic drugs use in patients with RA under biological agents
R. Roque, S. Ramiro, F. Vinagre, A. Cordeiro, P. Gonçalves, V. Tavares, J. Canas da Silva, M.J. Santos, *Portugal*

13:04-13:13 Can an integrated approach be a better choice in the management of osteoporosis? A pilot study
Y. Bali, *India*

13:13-13:22 Osteoporosis in thalassemia patients of north India: Status of 25-hydroxyvitamin D deficiency and effect of vitamin D receptor gene polymorphisms
S. Agarwal, R. Kumar, K. Singh, A. Shukla, S. Phadke, *India*

13:22-13:31 Risk factors in an origin of fractures of vertebral
Y. Varavko, *Russian Federation*

13:31-13:40 The cross-talk between osteoclasts and osteoblasts in response to strontium treatment: involvement of osteoprotegerin
S. Peng, *China/USA*

14:30-16:00 JOINT BIOLOGY

Chairperson: **P. Monahan**, USA

14:30-14:39 Key enzymes involved into steroid metabolism and idiopathic scoliosis: A possible genetic linkage
T. Esposito, **B. Varriale**, G.F. Di Martino, M. Chierchia, D. Ronca, *Italy*

14:39-14:48 Bone mineral density and lean body mass in young hyperthyroid men
A.P. Barbosa, M.R. Mascarenhas, A. Goncalves, V. Simoes, A.G. Oliveira, D. Santos Pinto, M. Bicho, I. do Carmo, *Portugal*

14:48-14:57 Condylar volume and surface in Caucasian adult subjects
S. Tecco, **E. Marchetti**, L. Tettamanti, S. Mummolo, F. Festa, G. Marzo, *Italy*

14:57-15:06 Volar locking plate versus K-wiring fixation of distal radius fractures in 20-65 year olds
C. Kiernan, *Republic of Ireland*

15:06-15:15 Scoliosis and dental occlusion
S. Tecco, **S. Mummolo**, L. Tettamanti, E. Marchetti, A. Monaco, G. Marzo, *Italy*

15:15-15:24 Three-phase bone scintigraphy with spect – diagnostic tool for avascular necrosis of the hip
S. Dugonjic, D. Stefanović, M. Ćirković, B. Ajdinović, *Serbia*

ORAL PRESENTATIONS

Hall C

15:24-15:33 Effect of radon upon the extracellular matrix and lipid peroxidation in patients with vertabral osteochondrosis
L. Kim, V. Melnikov, *Russian Federation*

15:33-15:42 A protocol for management of periprosthetic wound infection and soft tissue cover following total knee arthroplasty
M.A.A. Khan, **L. Gwozdziewicz**, R. Sehgal, B. Haughton, *UK*

16:30-18:00 OSTEOARTHRITIS

Chairperson: **M. Henriksen**, Denmark

16:30-16:39 Self-repair in degenerative joint disease
V. Di Nicola, *Switzerland*

16:39-16:48 Prevalence of low BMD and osteoporosis in male hypogonadism
M.R. Mascarenhas, A.P. Barbosa, A.G. Oliveira, A. Goncalves, V. Simoes, D. Santos Pinto, M. Bicho, I. do Carmo, *Portugal*

16:48-16:57 A new tool for measuring cup orientation in total hip arthroplasty from plain radiograph
C-K. Liaw, T-Y. Wu, R-S. Yang, S-M. Hou, *Chinese Taipei*

16:57-17:06 A simple mathematical standardized measurement of acetabulum anteversion after total hip arthroplasty
C-K. Liaw, **T-Y. Wu**, R-S. Yang, S-M. Hou, *Chinese Taipei*

17:06-17:15 Clarifying the role of adamts4 and adamts5 in human osteoarthritis: Fully selective and neutralizing monoclonal antibodies for characterization of the disease and development of a disease modifying therapeutic
J. Larkin, T. Lohr, L. Elefante, J. Shearin, R. Matico, J-L. Su, J. White, *USA*

17:15-17:24 Plowing in a Cartilage model of diarthrodial joints could induce catabolism
L. Gallo, V. Colombo, M.R. Correro-Shahgaldian, *Switzerland*

17:24-17:33 Investigating gastrointestinal function and microbiota profiles in patients with osteoarthritis: A role for glucosamine and green-lipped mussel
S. Coulson, P. Masci, P. Vecchio, L. Vitetta, *Australia*

17:33-17:42 Evaluation of separate quantitative radiographic features adds to the prediction of incident radiographic osteoarthritis in individuals with recent onset of knee pain: Five-year follow-up in the check cohort
M.B. Kinds, A.C.A. Marijnissen, K.L. Vincken, M.A. Viergever, K.W. Drossaers-Bakker, J.W.J. Bijlsma, S.M.A. Bierma-Zeinstra, P.M.J. Welsing, F.P.J.G. Lafeber, *Netherlands*

17:42-17:51 Clinical characteristics and medication use of patients with knee osteoarthritis selected for total joint replacement surgery
T de Boer, M. Stukstette, P. Welsing, M. Huisman, A. Polak, J. Bijlsma, S. Mastbergen, F. Lafeber, *Netherlands*

17:51-18:00 FGF2 and TGFB1 induce precocious maturation of articular cartilage: Implications for repair of osteoarthritic lesions
I. Khan, C. Archer, *UK*

Saturday January 21, 2012

08:30-10:00 **CONTROLLING PAIN IN MUSCULOSKELETAL DISEASES** Hall A

Capsule

Even though cartilage damage and bone changes are the central clinical description of OA, it is nevertheless pain that motivates the patient for consultation. Who cares about OA if it does not involve pain control? Can we devise an optimal treatment for OA-related pain?

Chairpersons

D. Hunter, Australia
D. Ferrer García, Spain

08:30-09:00 Selected presentations

Activation of the transversus abdominis, pain and functional disability in patients with chronic nonspecific low back pain and lumbar disc herniation
A. Maques, **F.J.R. França**, L. Ramos, T. Burke, Brazil

Joint-pain comorbidity is associated with unfavorable health status and medication use in hip and knee osteoarthritis: A cross-sectional study
T. Hoogeboom, A. den Broeder, B. Swierstra, R. de Bie , C. van den Ende, Netherlands

"Beating osteoarthritis": Development of a stepped care strategy to optimize utilization and timing of conservative treatment modalities for patients with hip or knee osteoarthritis
A. Smink, C. van den Ende, T. Vliet Vlieland, B. Swierstra, J. Kortland, J. Bijlsma, T. Voorn, H. Schers, S. Bierma-Zeinstra, J. Dekker, Netherlands

09:00-10:00 **Debate: Should pain be controlled centrally, peripherally, or both? Is chronic pain the most important part of the treatment of OA? Is OA pain just OA pain?**
Yes, yes: **S.B. Abramson**, USA
No, no: A.M. Malfait, USA
Discussion

Objectives

Upon completion of this session, the audience will have learned:
- *Whether there is any difference between musculoskeletal and visceral pain*
- *Central and local pain mediators*
- *Possible hormones interfering with pain*
- *Pain-specific medication*
- *Novel possibilities and strategies*

08:30-10:00 **Go to Hall A** Hall B

10:00-10:20 **Coffee break**

10:20-11:50 **FRAILTY SYNDROME AND SARCOPENIA** Hall A

Chairpersons

R.D. Altman, USA
A.M. Malfait, USA

10:20-11:00 **FRAILTY SYNDROME: THE NEW TARGET POPULATION WHEN CONSIDERING THE BASKET OF BENEFITS OF SELECTED TREATMENT OPTIONS**

Capsule

Unfortunately, aging is a natural consequence of life. Frailty syndrome is a neglected part of long term care for the elderly population. Frailty syndrome involves muscles, bone, cartilage and the cognitive state. Can we expect to reverse aging by mono therapy?

Is muscle wasting the cause or the consequence of frailty? Are there positive secondary effects of preventing sarcopenia?
Yes, yes to both: **M.C. Hochberg,** USA
Discussion

Objectives

Upon completion of this session, the audience will have learned about:
- *Muscles as a target tissue*
- *Muscles in OA and OP: A central part of fracture prevention?*
- *Muscles in metabolic syndrome*
- *Do we have treatment options?*
- *What are the secondary benefits of positive effects on muscles?*

11:00-11:50 **SARCOPENIA: THE EFFECT OF MUSCLE ON HEALTHY AGING AND THE QUALITY OF LIFE**

Capsule *It is becoming increasingly clear that muscles and muscle function are a central part of healthy aging. In addition, muscle physiology has profound effects on a range of other diseases, such as diabetes and osteoporosis. How may we better understand the role of muscles in healthy aging and muscle physiology as a target for pharmaceutical intervention? What could be the secondary positive effects of targeting muscles in bone, cartilage and other disease indicators?*

11:00-11:35 Sarcopenia trials: Lessons from osteoporosis and osteopenia
S.R. Cummings, USA

11:35-11:50 Presentation

Defining sarcopenia: The impact of different diagnostic criteria on the prevalence of sarcopenia in a large middle aged cohort
A.Y. Bijlsma, C.G.M. Meskers, C.H.Y. Ling, M. Narici, S.E. Kurrle, I.D. Cameron, R.G.J. Westendorp, **A.B. Maier**, Netherlands

10:20-11:50 **MONITORING PROGRESSION OR REMISSION: IMPLEMENTATION OF BIOMARKERS** Hall B

Capsule *The field of biomarkers is expanding, resulting in ample choices from different modalities for the assessment of biomarkers. How many biomarkers are really needed? Do imaging and biochemical approaches provide additional information?*

Chairpersons **Y. Henrotin**, Belgium
M. Østergaard, Denmark

10:20-11:20 **Debate: Imaging, biochemical biomarkers, or both: Can they provide information on the progression or remission of OP, OA and RA?**
For Imaging: **D. Hunter**, Australia
For Biomarkers: **R. Eastell**, UK
Discussion

11:20-11:50 Imaging in joint disease: Can this be further developed?
H.K. Genant, USA

Objectives ***Upon completion of this session, the audience will have learned the following:***
- *Can we better identify fast progressors in need of aggressive therapy?*
- *Biochemical markers in RA, OA and OP*
- *The molecular action mode of joint destruction*
- *The action mode of inflammation and immune systems in RA*

11:50-12:10 **Poster viewing**

12:10-13:05 **GLUCOCORTICOIDS AND SMALL MOLECULES FOR THE MANAGEMENT OF RHEUMATOID ARTHRITIS (RA)** Hall A

Capsule *A range of treatment opportunities exist for inflammatory diseases such as RA. Biological treatments offer sought out efficacy at a high cost. Can early RA be treated more cost efficiently with glucocorticoids or small molecules? With the apparent similarities in Ankylosing Spondylitis (AS) and RA, could any treatment opportunities for RA be extended to AS?*

Chairpersons **B.L. Langdahl**, Denmark
S. Castañeda, Spain

12:10-12:38 Glucocorticoids without the side effects: Is this the future for treating RA?
J.W. Bijlsma, Netherlands

12:38-13:05 Disease modification in Ankylosing Spondylitis: What evidence is there?
W. Maksymowych, Canada

Objectives ***Upon completion of this session, the audience will have learned as follows:***
- *Can we find a strategy to reach the goal?*
- *The cellular action mode of inflammation, including macrophages and osteoclasts*
- *Subcellular cascades and key components leading to chronic inflammation*
- *Small molecule options in RA*
- *The role of the osteoclasts and bone degradation in RA*

Saturday January 21, 2012

13:05-13:40 **CHOOSING THE RIGHT TREATMENT FOR PATIENTS WITH RHEUMATOID ARTHRITIS (RA)** Hall A

Capsule

Despite many years of research and many different choices of treatment, pathophysiology remains elusive and the response to treatment is unpredictable

Round Table Discussion

Discussants
M. Østergaard, Denmark
J.W. Bijlsma, Netherlands
W. Maksymowych, Canada

Tricks of the trade: Experts' opinion on:
1. When to treat?
2. When to start the biological intervention?
3. When to switch treatments before it's too late?
4. What risks do we need to consider and which can we assess?
5. Is there a difference between current available anti-inflammatory strategies in RA?

Objectives

The intervention possibilities discussed:
- *CD20*
- *Different anti-TNF treatments*
- *Anti-IL-6*
- *Anti-IL-1*
- *P38 MAP kinase inhibitors*
- *Other intracellular opportunities and future treatment opportunities*

14:30-16:00 **METABOLIC SYNDROME AND OSTEOARTHRITIS (OA)** Hall B

Capsule

There is increasing evidence linking metabolic syndrome and OA. What is the role played by fat tissue? What is the link between OA and diabetes?

Chairpersons

X. Chevalier, France
K. de Vlam, Belgium

14:30-14:50

Obesity
P. Richette, France

14:50-15:10

Chronic inflammation and adipokines
A. Ioan-Facsinay, Netherlands

15:10-15:30

Metabolic markers of pre-OA and early OA in hip and meniscus
L.J. Sandell, USA

15:30-16:00

Round Table Discussion

Discussants
P. Richette, France
A. Ioan-Facsinay, Netherlands
L.J. Sandell, USA

Questions to the panel:
1. Is OA a cause or a consequence of metabolic syndromes?
2. What is the role of fat tissue in OA pathogenesis?
3. Is metabolic syndrome a therapeutic target of OA therapy?

Objective

To better understand the molecular and biomechanical mechanism involved in OA, related to metabolic syndrome

13:40-14:30 **Lunch break**

Saturday January 21, 2012

14:30-16:00 DOES INFLAMMATION CAUSE SYNDESMOPHYTE FORMATION IN ANKYLOSING SPONDYLITIS? — Hall A

Capsule

Ankylosing Spondylitis involves a complicated and multifaceted pathogenesis of inflammation, tissue turnover and bone formation. These processes may interact and cause disease progression. How these processes best interact for the benefit of patients is much debated. Thus, the question at hand is, does inflammation cause syndesmophyte formation in Ankylosing Spondylitis?

Chairpersons

M. Østergaard, Denmark
S.B. Abramson, USA

14:30-15:20

Debate: Does inflammation cause syndesmophyte formation in Ankylosing Spondylitis?
Propostion: Inflammation causes syndesmophyte formation
W. Maksymowych, Canada
Opposition: Inflammation does not cause syndesmophyte formation
R. Meliconi, Italy
Discussion

15:20-15:50

Translational aspects of syndesmophyte formation
K. de Vlam, Belgium

15:50-16:00

Presentation

Striking prevalence of axial spondyloarthritis in primary care patients with chronic low back pain: A cross-sectional study
A. Weel, Netherlands

14:30-16:00 MUSCLE PERFORMANCE IN THE PHYSIOPATHOLOGY OF OSTEOARTHRITIS (OA) — Hall B

Capsule

Muscle atrophy, weakness and neuromuscular control deficiency are signs of OA diseases

Chairpersons

M. Marty, France
M.C. Hochberg, USA

16:30-17:00

Anatomo-pathological and biochemical aspects
S. Poiraudeau, France

17:00-17:30

Mechanical aspects
M. Henriksen, Denmark

17:30-18:00

Round table discussion

Discussants
M. Henriksen, Denmark
S. Poiraudeau, France

Questions to the panel:
1. What are the impacts of these signs on the onset and the progression of OA?
2. Are these signs determinants of OA pain?
3. Can we slow down OA progression by improving muscle performance?

16:00-16:30 **Coffee break**

16:30-18:00 LATE BREAKING NEWS AND HOT TOPICS — Hall A

Chairpersons

L.J. Sandell, USA
R. Eastell, UK

16:30-17:00

Bones as endocrine organs
TBA

17:00-17:30

Is osteoarthritis a metabolic disease?
F.J. Blanco, Spain

17:30-18:00

The use of biomarkers in the personalized management of OA patients: Myth or reality?
Y. Henrotin, Belgium

Saturday, January 21, 2012

ORAL PRESENTATIONS

Hall C

08:30-10:00 OSTEOPOROSIS

Chairperson: **S.R. Cummings,** USA

08:30-08:39 Relationship between early menopause, oestrogens receptor polymorphism and osteoporosis in a Mediterranean population
D. Ronca, T. Esposito, M. Chierchia, G.F. Di Martino, B. Varriale, *Italy*

08:39-08:48 Feature of the assessment of bone mineral density in postmenopausal women
V. Novikova, G. Penzhoyan, F. Autleva, S. Autleva, *Russian Federation*

08:48-08:57 Deferoxamine increase bone mineralization density of postmenopausal ovariectomy model and promote biological activity of osteoblast in vitro
Y. Ma, *China*

08:57-09:06 Relationship between neonate and maternal bone metabolism and anthropometric markers
R. Tenta, I. Bourgiezi, E. Aliferis, A. Gounaris, M. Skouroliakou, *Greece*

09:06-09:15 Assessment of osteoporosis by DXA and QUS in thalassemic patients
A. Argentiero, C. Neglia, A. Peluso, S. Di Rosa, V. Caiaffa, N. Agnello, A. Cozma, G. Chitano, D. Paladini, E. D'alò, M. Benvenuto, P. Piscitelli, A. Distante, *Italy*

09:15-09:24 Can the trabecular bone score (TBS) be considered as a major clinical risk factor (CRF) of osteoporotic fractures? A meta-like analysis
D. Hans, **R. Winzenrieth**, B. Aubry-Rozier, D. Stoll, O. Lamy, M-A. Krieg, *Switzerland*

09:24-09:33 Passive standing and functional electrical stimulation preserves bone strength in paraplegic rats following acute spinal cord injury
A. Zamarioli, R. Battaglino, L. Morse, S. Sudhakar, D. Maranho, R. Okubo, J. Volpon, A. Shimano, *Brazil/USA*

09:33-09:42 Influence of high-impact exercise on bone in osteopenic ovariectomized rats
R. Okubo, A. Zamarioli, V.A. Castania, F.J. Albuquerque de Paula, M.J. Quirino Louzada, J. Volpon, A. Shimano, *Brazil*

09:42-09:51 Susceptibility to osteopenia in obese subjects may modify by alteration of some important gene expression at involved pathway in osteoclastic differentiation
K. Mirzaei, A. Hossein-Nezhad, H. Ansar, Z. Maghbooli, M. Khosrofar, *Islamic Republic of Iran*

09:51-10:00 The effect of low-frequency pulsed electromagnetic fields on osteoporosis: A systematic review
L. Xia, China

10:20-11:50 OSTEOARTHRITIS

Chairperson: **S. Poiraudeau**, France

10:20-10:29 Should DXA t-scores or Z-scores be used for diagnosing and managing osteoporosis in premenopausal women and men aged 20 to 50 years?
J. Carey, M. Delaney, B. Richmond, T. Love, B. Cromer, A. Licata, P. Miller, *Republic of Ireland/USA*

10:29-10:38 A study of propranolol and SKZD on central depressant and anti-osteoporosic actions in ovariectomized rats
T. Ishida, W. Zhang, H. Fujieda, N. Nagaoka, N. Tanahashi, *Japan*

10:38-10:47 Manipulations of disulfide bonds in an amylin octapeptide: A mechanism to modify bioactivity
J. Cornish, D. Naot, R. Kowalczyk, M. Watson, K.E. Callon, P.W. Harris, M.A. Brimble, *New Zealand*

10:47-10:56 Cemented or uncemented fixation of proximal interphalangeal joint implants? A 2 year RCT of implant fixation, periprosthetic bone density and finger function
M. Stilling, K. Krøner, B. Munk, I. Helleberg, K. Ulstrup, O. Rahbek, L. Rømer, K. Soballe, *Denmark*

10:56-11:05 Joint resurfacing with decellularized type 1 collagen as an alternative to replacement or arthrodesis for hallux rigidus osteoarthritis
A. Landsman, *USA*

11:05-11:14 Minimal invasive procedures for the treatment of hip and knee osteoarthritis
S. Ventura, A. Musolino, M. Cancelli, M. Beatric, V. Verna, A. Borré, G. Massazza, *Italy*

11:14-11:23 Synovial fluid leptin level and joint pain in end-stage osteoarthritis: A potential explanation for increased pain in women and in obese patients
A. Lübbeke, A. Finckh, G. Puskas, D. Suva, A. Lädermann, S. Bas, D. Fritschy, C.Gabay, P. Hoffmeyer, *Switzerland*

ORAL PRESENTATIONS

Hall C

11:23-11:32 Implementation of clinical practice guidelines for management of nonsurgical knee osteoarthritis: A survey of physiotherapists in direct access practice settings in Ontario, Canada
N. MacIntyre, B. Hale, M. Bhandari, J. Busse, *Canada*

11:32-11:41 Beliefs among Canadian physiotherapists regarding the use of therapeutic ultrasound for management of mild to moderate knee osteoarthritis
N. MacIntyre, **M. Bhandari**, J. Busse, *Canada*

11:41-11:50 Precision of radiological methods novel in relation to resurfacing humeral head implants: Assessment by radiostereometric analysis, DXA, and geometrical analysis
I. Mechlenburg, M. Stilling, A. Amstrup, K. Soballe, T. Klebe, *Denmark*

12:10-13:40 TRANSLATIONAL SCIENCE/OSTEOARTHRITIS

Chairperson: **L.Yamamoto**, USA

12:10-12:19 An intervention to reduce psychosocial and biological indicators of stress in African American lupus patients: The balancing lupus experiences with stress strategies (bless) study
E. Williams, *USA*

12:19-12:28 Development of the "which health approaches and treatments are you using?" (what) questionnaires: A multidimensional assessment of complementary and alternative medicine use in children with juvenile arthritis
K. Toupin April, D. Moher, J. Stinson, B. Heather, D. Ciaran, P. Tugwell, *Canada*

12:28-12:37 Effects of cinnamon extract on blood glucose level in mice
N. Djaya, J. Hidayat, J. Hueichi, Y. Gerald, *Indonesia*

12:37-12:46 Obesity influences the clinical outcome and the quality of life following primary total knee arthroplasty
A. Liljensøe, I. Mechlenburg, J.O. Laursen, *Denmark*

12:46-12:55 Potentiating the osteogenic capacity of bone marrow stem cells using nell-1 in an osteoporotic rat model
J. Zara, J. Kwak, R. Ngo, M. Chiang, J. Shen, A. James, X. Zhang, K. Ting, C. Soo, *USA*

12:55-13:04 Demineralized calf foetal growth plate effects on experimental bone healing
A. Bighamsadegh, Z. Shafiei-Sarvestani, *Islamic Republic of Iran*

13:04-13:13 Oxidative stress in bone remodeling
E. Filaire, *France*

14:30-16:00 RHEUMATOID ARTHRITIS

Chairperson: **F.J. Blanco**, Spain

14:30-14:39 Assessment of blood tyrosine level as an approach to individualized rational prescribing and monitoring glucocorticoid therapy in rheumatoid arthritis
I. Rass, *Russian Federation*

14:39-14:48 IL-17/RANKL interplay provided by neutrophils
V. Milanova, N. Ivanovska, P. Dimitrova, *Bulgaria*

14:48-14:57 A proposed approach to treat active rheumatoid arthritis (RA) with concomitant hepatitis viremia
O. Noguchi, *Japan*

14:57-15:06 Efficacy and safety of adalimumab treatment in juvenile idiopathic arthritis
E. Mitenko, E. Alexeeva, R. Denisova, S. Valieva, T. Bzarova, T. Sleptsova, K. Isaeva, *Russian Federation*

15:06-15:15 Safety and efficacy of tocilizumab treatment in children with systemic onset of juvenile idiopathic arthritis
E. Alexeeva, **R. Denisova**, S. Valieva, T. Bzarova, T. Sleptsova, E. Mitenko, K. Isaeva, *Russian Federation*

15:15-15:24 Co-medications with steroids in patients with rheumatoid arthritis under biologic agents
S. Ramiro, R. Roque, F. Vinagre, P. Gonçalves, A. Cordeiro, V. Tavares, J. Canas da Silva, M.J.Santos, *Portugal/Netherlands*

15:24-15:33 Efficacy of infliximab treatment in patients with early and long-standing juvenile idiopathic arthritis
T. Sleptsova, *Russian Federation*

15:33-15:42 Serum cartilage oligomeric matrix protein (comp) levels in knee osteoarthritis in an Indian population
P. Verma, K. *Dalal, India*

Saturday, January 21, 2012

ORAL PRESENTATIONS

Hall C

16:30-18:00 **OSTEOARTHRITIS**

Chairperson: **S. Castañeda**, Spain

16:30-16:39 Hip revision surgery using the bipolar cup advantage
W. Steens, C. Götze, *Germany*

16:39-16:48 Comparison between serum DKK1 (dickopff-1) and bone mineral density in patients receiving bisphosphonate treatment and patients without treatment
A. Memon, J.Harty, *Republic of Ireland*

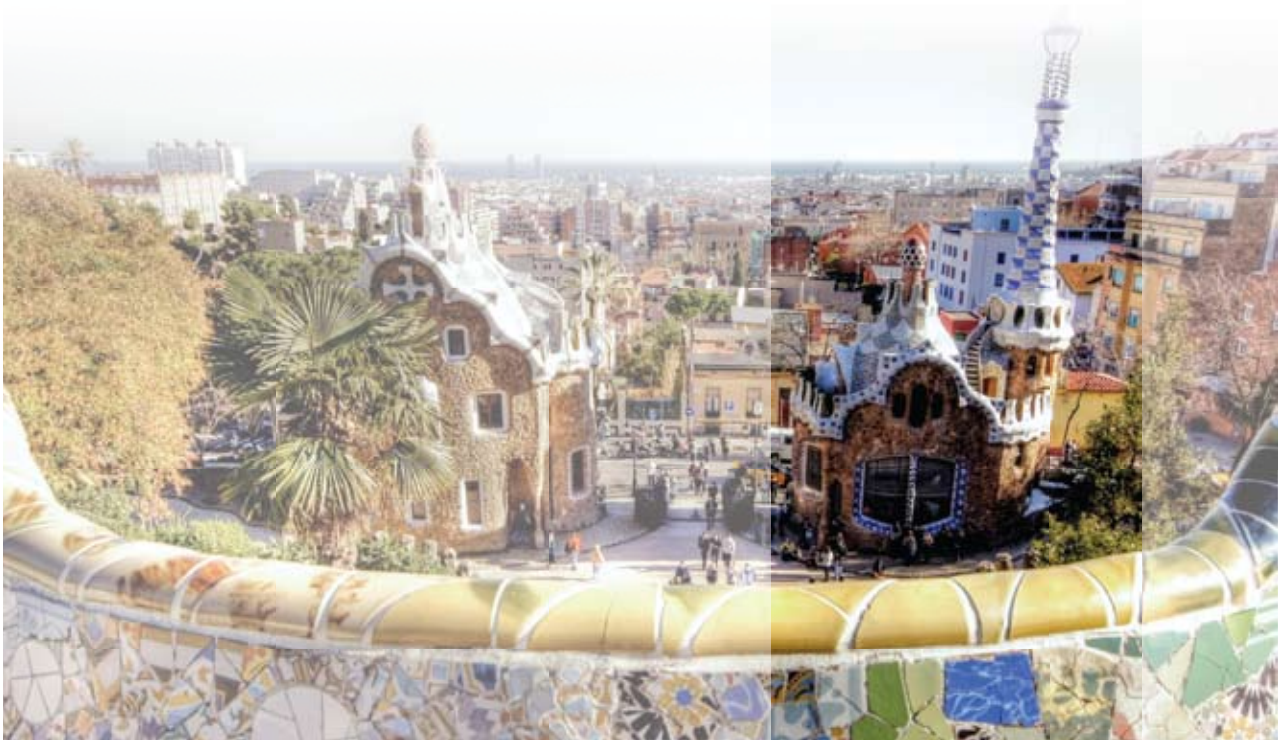
16:48-16:57 Association of single nucleotide polymorphisms in 4 genes (VDR, COL1A1, CALCR and BGLAP) with susceptibility to steroid osteoporosis in patients with idiopathic pulmonary fibrosis (IPF)
A. Ulitina, D. Dzadzua, L. Novikova, I. Pavlenko, J. Ilkovich, D. Ghorab, M. Dubina, *Russian Federation*

16:57-17:06 Induction of an osteoporotic phenotype with nell-1 deficiency
J. Zara, **J. Aaron**, M. Chiang, A. Askarinam, A. Nguyen, X. Zhang, K. Tin, C. Soo, *USA*

17:06-17:15 Cementless arthroplasty for osteoporotic intertrochanteric fracture in the elderly
Y.Y. Chung, *Republic of Korea*

17:15-17:24 Evaluation of frequency of osteoarticular complications of brucellosis in patient admitted to Beheshti hospital, Kashan
Z. Soleimani, *Islamic Republic of Iran*

17:24-17:33 Erythrocyte sedimentation rate (ESR) and leukocyte changes in canine model of osteoarthritis
A. Ajadi, *Nigeria*



08:30-10:00 "BONE BEYOND OSTEOPOROSIS" PORTUGUESE SOCIETY OF OSTEOPOROSIS AND BONE METABOLIC DISEASES (SPODOM)

Hall A

Chairpersons
J. Monteiro, Portugal
C. Vaz, Portugal

Effects of thyroid dysfunction in bone
A.P. Barbosa, Portugal

Male hypogonadism and bone
M.R. Mascarenhas, Portugal

Paget disease of bone: A Portuguese experience
M.E. Simões, Portugal

Effects of breast cancer in bone
R. Sousa, Portugal

Discussion

08:30-10:00 JAPANESE OSTEOPOROSIS FOUNDATION/ JAPANESE OSTEOPOROSIS SOCIETY (JOF/JOS)

Hall B

Chairperson
H. Orimo, Japan

Part I: **Bone metabolic markers**

Present status of bone metabolic markers for treatment of osteoporosis in Japan. The Japanese guidelines for the use of bone metabolic markers (2011 Edition)
M. Miura, Japan

Bone metabolic markers and vertebral fracture risk in type 2 diabetes mellitus
T. Yamaguchi, Japan

Influence of chronic kidney disease on the measurement of bone metabolic markers
M. Inaba, Japan

Part II: **The combination therapy for osteoporosis**

Fracture risk reduction by the combination therapy of alendronate with alfacalcidol in osteoporosis patients: The Japanese Osteoporosis Intervention Trial (JOINT)-02
T. Hosoi, Japan

Serum 25 hydroxy vitamin D level associates with quality of life in osteoporosis: The Japanese Osteoporosis Intervention Trial (JOINT)-02
S. Mori, Japan

10:00-10:20 **Coffee break**

10:20-11:20 BIOTHERAPY IN OSTEARTHRITIS (OA) TREATMENT: DREAM OR REALITY?

Hall A

Capsule
Biotherapy targeting cytokines or neuromediators have been studied in the OA population. This session reviews the evidence of this and discusses the relevance of biotherapy in the treatment of OA considering the cost/benefit and risk/benefit ratio

Chairpersons
P. Richette, France
S.B. Abramson, USA

Should we use biotherapy for treatment of OA?
X. Chevalier, France
Discussion

Objectives
Upon the completion of this session, the audience will have found answers to the following questions:
- *What is the evidence for efficacy of biotherapy?*
- *What are the indications and contra-indications for biotherapy?*
- *What is the place of biotherapy in the algorithm of OA patients therapy?*

Saturday, January 21, 2012

11:20-12:20 **FOOD SUPPLEMENTATIONS: ARE THEY OF ANY VALUE? Hall A** Hall A

Capsule

The scientific requirements proposed by the EFSA for health claims related to maintenance of joints and to reduction in the risk of osteoarthritis are clinical trials designed to demonstrate a beneficial physiological effect on joint or a reduction of joint degeneration in people without osteoarthritis

Chairperson

Y. Henrotin, Belgium

Debate: How to evaluate the beneficial physiological effects of food supplements on joint health?
Proposition: Only clinical trials designed to demonstrate a beneficial physiological effect on joints or a reduction of joints degeneration in people without osteoarthritis should be accepted as indicative
A. Mobasheri, UK
Opposition: Which are the useful alternatives of randomized clinical trials to demonstrate beneficial physiological effects on joints or a reduction of joints degeneration in people without osteoarthritis, and how to do it?
M. Marty, France
Discussion

Objectives

Upon completion of this session, the audience will have learned:
- *EFSA requirements for claims related to maintenance of joint health*
- *The design of a clinical trial targeting normal joint health*
- *The population required for this clinical trial*
- *The primary clinical outcome for measuring beneficial physiological effects*

WORLD CONGRESS

on Debates & Consensus

in Bone, Muscle & Joint Diseases

ABSTRACTS

BMJD

World Congress

on Debates & Consensus

INVITED SPEAKERS' ABSTRACTS

GLUCOCORTICOIDS WITHOUT THE SIDE EFFECTS: IS THIS THE FUTURE FOR TREATING RA?

J.W.J. Bijlsma
University Medical Center, Utrecht, Netherlands

Objectives:

- To value the efficacy of glucocorticoids in many immune mediated diseases
- Specific in rheumatoid arthritis: glucocorticoid treatment decreases not only symptoms, but also inhibits progression of erosions
- The adverse effects of chronic low dose glucocorticoids are limited and for a large part manageable
- Most frequent are: occurrence of osteoporosis; guidelines are in place and effective; occurrence of infections; occurrence of diabetes
- To learn how to diagnose and monitor these
- To learn about new glucocorticoid preparations

New insights in the efficacy and safety of glucocorticoids in the treatment of rheumatoid arthritis have led to a more prominent place of this drug in the treatment strategies of RA. EULAR has developed guidelines on monitoring these drugs and formulated recommendations how to use these drugs. Different activities have led to a better understanding and more responsible use; these will be discussed. Glucocorticoids are still the most effective and cheap immunosuppressive drugs for many rheumatic diseases. Responsible use will also be relevant with regard to the sequellae for bone-problems. New glucocorticoid preparations have been developed and are under development in order to reduce the possible adverse events; these will be discussed, with the targeted release preparation Lodotra as a clear example.

BIOTHERAPY FOR OSTEOARTHRITIS: IS IT THE QUEST OF THE GRAAL….

X. Chevalier
Department of Rheumatology, Hopital Henri Mondor, Creteil, France

Osteoarthritis is the most prevalent form of articular disease involving billions of people. Several conference consensuses on the management of knee, hip and digital osteoarthritis have been published and figured out the point that there is a need for a targeting treatment. OA is marked by an imbalance between repair process and processes mediating degradation of the cartilage matrix in favour of the latest. There are a lot of pro inflammatory mediators such interleukins, prostaglandins, free radicals, enzymes which are coordinated to degrade the cartilage matrix. Interleukin-1 (its soluble form IL-1 b and it cytoplasmic form (IL-1 a)) appears as the chief orchestrators of the destructive process because they can inhibit the anabolism of the chondrocyte, increase the production of NO, enzymes and free radicals. Il-1 b synergizes with other cytokines such as TNF a, oncostatin M, IL-6. Furthermore IL-1 and others cytokines are produced not only by the cartilage but also by the synovial membrane. Thus they could be present in the synovial fluid. While it was logical to block IL-1 in OA, two main trials performed in knee OA, one by local injection of IL-1 ra, the other by systemic administration of a monoclonal antibody failed to demonstrate any efficacy on pain and function. Similarly, the anti TNF strategy in hand OA do not demonstrate its capacity to slow down the progression of the disease as well failed to improve the evolution of pain. It is now time to understand why the biotherapy failed in OA. There are a lot of explanations. First it is possible that it is not sufficient to block one cytokine IL-1 or TNF a alone. It is also possible that the role of cytokine may fluctuated over time and that the ratio of antagonist of cytokine/cytokine may also fluctuate. A recent work shows that in knee OA the synovial fluid is already saturated in IL-1ra. Cytokine may also not be the right target. Recent in vivo works in animal's models of OA demonstrate that blocking IL-1 is not always efficient and depends on the model used. Other mediators such as alarmins may be better targets. If we still consider cytokines as appropriate targets, it does mean that using the same strategy based on anti-cytokine works at an individual level. Indeed OA should be regarded as a multi side's disease involving several tissues: bone, synovial membrane, cartilage. The weight of each tissue in the disease process may change over time in a one individual, but also may change from one individual to another. This may explain that the response to anti-cytokine may show inter individual variations. In other words it a little bit speculative to find one single therapy from all patients. Another problem consists in variations in OA presentations among different localizations. It is not possible to compare hand OA with knee OA and hip OA. Similarly, it is not possible to compare rapid atrophic form of OA with slow hypertrophic forms of the same disease. It means that the best target may change owing to the presentation of OA. Finally, one of the most difficult problems which may limit the use of biotherapy consists to find the good balance of anti-cytokine strategy between the potential of severe side effects and the benefit of drug. In conclusion, we need to better explore the biotherapy in OA not only in terms of target but also in terms of patients selection and to choice the best period and the best route of administration of the drugs.

ESTROGEN AND ESTROGEN-LIKE MOLECULES: DO THE BENEFITS OUTWEIGH THE RISKS? NO

R.T. Chlebowski
Los Angeles Biomedical Research Institute at Harbor-UCLA Medical Center, Torrance, CA, USA

The Women's Health Initiative (WHI) investigators have conducted two full scale, randomized, placebo-controlled clinical trials separately evaluating estrogen plus progestin in 16,608 postmenopausal women with no prior hysterectomy and estrogen alone in 10,739 postmenopausal women with prior hysterectomy to determine long-term effects of therapy use on clinical disease processes. After about five years of intervention and over a decade of follow-up, results were seen to substantially differ based on specific hormone therapy used and the age of therapy initiation. In the WHI randomized, placebo-controlled clinical trial evaluating estrogen plus progestin intervention ended after a mean of 5.6 years when overall harm for estrogen plus progestin therapy was seen. In addition to increased breast cancer risk, adverse effects on coronary heart disease, stroke and pulmonary emboli were seen along with a lower risk of fracture and colorectal cancer. Estrogen plus progestin interfered with mammographic cancer detection, delayed diagnosis leading to more advanced stage breast cancer ultimately resulting in a statistically significant increase in breast cancer mortality. Subsequent analyses identified a statistically significant increase in lung cancer mortality as well. With additional follow-up, despite a 44% lower colorectal cancer incidence no reduction in colorectal cancer mortality was seen suggesting diagnostic delay rather than true incidence reduction. Thus, estrogen plus progestin use significantly increased mortality in the two leading causes of cancer death in women. The increase in breast cancer incidence was somewhat larger for women initiating therapy closer to menopause. While estrogen plus progestin's adverse effect on coronary heart disease was not seen in women initiating therapy closer to menopause, no beneficial effect emerged. The strong negative effect on common cancers in women associated with estrogen plus progestin use suggest extreme caution when prescribing for climacteric symptom management. Findings in the estrogen alone WHI clinical trial were substantially different. Intervention in that trial ended after 7.1 years (mean) intervention because of increased risk of stroke and absence of overall clinical benefit despite a decrease in fracture risk. Other monitored outcomes including coronary heart disease, pulmonary emboli, and colorectal cancer were not influenced by estrogen alone and there was a non-significant trend for fewer

breast cancers in the estrogen alone group. With further follow-up the lower incidence of breast cancer in the estrogen alone compared to placebo group became statistically significant. In addition, exploratory subgroup analyses indicated, for women entering between 50-59 years of age, fewer coronary heart disease events (myocardial infarction or death from heart disease) were seen, the breast cancer incidence was lower and a trend for longer overall survival was seen. Opposite and negative effects on coronary heart disease were seen in older women in the trial. Thus, for younger (50-59 year old) postmenopausal women with prior hysterectomy, estrogen alone use may well reduce breast cancer incidence and be associated with overall net health benefit. Although only one dose and schedule of estrogen plus progestin and estrogen use was evaluated in the WHI trial, the breast cancer findings using other combined hormone therapy regimens in observational studies are quite similar. Micronized progesterone (used largely in France) has been associated with less adverse effects on breast cancer when used together with estrogen in observational studies but did not mitigate fully estrogen plus progestin's adverse effect on endometrial cancer incidence. In summary estrogen plus progestin in postmenopausal women with an intact uterus increases breast and lung cancer mortality and should only be used in the lowest dose and shortest duration necessary to manage limiting menopausal symptoms. In contrast, estrogen alone in postmenopausal women with prior hysterectomy when used for about five years in younger postmenopausal women may reduce breast cancer incidence and result in overall health benefit.

TRANSLATIONAL ASPECTS OF SYNDESMOPHYTES FORMATION

K. de Vlam
Dept. of Rheumatology, University Hospitals Leuven, Belgium

To understand the pathogenesis of syndesmophyte formation , one should reconsider the process of bone formation. During the embryonic development two types of bone formation are described: endochondral bone formation and membranous bone formation. Endochrondral bone formation is responsible for de length growth and originates from mesenchymal cells differentiating into chondrocytes before bone matrix is desposited. Membranous bone formation is important for the …….. and is the result from mesenchymal cells differentiation directly into osteoblasts. These osteblasts are responsible for the bone matrix and the mineralization process. Recent findings suggest that both types of bone formation occur at the site of syndesmophyte formation.
Syndesmophyte is the ultimate structural outcome in the disease process in ankylosing spondylitis and may lead to ankyosis of the spine after bridging with the opposite syndesmophyte. The presence or absence of syndesmophytes contributes importantly to score in radiographic scoring methods. Syndesmophytes can be considered as an attempt to tissue regeneration or repair as a specific tissue respons to damage in AS but in an exaggarated and untimely way, resulting in damage. Radiographic scoring systems focus heavily on scoring damage. Recently spinal mobility impairment in AS is attributed to the presence of inreversible spinal radiographic damage and to a lesser extent to reversible inflammatoin. Specifically syndesmophytes are orthotopic bone formation and originate from the cartilage-bone edge (enthesis) or periosteum. Both types of bone formation , endochondral and direct bone fomation contributes to the development of the syndesmophytes. Recentely different molecular mechanisms and cell types are identified contributing to the bone forming process, including synesmophyte formation and ankylosis, in AS. Several animal models and ex-vivo models are available to study these aspects. The bone morphogenetic proteins and Wnt proteins seems to play an important role in respective endochondral and membranous bone formation. Different cell types , including mesenchymal cell derived from synovium and periosteum , and neutrophils are important for the disease process. One of the main questions remains the interplay between the inflammatory process and the bone forming process. It is actually suggested that both processes occurs simulataneously but are uncoupled. AT the early stage inflammation seems to be the initiator of the process but during further stages inflammation seems to be rather a negative regulator of the bone forming process. Abolishing inflammation in later stages pushes the process towards the completion of this bone formation. Targetting inflammation solely as therapeutic strategies may just be insufficient to prevent structural damage (represented by syndesmophyte formation and ankylosis) in AS. Additional strategies may be needed.

CURRENT STATUS AND FUTURE DIRECTIONS FOR IMAGING IN OA

H.K. Genant
Professor Emeritus of Radiology, Medicine and Orthopaedic Surgery, University of California, San Francisco, CA, USA

Prospective clinical studies of new treatment options in OA are lengthy and difficult due to lack of sensitive methods to investigate disease progression and difficult patient selection process. There is an substantial need for reliable, sensitive and specific tools to promptly assess the progression of this disease. Radiography is currently acknowledged as the best validated method to assess damage in OA patients. This technique allows the measurement of changes in joint space width (JSW), which currently remains the gold standard for the evaluation of structure modifying drugs in OA. However, JSW measurement does not allow detection of early structural damage nor does it constitute an effective way of monitoring the progression of OA in daily practice. Magnetic resonance imaging (MRI), with its excellent soft tissue contrast, is the ideal technique for assessment of normal articular cartilage and cartilage lesions. Joint imaging has the potential to provide morphologic information, such as the presence of fissuring, partial or full thickness cartilage defects and signal changes within residual cartilage. Moreover, MRI, with its ability to discriminate the different articular tissues, holds the greatest potential as a method for whole-organ imaging of the joint in OA. Several different semi-quantitative scoring systems using a variety acquisition protocols have been developed and proposed to assess cartilage defects in knee OA patients, including the Whole-Organ Magnetic Resonance Imaging Score (WORMS), the Knee Osteoarthritis Scoring System (KOSS), the Boston Leeds Osteoarthritis Knee Score (BLOKS), and the MRI Osteoarthritis Knee Score (MOAKS). These scoring systems have been used to provide a better understanding of the pathophysiology of OA and the relationship between joint tissue structural changes and disease symptoms. The common contrast mechanisms used in MR imaging are two-dimensional or multi-slice T1-weighted, proton-density, and T2-weighted imaging. The appearance of these has changed over time with the introduction of fast or turbo spin-echo imaging and the use of fat saturation and water excitation. Three-dimensional spoiled gradient recalled echo imaging with fat suppression (3D-SPGR) produces high cartilage signal, but low signal from adjacent joint fluid. Currently, this technique is the standard for morphologic imaging of cartilage. Newer high-field MRI at 3.0 Tesla enables the acquisition of morphologic images at resolution that cannot be achieved in a reasonable scan time at 1.5 Tesla. In the area of morphologic imaging, further advances have been made with techniques such as Double-echo steady-state (DESS) imaging with water excitation, which has appeal because of the faster acquisition time and lower slice thickness that can be achieved. Other advanced sequences include Driven equilibrium Fourier transform (DEFT) imaging, Steady State Free Precession SSFP imaging, Fluctuating Equilibrium Magnetic Resonance (FEMR), along with various improved fat-water separation capabilities. Further, a wide array of image processing approaches has been applied to these image data sets to display and quantify regional and global cartilage thickness and volume. In the area of physiologic cartilage imaging, several techniques have been developed The T2 relaxation time of articular cartilage is a function of the water content, and collagen ultra-structure of the tissue. Measurement of the spatial distribution of the T2 relaxation time reveals areas of increased or decreased water content, correlating

with cartilage damage. Recent work also shows the potential for Diffusion Weighted Imaging (DWI) of cartilage for assessing composition in OA. A technique referred to as delayed Gadolinium Enhanced MRI of Cartilage (dGEMRIC) has been validated in both basic science and clinical studies as being a reflection of the status of glucosamine glycans (GAG). Another simpler, more practical approach to assessing cartilage compositional changes in OA is the so-called T1rho imaging. Overall, many advances in MR imaging acquisition and analysis have continued to occur for morphologic and functional imaging of cartilage in osteoarthritis, and these methods promise to further improve our ability to study and understand this important disease and its potential treatments.

References:
Peterfy CG, Guermazi A, Zaim S, Tirman PF, Miaux Y, White D, Kothari M, Lu Y, Fye K, Zhao S, Genant HK. Whole-Organ Magnetic Resonance Imaging Score (WORMS) of the knee in osteoarthritis. Osteoarthritis Cartilage 2004;12(3):177–190.
Gold GE, Burstein D, Dardzinski B, Lang P, Boada F, Mosher T. MRI of articular cartilage in OA: novel pulse sequences and compositional/functional markers. Osteoarthritis Cartilage. 2006;14 Suppl A:A76-86. Epub 2006 May 23.
Gold GE, Chen CA, Koo S, Hargreaves BA, Bangerter NK. Recent advances in MRI of articular
cartilage. AJR Am J Roentgenol 2009;193(3): 628–638.
Eckstein F, Guermazi A, Roemer FW. Quantitative MR imaging of cartilage and trabecular bone in osteoarthritis. Radiol Clin North Am 2009;47(4): 655–673.
Michel D. Crema, MD, Frank W. Roemer, MD, Monica D. Marra, MD Deborah Burstein, PhD, Garry E.Gold, MD, MSEE, Felix Eckstein, MD, Thomas Baum, MD, Timothy J. Mosher, MD, John A. Carrino, MD,MPH, Ali Guermazi, MD. Articular Cartilage in the Knee: Current MR Imaging Techniques and Applications in Clinical Practice and Research. RadioGraphics 2011; 31:37–62

BIOMECHANICAL ASPECTS OF MUSCULAR PERFORMANCE DEFICIENCIES IN RELATION TO OSTEOARTHRITIS ONSET AND PROGRESSION

M. Henriksen
Clinical Motor Function Laboratory, The Parker Institute, Copenhagen University Hospital at Frederiksberg, Denmark

This presentation is a view of the biomechanical aspects of muscle weakness and neuromuscular control deficiencies in knee osteoarthritis (OA) and its association with clinical and structural signs of the disease. Theories and empirical data on the impact of these signs on mechanically factors in disease progression are condensated and discussed to give a clearer picture of current knowledge about the relationship between muscle weakness and neuromuscular control deficiency and knee OA. In existing theories, deficiencies in neuromuscular control and muscle strength, is linked with OA through aberrant or increased joint loadings that are associated with disease progression. However, due to the slow disease progression rate with a long subclinical phase, and difficulties in designing appropriately controlled studies, very sparse longitudinal data exist to confirm the hypotheses. Adequate muscle function is crucial for joint mobility, stability and function. Hence, muscle weakness is believed to be one of the earliest signs of OA and is thought to induce degenerative changes as a result of poorer shock absorption and increased joint loads. However, impulse-forces have not been reported as elevated among knee OA patients and the relationship between muscle strength and joint loads is vague and inconsistently reported. Neuromuscular control deficiencies are also hypothesised to participate in OA onset and progression, but an association with joint loads and forces remains elusive and no clear associations with OA onset and progression have been presented. While deficiencies in neuromuscular control and muscle strength are well established as associated with OA, little is known about their interaction with mechanical factors in OA onset and progression. Most relevant studies are observational or cross sectional, precluding confident conclusions about a pathogenic role of muscle weakness and neuromuscular deficits in OA onset and progression. The roles of muscle weakness and neuromuscular deficiencies have in most cases been studied independently but recent experimental and clinical studies that incorporate clinical, biological and structural signs of OA can help elucidate the relationships between muscle weakness, neuromuscular deficiencies and OA. Clinically important signs of OA, such as pain, inflammation and effusion, are consistently described as potent factors that significantly impair muscle strength, neuromuscular function and joint mechanics. In experimental studies, muscle strength and force control is impaired during muscle and joint pain. Similarly, muscle coordination and joint biomechanics are also impaired during experimental pain and joint effusions. In experimental inflammation research studies show plastic changes in both peripheral and central nervous systems in the presence of inflammation. The inflammation causes mechanosensitive joint afferents to increase sensitivity and changing their function to convey nociception. Further, the effects of an exercise regime on pain, physical function and muscle strength decline soon after cessation of an exercise program. This indicates that some underlying mechanisms (e.g. inflammation) are suppressed during exercise but re-emerges to resume impairment of muscle strength and neuromuscular dysfunction. This indicates that pain and inflammation are determinants of functional and neuromuscular deficiencies – not vice versa. Studies on the impact of improved muscle function on disease progression are very few in numbers. Exercise is recommended as a treatment of knee OA and successfully improves muscle function, pain and disability. A generally accepted assumption is that muscle strengthening results in redistribution of load from the cartilage to the muscle. While such mechanism for treatment efficacy is intriguing, muscles act as tension springs defined as operating under tension load and thus cannot serve as 'cartilage unloaders'. Therefore any improvement in pain, inflammation, muscle strength, neuromuscular function and disability raises concern of the risk of increased knee joint loading that is thought to be detrimental to knee OA and accelerate structural changes. The acceptance of increased joint loads as being detrimental questions the current recommendation about pain relief and exercises as serving the best interest of the patients. However, pilot studies challenge this as moderate exercise has been indicated to have positive effects on cartilage glycosaminoglycan-content. Further, results from a recent study offered the opportunity to address the concern of increase loads following improvements in physical function since approximately 1/3 of the participants responded to a significant weight loss by improving physical function in a manner that increased loading at the knee during walking. In summary, observational studies suggest muscle weakness and neuromuscular dysfunctions to be predictive of onset and progression of OA via mechanical pathways, but the data are conflicting and proper study designs are difficult to realize. In contrast, experimental data more consistently suggest muscle weakness and neuromuscular deficits to be caused and determined by biological and structural signs and symptoms of OA. Treatments successfully targeting muscle dysfunctions are successful in alleviating pain and improving physical function, yet the concerns of undesirable increase in joint loadings and subsequent disease progression are rarely considered in trials, but so far improvements in physical function and neuromuscular deficits does not seem to provide detriments to OA progression.

THE USE OF BIOMARKERS IN THE PERSONALIZED MANAGEMENT OF OA PATIENTS: MYTH OR REALITY?

Y. Henrotin
Bone and Cartilage Research Unit, University of Liège, CHU Sart-Tilman, Institute of Pathology, Liège, Belgium

Diagnostic of osteoarthritis is based on history, physical examination and radiographic features. Cartilage damage in OA is detected radiographically by a decrease in joint space width. However, radiographic evidence is seen only after significant cartilage degradation has already taken place. At this late stage, cartilage lesions are irreversible. The early stages of the disease may be asymptomatic for many years and are characterized by molecular/metabolic changes in joint tissues. To detect this molecular/metabolic phase before the occurrence of imaging signs is a key challenge for the next decade. Therefore, there is an acute need for reliable biological markers that can facilitate earlier diagnosis of OA, and inform the prognosis, monitoring and

therapeutic strategies for chronic and disabling forms of the disease. Biomarkers of tissue turnover in joints have the capacity to reflect disease relevant biological activity and provide information that may be useful diagnostically and therapeutically, potentially enabling a more rational and personalized approach to healthcare management. Type II collagen is the ideal source of biomarker for studying cartilage remodeling. First, this collagen is relatively specific to articular cartilage, although it is also present in the vitreous humour of the eye, the nucleus pulposus of vertebral discs and the meniscus. Second, it is the most abundant protein in cartilage, representing 25% of the wet weight, 50% of the dry weight, and 90-95% of the total collagen content. Recently, we have developed a method for the assessment of oxidative damage of type II collagen in cartilage and biological fluids (serum, urine and synovial fluid). This original approach is based on the detection in biological fluids or in tissue of a nitrated peptide release from type II collagen during proteolytic and/or oxidative cartilage degradation. Our strategy was based on the following points: 1) type II collagen is specific for cartilage and is the most abundant collagen in the extracellular matrix, 2) peptide nitration results from the reaction of aromatic acid with -ONOO-, 3) in pathological circumstances, chondrocytes, but also synovium cells (mainly macrophages) produced high levels of $^{\bullet}NO$ and $O_2^{\bullet-}$, 4) type II collagen contains two tyrosine residues, but not other aromatic amino acid, one located in the triple helix (Coll2-1) and the other in the telopeptide of the C-terminal end (Coll2-2). We have then developed specific immunoassays, one for the peptide ^{108}HRGYPGLDG^{116} (Coll2-1) and the other for the nitrated form of this peptide ^{108}HRGY(NO2)PGLDG^{116} (Coll2-1NO_2). This strategy allows the calculation of the ratio Coll2-1NO_2/ Coll2-1 which reflects the oxidative-related damage of the triple helical area of the molecule. These immunoassays have been validated in animal models and in human clinical surveys. For the first time, we show data from two independent NHI studies named “Progression” and “Doxycycline”. Coll2-1NO2 appears be a relevant prognosis biomarker. Coll2-1NO2 variation over one month in urine is highly predictive of joint space width changes over three years. These data support the use of Coll2-1NO2 in the daily practice to predict knee OA progression at an individual level.

MONITORING PROGRESSION OR REMISSION - IMPLEMENTATION OF BIOMARKERS IMAGING, BIOCHEMICAL BIOMARKERS, OR BOTH: CAN THEY PROVIDE INFORMATION ON THE PROGRESSION OR REMISSION OF OP, OA AND RA? FOR IMAGING

D.J. Hunter
The University of Sydney, Sydney, Australia

Imaging has a number of different applications for osteoporosis (OP), osteoarthritis (OA) and rheumatoid arthritis (RA). Firstly and most importantly the utility of biomarkers (whether imaging or biochemical) is not generic for all musculoskeletal diseases and we particularly need to treat the application of biochemical and imaging markers for systemic diseases such as osteoporosis and rheumatoid arthritis quite distinctly from osteoarthritis which is frequently limited to one joint. There are a number of characteristics of a biomarkers that underlie their potential clinical utility including their biologic rationale, clinical relevance, sensitivity and specificity, reliability, practicality (invasiveness and safety) and simplicity for routine utilization. A perfect biomarker is easily measurable, fast, accurate, reproducible, cost-effective and easy to interpret by the clinician. Integral to the utility of a biomarker being clinically useful, it has to answer a clinically relevant question and provide information that is not available in a more simple and cost-effective way. Imaging has a number of distinct advantages especially as it regards direct visualization of the pathology at hand, general clinical acceptance and a wide body of supportive validating literature. For clinicians managing these diseases the main applications of biomarkers pertains to diagnosis, assessing prognosis/ progression and determining the efficacy of interventions used to treat these diseases. Disease diagnosis markers are defined by the ability to classify individuals as either diseased or non-diseased. The key feature of an Intervention/Therapeutic biomarker is that among those with disease or at high risk of developing it, measurable biomarker changes occur as a result of pharmacologic or other intervention, and those changes differ from those who do not receive the intervention. Recent advances in musculoskeletal imaging have enriched our knowledge of disease etiopathogenesis, diagnosis, prognosis prediction and therapeutic efficacy. The last decade has seen major advances in the therapy of rheumatoid arthritis in which imaging determines whether individual agents or therapeutic regimens are structure-modifying. Although the conventional radiograph remains the gold standard for assessing structural progression in RA, growing work on the performance metrics of MRI have resulted in its increasing use in trials. The conventional radiographic erosion remains one of the hallmarks of RA, although erosions may only be present in about 40% of patients at time of clinical diagnosis. Plain X-rays of the hands and feet remain the gold standard for assessment of joint damage progression, as estimated by joint space narrowing and erosions. The increased sensitivity of MRI over clinical examination in detecting synovial inflammation and tenosynovitis, as well as its increased sensitivity over conventional radiographs in detecting bony damage means MRI has attracted considerable attention as an outcome measure for RA clinical trials. Conventional radiography allows qualitative and semi-quantitative evaluation of osteoporosis, whereas other imaging techniques allow quantification of bone loss (e.g., dual-energy x-ray absorptiometry (DXA) and quantitative computed tomography [CT]), assessment for the presence of fractures (morphometry), and the study of bone properties (ultrasonography). In the assessment of osteoporosis, the measurement of bone mineral density (BMD) obtained from dual energy X-ray absorptiometry (DXA) is the most widely used parameter. However, bone strength and fracture risk are also influenced by parameters of bone quality such as micro-architecture and tissue properties. Newer imaging modalities are providing critical insights into the importance of assessing the biomechanical properties of bone architecture. In recent years, new imaging modalities such as micro-CT and high-resolution magnetic resonance imaging have been developed in an attempt to help diagnose osteoporosis in its early stages, thereby reducing social and economic costs and preventing patient suffering. Osteoarthritis (OA) is at the cusp of tremendous advance with a diverse number of parties (including government and industry sponsors) demonstrating a commitment to making inroads into this disabling disease. Recent imaging advances in OA have offered insights into fundamental questions including the etiology of pain and reasons for disease progression. Although ongoing disease modification clinical drug trials in OA mostly use standardized plain radiographs to monitor structural changes in the joint, magnetic resonance imaging is rapidly evolving as a method to monitor joint structure, and with time may become the preferred method to monitor this feature in OA clinical trials. Recent advances in musculoskeletal imaging have enriched our knowledge of disease etiopathogenesis, prognosis prediction and therapeutic efficacy for these diseases and will play an increasingly prominent role in clinical practice. A number of complex challenges face us over the coming years as both clinicians and researchers grapple with the use of these new imaging techniques.

CHRONIC INFLAMMATION AND ADIPOKINES

A. Ioan-Facsinay
Dept. of Rheumatology, Leiden University Medical Center, Leiden, Netherlands

The obesity epidemics is rapidly expanding and has become one of the major health threats in the world, as over 1.5 billion adults and over 43 million children under the age of five are either obese or overweight. Diseases associated with obesity include cardiovascular diseases and diabetes, but also different types of cancer and chronic inflammatory diseases. The biological mechanisms involved in the association between obesity and chronic inflammatory diseases are still unknown. It has, however, become clear during the last 10 years that the adipose tissue is a regulator of whole-body metabolism and not merely a site for energy storage and release. Besides lipids, the adipose tissue can release a high number of cytokines and other soluble mediators that generate a low-grade inflammatory state that could mediate the

systemic effects of obesity. These soluble mediators include inflammatory cytokines such as IL-6 and TNFα, but also adipokines, such as adiponectin, leptin, resistin and others. Adipokines were originally described as adipose tissue-specific cytokines, but have been more recently shown to be secreted by a several cell types and tissues in the human body. In fact, most of the known adipokines are secreted rather by cells infiltrating the adipose tissue than the adipocytes themselves. Moreover, although the characterization of the pro- and anti-inflammatory properties of adipokines is still ongoing, there is accumulating evidence that adipokines can modulate inflammation and the immune system, thereby playing a potentially important role in chronic inflammatory diseases. In this review, current knowledge about the role of adipokines in chronic inflammatory diseases of the joint (Osteoarthritis and Rheumatoid Arthritis) will be summarized, as well as the possible mechanisms involved in these associations.

CAN EFFECTIVE TREATMENTS IN OSTEOPOROSIS AND RHEUMATOID ARTHRITIS ALSO BE EFFECTIVE IN A SELECTED POPULATION WITH OA?

B.L. Langdahl
Department of Endocrinology and Internal Medicine, Aarhus University Hospital, Denmark

Osteoarthritis (OA) is the most common form of arthritis and the prevalence is increasing. The need for effective preventive and treatment measures are therefore urgent. OA is characterized by progressive degeneration of articular cartilage, synovitis and changes to the subchondral bone characterized by increased turnover, thinning of the trabecular structures, sclerosis of the subchondral plate, osteophytes and bone marrow lesions. Pain in OA is associated with synovitis and increased subchondral bone turnover. Based on these observations it has been suggested that drugs that either inhibit synovitis or bone turnover may have beneficial effects on already existing OA and/or be able to prevent the development of OA. Several antiresorptive therapies are available for the treatment of osteoporosis. Bisphosphonates, strontium ranelate and calcitonin have been investigated in clinical studies for their effect on progression of OA. The effects of bisphosphonates on OA have been investigated in two long-term prospective studies with effect on OA as primary endpoint. The BRISK study included 284 women with mild to moderate knee OA treated with risedronate (RIS) 15 mg daily for 12 months. Treatment with RIS resulted in improvement of the WOMAC index, particularly of physical function, and improvement in patient global assessment. Subsequently, a larger study, KOSTAR, was undertaken. 2483 patients with mild to moderate knee OA were included and randomized to different doses of RIS or placebo. Overall, no improvement in signs and symptoms of OA was observed and progression of OA was unaffected by treatment allocation. Serum levels of CTX-II were dose dependently decreased. Posthoc analyses revealed that more pronounced suppression of CTX-II was associated with less progression of the disease. A subgroup analysis of patients with progressive disease demonstrated that RIS preserves structural integrity of the subchondral bone. The effect of strontium ranelate (SR) on OA has been investigated in the TROPOS study, a study designed to examine the effect of SR on fracture prevention. SR reduced serum levels of CTX-II, a marker of cartilage degradation with 15-20% and deterioration of spinal OA with 42%. Back pain was reduced but there was no effect on health-related quality of life. Calcitonin has been demonstrated to reduce serum levels of CTX-II and improve functional disability despite no change in pain in patients with knee OA over 3 months. Also, the use of anti-cytokine therapies has been investigated in OA. In a non-controlled investigation of the effect of intra-articular anakinra, an IL-1R antagonist, in 13 patients with knee OA, anakinra reduced pain and the WOMAC score. The same drug was later on tested in a placebo-controlled study in patients with knee OA and despite a rapid improvement in symptoms in the actively treated patients, no lasting differences between patients treated with anakinra and placebo were found. Inhibition of TNF-alpha with adalimumab has been investigated in a small non-controlled study comprising 12 patients with hand OA. A significant reduction in the number of swollen joints was seen after 12 weeks. No significant changes were seen in any other OA parameters. In order to further investigate the potential of antiresorptive and anti-inflammatory treatments on prevention or treatment of OA, future research should be focused on 1. developing clinical relevant animal models, 2. identifying the pathogenic mechanisms that can be modified by intervention and 3. targeting pharmacological intervention towards those mechanisms in the right patients at the right time.

OSTEOARTHRITIS: THE JOINT IS THE SOURCE OF CHRONIC PAIN. TREAT THE JOINT, TREAT THE PATIENT.

A-M. Malfait
Rush University Medical Center, Chicago, IL, USA

As the most common joint disorder, osteoarthritis (OA) represents a major unmet medical need. A recent American College of Rheumatology task force concluded that pain is the most common symptom of patients with rheumatic disorders, including OA, and pain is the major reason for seeking medical care (Arthritis Care Research 2010). Available pharmacologic approaches include NSAIDs or analgesics, and intra-articular viscosupplementation or steroids, which can alleviate mild-to-moderate pain in OA. Treatment of severe OA pain remains inadequate and pain is a major reason for seeking surgical intervention. The International Association for the Study of Pain defines pain as “An unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage”. Pain occurs when afferent nociceptive neurons are activated by a noxious stimulus of a mechanical, thermal, or chemical nature, and conduct this information to the central nervous system (CNS). Persistent pain in association with injury or disease (such as arthritis) results from alterations in the peripheral nervous system, known as peripheral sensitization, which is commonly caused by inflammation-associated changes in the biochemical environment of the sensory nerve fibers. In addition, changes in the CNS lead to enhanced processing of nociceptive messages, a process known as central sensitization (reviewed in Basbaum et al, 2009). Pain serves a vital role in maintaining the integrity of the body, because it is what forces us to adopt protective behavior when confronted with harmful stimuli. Therefore, when faced with a long-term chronic pain problem like OA, where patients may need to be treated for many years, it is conceivable that profound pain relief may promote joint destruction, analogous to Charcot neuro-arthropathy. Therefore, symptomatic treatment without disease-modifying intervention may cause problems in the long run, especially in an already compromised joint. It has been described that NSAID treatment in patients with knee OA results in reduction in pain and increased loading of the knee (Schnitzer et al, 1993). Furthermore, pain relief without protecting joint integrity will not restore joint function, and ultimately, patients will still need total joint replacement. Current understanding of the origin and mechanisms of pain generation in OA is limited. As in most chronic pain conditions, the correlation between the extent of tissue damage and symptoms appears weak, and this has been mostly studied for knee OA (Dieppe and Lohmander, 2005). Particularly for knee OA, multiple studies have examined the association between radiographic severity and pain, concluding that the correlation is low (Bedson and Croft, 2008). Many recent studies have attempted to find correlations between pain and specific tissue changes in the joint. A relationship between specific radiographic changes and pain experienced by patients has been reported (Duncan et al, 2007; Neogi et al, 2009). Other imaging techniques such as magnetic resonance imaging (MRI) can visualize joint tissues that cannot be seen on radiographs, and many studies have related structural changes including bone marrow lesions, sub-articular bone attrition, synovitis and effusion to knee pain (reviewed in Hunter et al, 2009). Interestingly, people with chronic symptomatic knee OA experience fluctuations both in the presence and the intensity of knee pain, and a recent study has shown that changes in bone marrow lesions and synovitis are associated with these fluctuations – pain resolution occurs more frequently when bone marrow lesions become smaller (Zhang et al, 2011). Further studies like these will provide the foundation for interventions that target specific structural

abnormalities. Pain requires sensory input from the damaged tissue. The source of pain in the arthritic joint is not clear. OA is a slowly progressing pathology, and molecular events in the joint predate radiographic changes, possibly by many years. During this time, molecular and cellular changes in joint tissues may affect the joint's sensory innervation and thus trigger changes that may ultimately lead to chronic pain. OA affects all tissues in the joint, including the subchondral bone, the synovium, the fat pad, the ligaments (all of which are richly innervated), and of course the articular cartilage. As an aneural and avascular tissue, cartilage is not likely a direct source of pain, but it consists of an exquisite network of extracellular matrix molecules that are degraded and released into the synovial cavity during the OA pathological process, and we can assume that matrix fragments will interact with nociceptors in the synovium and elsewhere. Moreover, episodic synovitis is a frequent feature of OA, and inflammatory mediators are part of the pathology. Animal models of OA, particularly in rodents, are often too aggressive to allow for a careful evaluation of the correlation between joint structure and symptoms, and very few animal studies have properly examined mechanisms of chronic pain in OA. We recently reported that destabilization of the medial meniscus (DMM) (Glasson S et al, 2007) offers an appropriate murine model to study the relationship between structural changes and pain. We observed a robust and progressive decrease in withdrawal threshold to a mechanical stimulus in the hindpaw after DMM but not sham surgery. This secondary mechanical allodynia (= a pain response to an innocuous stimulus, indicating central sensitization) was apparent as early as 14 days post-surgery and was progressive over 8 weeks. *Adamts5* null mice, which are protected from cartilage degeneration and OA progression in this model (Glasson et al, 2005), did not develop mechanical allodynia (Malfait et al, 2010). Further studies are required to understand the dynamic relationship between structural changes in this model (e.g. cartilage changes, changes in the subchondral bone) and pain-dependent measures. It will be of paramount importance to test potentially disease-modifying compounds such as ADAMTS-5 inhibitors in preclinical models, to investigate whether structural protection of the joint will be accompanied by analgesia. Currently, disease-modifying treatments for OA are not yet available, but clinical and preclinical data listed above warrant their future development. Chronic pain associated with OA is the result of a complex interaction between local events in the joint, peripheral and central sensitization, the brain, psychological and social factors, and co-morbidities. Therefore, the approach to treating the patient with chronic OA pain should integrate these different aspects, including joint protection. This will become increasingly important as more efficacious analgesic approaches become available, because at that time, preservation of joint function will become the main concern.

FOOD SUPPLEMENTS: WHICH ARE THE USEFUL ALTERNATIVES OF RANDOMIZED CLINICAL TRIALS TO DEMONSTRATE BENEFICIAL PHYSIOLOGICAL EFFECT ON JOINTS OR A REDUCTION OF JOINTS DEGENERATION IN PEOPLE WITHOUT OSTEOARTHRITIS?

M. Marty

Rheumatology Department, Teaching Hospital Henri Mondor, Cretiel, France

Osteoarthritis (OA) is a common chronic health problem, leading to pain, disability, impaired health-related quality of life, work loss and high cost burden. Treatment is primarily symptomatic and at present there is no known cure. Then all opportunities which can prevent or reduce onset of OA should be developed. Present topic is focused on the primary prevention by food supplements (FS) in individuals without osteoarthritis. OA is chronic disease which represents a good paradigm of physiopathology in which nutrition could play a crucial role to prevent it. Beyond the regulation many words are used to named FS : dietary supplement, functional supplement, nutritional supplement, nutrient, nutraceuticals...For some FS, the borders between drugs and food supplement is blurred depending of the daily dose, galenic formulation, country.....Dietary supplement, food supplement, functional supplement, nutritional supplement are required to keep good health then nutraceuticals have a preventive medical approach. This point highlights also the fuzziness of the definition of a physiological effect to decrease the onset of a disease. Contribution to the maintenance of normal joints is considered to be a beneficial physiological effect (1). Health claims should have been based on a high standard of evidence. Among FS, good candidates for prevention of OA could be those which have already demonstrated relevant preclinical evidence in *in vivo* experimental studies and above all clinical evidence of efficacy and good safety in patients with OA (2). On the whole, international agencies as EFSA consider that evidence demonstrated in patients with OA with a FS cannot be extrapolated to the target population of patient without OA (1). According to EFSA, studies measuring the rate of cartilage degeneration (e.g. changes in joint space width) in individuals without osteoarthritis could be used for the scientific substantiation of disease risk reduction claims (1). In 2011, the Working Group for Prevention and Risk Reduction of OARSI-FDA initiative published methodological issues in clinical trials for prevention or risk reduction in OA (3). Prevention refers to agents or actions that curtail or delay the onset of OA. Risk reduction refers to decreasing specific and modifiable risk factors associated with the development of OA, in an attempt to decrease the likelihood of developing OA or to delay its onset. Ideally, to demonstrate beneficial physiological effect on joints or a reduction of joints degeneration in people without osteoarthritis, aims of trials should be to demonstrate that an action prevents structurally-defined OA or symptoms OA or even surgery. The optimal target population would be at risk for future OA meaning free of full evidence satisfying definition of OA. The Working Group highlighted the drawbacks to define such population. Disease continuum between well-being populations, at risk populations, established disease and controlled chronic disease leads to the question of the concepts of normality and the norm which are at the heart of French physician René Canghuilhem's work (4). The double blind randomized controlled (placebo or other) trial (DB-RCT) is acknowledged as the most scientific rigorous study design for evaluating interventions on health. FS allow using of complete blind. The key points of a high quality RCT protocol are now well defined to avoid bias of effect. Nevertheless, evidence drawn from a RCT depends on the protocol but also the conduct of the clinical trial, the data analysis and the reporting of results. Main features can leading to bias in RCTs assessing prevention of OA with FS: 1/ duration of the trial (several years and depending of the primary end points) 2/ co- interventions which interfere with the expected effect 3/ management of missing data related to withdrawal and loss of follow up for an ITT analysis 4/ level of observance FS including 5/ needing to adjusted analysis on known risk factors 6 / choice of the primary end point and the minimal difference expected between FS group and control group 7/ assessment of safety 8/ ethical problems. All this pitfalls must be making careful on the conducting of this kind of study. Means to counteract all this source of bias could be: 1) To optimize the definition of pre-clinical OA and OA (for research) using genomics, biochemical (5) or imaging biomarkers. The predictive validity of these genomics, biochemical or imaging biomarkers should be developed. These parameters can used as to define target population. Then use of validated surrogate end points could shorten the duration of study. Collections of extensive biological specimens e.g. serum plasma, urine should be part of future studies. 2) To choose statistical analysis using time-to-event endpoints taking account time and incidence. 3) To use modern tools of communication to follow up patient. 4) To use a design other than DB-RCT to demonstrate beneficial physiological effect on joints or a reduction of joints degeneration in people without osteoarthritis: cluster randomized trial, special method of contentment of consent, no randomized comparative study. 5) To conduct observational study to assess effect of FS on joint health. Many possibilities are available to limited bias. But causation and causal inference remains always a subject of debate (6). 6) To conduct observational study to improve scientific knowledge on clinical course of OA (over 10, 20 or more years) to improve scientific knowledge on clinical course of OA and to develop risk prediction model (7). Finally, DB-RCT remains the gold standard using clinical validated end point to demonstrate the effect of an intervention on onset of OA. But conducting such trials needs very long period of follow up and highlights many potentials pitfalls.

Using surrogate end points as validated imaging markers or biomarkers in DB-RCT or conducting study with other design than DB-RCT could be provide sufficient evidence to support health claims and avoid that scientific progress was not translated in practice. Nevertheless safety FS vigilance should be developed as the same time. It would be suitable than guidelines should be established.

References:

1. EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA); Draft guidance on the scientific requirements for health claims related to bone, joints, and oral health released for public consultation. EFSA Journal 20xx;x(x):xxxx. [11 pp.]. doi:10.2903/j.efsa.20NN.NNNN. Available online: www.efsa.europa.eu/efsajournal.
2. Henrotin Y, Lambert C, Couchourel D et al. Nutraceuticals: do they represent a new era in the management of osteoarthritis ? A narrative review from the lessons taken with five products. Osteoarthritis Cartilage 2011;19:1-21.
3. Jordan JM, MF Sowers MF, Messier SP et al. Methodological issues in clinical trials for prevention or risk reduction in osteoarthritis. Osteoarthritis Cartilage 2011;19:500-508.
4. Horton R. Georges Canguilhem: philosopher of disease. J R Soc Med 1995;88:316-319.
5. Mobasheri A, Henrotin Y. Biomarkers of osteoarthritis: a review of recent research progress on soluble biochemical markers, published patients and areas for future. Recent Patents on biomarkers. 2011;1-1-19.
6. Rothman KJ, Greenland S. Causation and causal inference in epidemiology. Am J Public health 2005;95:S144-S150.
7. Zhang W, McWilliams DF, Ingham SL et al. Nottingham knee osteoarthritis risk prediction models. Ann Reum Dis 2011;70:1599-1604.

INFLAMMATION DOES NOT CAUSE SYNDESMOPHYTES FORMATION

R. Meliconi
Rizzoli Orthopaedic Institute and University of Bologna, Italy

Mechanisms leading to syndesmophyte formation and ankylosis in Spondyloarthritis (SpA) are partially unknown: molecules regulating new bone formation, such as Transforming Growth Factor-β (TGF-β) Bone Morphogenic Protein (BMP), Wnt signaling pathway and its inhibitors (Dickkopf -DKK- 1 and sclerostin) (Schett g, Am J Med Sci, 2011; Diarra D et al., Nat Med, 2007) may have a key role in driving bone overgrowth in SpA. Noteworthy TNFα is a key inducer of DKK-1. Growing body of evidence concerning DDK-1 and sclerostin involvement in spine joint remodeling has been reported:

- DKK-1 blockade promotes ankylosis of the sacroiliac joint in an animal model (Uderhard S et al., Ann Rheum Dis, 2010) - DKK-1 and sclerostin serum levels are lower in patients with ankylosing spondylitis (AS) than in healthy subjects (Kwon SR, Rheumatol Int, 2011; Appel H, Arthritis Rheum, 2009) - Functional DKK-1 levels appear to be significantly higher in AS patients with no syndesmophyte formation compared to those with syndesmophyte occurrence (Heiland GR, Ann Rheum Dis, 2011)
- lower levels of DKK-1 in patients with AS are unmodified after 3 months of anti-TNFα therapy (Kwon SR, Rheumatol Int, 2011).

These data are related to the evidence that TNFα blockers in AS, despite their strong anti-inflammatory effect, do not influence new bone formation. These findings, together with data obtained from animal models (Lories RJ, Arthritis Rheum, 2007), may support the concept that bone response in SpA is not entirely related to inflammation. They suggest a more complex, and still unraveled interplay of various inflammatory and metabolic (growth factor) molecules, unlike the apparently straightforward mechanism of bone erosion in Rheumatoid Arthritis

RECOMMENDATIONS ON THE MANAGEMENT OF FRAGILITY RISK FRACTURE WOMEN THAT ARE YOUNGER THAN 70 YEARS

S. Palacios
Palacios Institute of Woman's Health, Madrid, Spain

Osteoporosis is predictable and treatable, but the lack of warning signals before a fracture means that few patients are diagnosed in the early phases of the disease and effectively treated. It is women under 70 years of age that make up this group. Osteoporosis is the most significant risk factor, and the one with the highest predictive value, for fragility fractures (nontraumatic or minimally traumatic). Knowledge of the risk factors for detecting those patients most likely to have the disease is important for detecting those patients most likely to develop the disease. Nevertheless, correcting the modifiable factors also has considerable therapeutic implications. When the risk factors and BMD for each woman have been determined, the clinician will be in a position to be able to speak with the patients about their risk level for fractures. That notwithstanding, it will also be the clinician's obligation to encourage changes in patient lifestyles, predict which health resources to use and carry out a minimal cost/utility analysis for the intervention alternatives for the disease. The need to treat osteoporosis is justified by the reduction in the risk for fracture by increasing the bone strength with this intervention. There are no fixed rules or established protocols about which drug or model to use. The decision to initiate and the type of treatment should be based on the necessity to reduce the risk for fracture. In each case, and aside from the BMD and other more important risks, the following factors should be taken into account: renal function, drug allergies, comorbidities, previous treatments, contraindications, secondary effects of drugs and cost. This way, establishing the risks and benefits of a drug is possible for each patient. Furthermore, it is important to take into consideration how to improve adherence. Osteoporosis, being a chronic disease that requires treatment over many years, makes it necessary to use individualized measures and sequential treatments. In theory, treatment in the first few postmenopausal years could start with the use of drugs aimed at the physiopathology of the rapid loss of bone mass produced by the increase in bone resorption as a result of the decrease in estrogens. The most appropriate drugs for these women are HRT, and, for asymptomatic women, SERMs. Another possibility would be to first use HRT for two or three years, followed by SERMs. Afterwards, there is a period where there is an increase in the resorption and a decrease in formation. This coincides with >10 years postmenopause and with a greater risk for hip fracture. This is when drugs such as the bisphosphonates, strontium ranelate and denosumab have clearly shown their effectiveness. Finally, and in women older than 70-75 years of age, there is an important decrease in formation. PTH should be used in women who continue to fracture while being on antiresorptive therapy.

INHIBITION OF SCLEROSTIN IN THE TREATMENT OF OSTEOPOROSIS; WILL IT SOLVE THE PROBLEM OF ANABOLIC THERAPY?

S.E. Papapoulos
Department of Endocrinology & Metabolic Diseases, Leiden University Medical Center, Leiden, Netherlands

During the past few years there have been significant developments in the pharmacotherapy of osteoporosis. These developments were paralleled by significant progress in our understanding of the local regulation of bone metabolism. Particularly, studies of human and animal genetics have led to identification of novel, more specific, signaling pathways in bone cells that can provide targets for new therapeutics for osteoporosis. Such novel targets in osteoclasts include, among others, RANKL and cathepsin-K. A fully human monoclonal antibody to RANKL (denosumab) was developed and approved worldwide for the treatment of osteoporosis while cathepsin-K inhibitors have been evaluated in phase 2 studies and are currently in phase 3 clinical development. The PTH paradigm illustrated the possibility of stimulating bone formation in osteoporotic patients and opened the way for the development of bone forming agents and novel forms of PTH or PTHrP are at

different stages of clinical development. The most exciting development of recent years has been, however, the recognition of the central role of the Wnt signaling pathway in the regulation of bone formation which, in turn, provided a number of attractive targets for the development of pharmaceuticals for the specific stimulation of bone formation. Fundamental for this development have been studies of two bone sclerosing dysplasias, sclerosteosis and van Buchem disease that led to the identification of sclerostin, an important negative regulator of bone formation. Sclerosteosis and van Buchem disease are two rare bone disorders with closely related phenotypes characterized by overgrowth of bone of excellent quality which are due to defective production of sclerostin. Sclerostin is a glycoprotein that binds to LRP5/6 and inhibits Wnt signaling by a not yet identified molecular mechanism. Its expression is restricted to osteocytes and is modified by mechanical loading and PTH treatment. Sclerostin deficiency reproduces the findings of the human diseases in mice, while sclerostin excess leads to bone loss and reduced bone strength. An antibody to sclerostin given to OVX rats or intact monkeys increased bone formation dramatically at all bone envelopes, including the periosteum, without affecting, or even decreasing, bone resorption and improved bone strength. In initial human studies, a single injection of the antibody to healthy postmenopausal women increased serum P1NP and transiently decreased serum CTX. Clinical phase II studies with this, and other, sclerostin inhibitors are currently underway. The restricted expression pattern of sclerostin in bone, the excellent bone quality of patients with sclerosteosis and van Buchem disease and the lack of abnormalities in organs other than the skeleton in these patients are reassuring for the efficacy and safety of sclerostin inhibition in humans. It should be noted, however, that the kinetics of bone remodeling in response to repeated administration of sclerostin inhibitors to humans have not yet been established and there is no information about the nature and the magnitude of the response (transient or sustained) which will ultimately determine their use in clinical practice. Apart from establishing the efficacy and optimal way of administration of these new molecules, a critical issue for their introduction into clinical practice will be their tolerability and safety profile in as much as very little is known about potential outcomes of sustained exogenous stimulation of Wnt signaling. Stimulating bone formation in patients with osteoporosis by approaches as this, may allow in the future tailoring pharmacotherapy to the specific needs and pathophysiological profile of the individual patient.

METABOLIC DISEASES AND OSTEOARTHRITIS

P. Richette
Assistance Publique-Hôpitaux de Paris (APHP), Hôpital Lariboisière, Paris, France

Recent data have shown that primary osteoarthritis (OA) is not simply a disease related to aging or mechanical stress of joints. Indeed, OA has been linked in epidemiological studies not only to obesity but also to other cardiovascular risk factors, namely, diabetes mellitus, dyslipidemia, hypertension, and insulin resistance, suggesting that systemic factors could also play a role in the genesis of OA joint damage.

METABOLIC MARKERS OF PRE-OA AND EARLY OA IN HIP AND MENISCUS

L.J. Sandell[1], F. Rai[1], R. Brophy[1], S. Hashimoto[1], J. Clohisy[1]
[1]*Department of Orthopaedic Surgery, Washington University School of Medicine, St. Louis, MO, USA*

Introduction: Treatment of osteoarthritis (OA) requires early detection of the disease when cartilage and other joint structures are pretty much intact. The classic method of detection of OA requires the narrowing of the joint space such that it can be detected on an X-ray. By this time, a great deal of time has been lost since the early stages of the disease and the tissue is beyond repair. In order to look for early stages of osteoarthritis, we choose to look at two joint problems that are known to predispose the patient to osteoarthritis, but still have intact cartilage: meniscal repair and femoral-acetabular impingement (FAI) of the hip. FAI is a frequent cause of hip pain in young adults and may increase the risk of developing secondary OA. Little is known about the cellular and molecular events linking mechanical hip impingement and biologic degeneration of affected articular cartilage. The meniscus functions as a load-bearing and shock-absorbing part of the tibiofemoral joint. Surgical procedures on the meniscus are the most commonly performed procedures in orthopaedics and approximately 50% of people with meniscal tears have radiographic evidence of OA ten to twenty years after injury. For this study, we hypothesized that these two syndromes may exhibit molecular events that predispose the tissue to OA and that the cells could be metabolically active in degrading or replacing the cartilage extracellular matrix. Methods: RNA was isolated from meniscal tissue retrieved at the time of surgery to remove a portion of the damaged meniscus (N=40). For meniscus analyses, samples were separated into meniscal tears alone or meniscal tear plus rupture of the anterior cruciate ligament. For FAI, tissue was obtained femoral neck at the time of surgery to preserve the joint and capsule (N=32). Each frozen tissue specimen was thawed and homogenized directly in TRIzol reagent using a Polytron homogenizer. RNA was extracted and purified using chloroform with a final purification by RNAeasy Mini Spin Columns (Qiagen). Specific mRNA was detected using real time PCR. Other parameters were measure as appropriate for each tissue. For gene analysis, candidate genes representing inflammation, matrix synthesis and matrix degradation were monitored. We quantitated gene expression of inflammatory cytokines and chemokines (IL-1β, IL-8, CXCL1, CXCL2, CXCL3, CXCL6, CCL3 and CCL3L1), degradative enzymes (MMP-13, ADAMTS4) and major cartilage extracellular matrix structural proteins (COL2A1, Aggrecan). Results: **Meniscus.** For the meniscus studies, mRNA levels were compared in patients over 40 years and under 40 and with and without ACL tear. We found significantly higher levels of pro-inflammatory cytokines and chemokines in the younger patients, but more enzyme and extracellular matrix synthesis in the older patients. For the meniscal tear plus ACL tear, the cytokines and chemokines were higher in the combined injuries, while matrix synthesis was lower. The type II collagen degrading enzyme, MMP-13, was higher in the combined injuries. **FAI.** Articular cartilage from hips with FAI expresses high levels of factors that increase inflammation, promote destruction of cartilage matrix and synthesize matrix. These factors are upregulated early in the disease process and represent a heightened metabolic state of cartilage in response to the abnormal mechanics of FAI. All were higher than normal control cartilage. IL-1β, CXCL3, and MMP13 were similar to expression levels from cells of OA patients taken at the time of total joint replacement. IL-8, CXCL1, CXCL2, CXCL6, CCL3, CCL3L1 ADAMTS4 COL2A1 were all higher in FAI than OA chondrocytes. Discussion and Conclusions In both of these syndromes, one knee and one hip, the inflammatory cytokines and chemokines were higher potentially indicating a high degree of cellular activity of these tissues that may lead to OA. The ability to synthesize extracellular matrix was significantly lower in the combined meniscus plus ACL injury potentially suggesting that this injury in more likely to result in OA. The finding that the hip syndrome FAI has such active articular cartilage also indicates that this tissue is responding to the impingement by increasing activity. A weakness of this study is that we cannot return to the same joint to determine whether surgery has changed gene expression. However, certain molecules that are increased such as CCL3, CCL3L1, IL-8 and CXCL1 can be measured in serum and future studies will address the question of using these up-regulated molecules are biomarkers of the increased joint metabolism stimulated by injury and impingement.

CHONDROITIN SULFATE: REVIEW OF THERAPEUTIC EFFICACY

D. Uebelhart
Medical Director and Head of Musculo-Skeletal Rehabilitation, Valmont, Private Rehabilitation Clinic, Glion sur Montreux, Switzerland

Symptomatic Slow-Acting Drugs for the treatment of Osteoarthritis (SYSADOA) are compounds which are prescribed as drugs in European countries since many years, whereas they are sold as nutraceuticals in USA. In Europe, the publication of the EULAR

Recommendations for the treatment of knee OA in 2003 has listed oral chondroitin sulphate as evidence 1A and strength of recommendation A which represents the highest level for a therapeutic strategy. Symptomatic slow-acting drugs are intended to be used as ground therapy for osteoarthritis; these compounds are not rapidly acting agents such as NSAID's and their clinical efficacy on algo-functional symptoms can only be demonstrated after a couple of weeks of regular intake. Interestingly, once the administration is stopped, they do show a carry-over effect of various durations from about 3 months with the oral formulations to 6-9 months with intra-articular formulations. The main rationale behind the use of the SYSADOA therapeutic class is the reduction of NSAID's in the overall drug management of OA disease and therefore consequently to limit the very significant risks of upper GI tract erosions, ulcers with bleeding and/or deleterious renal effects in elderly patients. **Oral Chondroitin Sulfate as a Symptomatic Slow-Acting Drug for the treatment of osteoarthritis (SYSADOA):** Chondroitin sulfate (CS) belongs to the oral SYSADOA and the substance does have a delayed mode of action in OA which means that the first effects on pain and mobility can only be assessed after a couple of weeks of therapy (2-3 weeks) in sharp contrast with analgesics and NSAIDs which do act more rapidly (1-3 days). Importantly, when stopped after 3 months of continuous daily administration, CS will present in most cases with a remnant effect which can last for a couple of months in some cases, a feature which is never observed with analgesics and NSAIDs, substances which need to be continuously administered in order to provide relief in pain and increased mobility in OA patients. An important consideration to be made at this stage is that oral CS is registered as a drug in many European countries whereas it is sold as a prescription free and over-the-counter (OTC) substance in all drugstores in the USA since many years. The differences between both markets are obvious. The oral CS sold and used on the European market has been fully registered as a drug which means that it had to fulfil severe criteria of quality and safety and was fully analysed regarding its pharmacotoxicologic characteristics and industrial processing. These requirements are not applied to the CS sold as OTC on the American market. There is no doubt that the actual content of active substance and its quality in various brands of CS sold on the US market is not directly comparable with the CS at disposal in the European countries, which might also explain why the results of the clinical trials might differ significantly between both North America and Europe. We did a survey of the available randomized clinical trials (RCTs) to assess the clinical efficacy and tolerability of oral CS and did choose to review the evidence on the basis of the published literature which was critically analyzed. The results of this review were published in 2006 (Uebelhart D et al, 2006). Briefly, the authors did assess the effects of oral CS on osteoarthritis of the knee using the available outcome criteria such as the Lequesne's Algofunctional Index (AFI), the Huskisson Visual Analog Scale for Pain, the Walking Time, the WOMAC Score as well as analysing the safety and tolerability data. The literature search yielded 11 reports that met the basic eligibility criteria of being an RCT which assessed the effects of oral CS on knee OA. A total of 1443 patients were included originating from France: Mazières et al, 2001; Bourgeois et al, 1998; Conrozier, 1998; and l'Hirondel, 1992; Switzerland: Michel et al., 2005; Uebelhart et al., 2004; Uebelhart et al., 1998, and Uebelhart et al (unpublished); Belgium: Malaise et al., 1999; Hungary: Bucsi and Poor, 1998; Tschech Republic: Pavelka et al., 1999..Several varieties of CS were used (bovine, shark, avian) which also differed in dosage (500 to 1200 mg/day), treatment time (3 to 24 months) and mode of administration, daily continuously (3 to 24 months) or intermittently (2 x 3 months). The results of this survey taking into account exclusively RCTs, 10 published in peer-reviewed journals and one study still not published so far, having the highest methodological quality, can be qualified in the overall as very positive for CS as an oral SYSADOA for the treatment of knee OA. Indeed, they did prove that the long-term administration of oral CS is safe, well tolerated and fully indicated to control the symptoms of pain and increase the overall mobility of knee OA patients. More recently, Gabay et al. did perform a well-designed RCT to access the symptomatic effects of 800mg/daily of CS 4&6 versus Placebo in 162 patients suffering from hand OA over 6 months. This study did provide the evidence that oral CS 4&6 significantly improved both hand pain and function in patients with symptomatic OA of the hand combined with a good safety profile (Gabay et al. 2011) **Meta-analyses on Chondroitin Sulfate in OA:** Before the meta-analysis of Reichenbach et al., 2007 was published, two other ones were available. Based on data originating from published studies available at the time of the publication, both Leeb et al., 2000 and McAlindon et al., 2000 did provide some positive effects (moderate to large) of oral CS on the relief of painful symptoms in OA patients. The latest published meta-analysis by Reichenbach et al, 2007 did provide some more critical insights in the effects of oral CS in OA pain. The authors did analyse 20 trials including a total of 3846 patients originating from randomized and quasi-randomized published studies focusing on pain relief in patients suffering from knee and hip OA as well. The authors did find for CS a pooled effect size of -0.75 (95% CI, -0.99—0.50) corresponding to a large symptomatic effect of the substance. This very positive result definitively goes along with the previous published meta-analyses, but the final interpretation of the authors was surprisingly negative about a symptomatic effect of the substance. It is worth noting that this meta-analysis presented with numerous bias and methodological problems which were also addressed as sound critics by some experts in the field of OA therapy who wrote letters to the Editor. One way to solve the problem raised by this controversial publication and to become a clear picture of the effects of oral CS in OA patients would be to perform a high-quality meta-analysis based on the raw data of the RCTs on CS and not based on the extracted data from the publications which are always incomplete. This was performed using the setting of the published RCTs performed with CS4&6 (Condrosulf™), but not including so far the last symptomatic data provided by the hand OA study of Gabay et al. The results of this analysis based upon 10 RCTs provided an effect size of CS 4&6 versus PBO at 6 months = 0.66 (95%CI: 0.37-0.95) as an ITT analysis (Uebelhart et al. unpublished results). Conclusion: Based upon published peer-reviewed RCT's and all available meta-analyses (published and upcoming, oral CS has so far proven efficacy in symptomatic knee and hand OA. In addition, the tolerability and the safety profile of the substance was found to be good in all available RCT's performed.

References:

1. Uebelhart D, Knols R, de Bruin ED, Verbruggen G. Treatment of knee osteoarthritis with oral chondroitin sulfate. In: Chondroitin Sulfate: Structure, role and Pharmacological Activity. Amsterdam: Elsevier Inc; 2006
2. Mazieres B, Combe B, Phan Van A, Tondut J, Grynfeltt M. Chondroitin sulfate in osteoarthritis of the knee: a prospective, double blind, placebo controlled multicenter clinical study. J Rheumatol 2001;28:173-81.
3. Bourgeois P, Chales G, Dehais J, Delcambre B, Kuntz JL, Rozenberg S. Efficacy and tolerability of chondroitin sulfate 1200 mg/day vs chondroitin sulfate 3 x 400 mg/day vs placebo. Osteoarthritis Cartilage 1998;6A:25-30.
4. Conrozier T. Anti-arthrosis treatments: efficacy and tolerance of chondroitin sulfates (CS 4&6). Presse Med 1998;27:1862-5.
5. Michel BA, Stucki G, Frey D, De Vathaire F, Vignon E, Bruehlmann P, *et al.* Chondroitins 4 and 6 sulfates in osteoarthritis of the knee: a randomized controlled trial. Arthritis Rheum 2005;52:779-86.
6. Uebelhart D, Malaise M, Marcolongo R, De Vathaire F, Piperno M, Mailleux E, *et al.* Intermittent treatment of knee osteoarthritis with oral chondroitin sulfate: a one-year, randomized, double-blind, multicenter study versus placebo. Osteoarthritis Cartilage 2004;12:269-76.
7. Uebelhart D, Knüsel O, Osterkorn K, Berz S, Przybylski C, Theiler R. Oral chondroitin Sulfate in patients with femorotibeal osteoarthritis: A six-month multicentre, randomised double-blind, placebo-controlled, parallel-group study, Unpublished (personal communication).
8. Malaise M, Marcolongo R, Uebelhart D, Vignon E. Efficacy and tolerability of 800 mg oral chrondroitin 4&6 sulfate in the treatment of knee osteoarthritis: a randomised, double blind, multicentre study versus placebo. Litera Rheumatologica 1999;24:, 31-42.

9. Bucsi L, Poor G. Efficacy and tolerability of oral chondroitin sulfate as a symptomatic slow-acting drug for osteoarthritis (SYSADOA) in the treatment of knee osteoarthritis. Osteoarthritis Cartilage 1998;6A:31-6.
10. Pavelka K, Manopulo R, Bucsi L. Double-blind, dose-effect study of oral chondroitin 4&6 Sulfate 1200 mg, 800 mg, 200 mg and placebo in the treatment of knee osteoarthritis. Litera Rheumatologica 1999;24:21-30.
11. Reichenbach S, Sterchi R, Scherer M, Trelle S, Bürgi E, Bürgi U, *et al.* Meta-analysis: chondroitin for osteoarthritis of the knee or hip. Ann. Int. Med. 2007;146:580-90.
12. Leeb BF, Schweitzer H, Montag K, Smolen JS. A meta-analysis of chondroitin sulfate in the treatment of osteoarthritis. J Rheumatol 2000;27:205-11.
13. McAlindon TE, LaValley MP, Gulin JP, Felson DT. Glucosamine and chondroitin for the treatment of osteoarthritis: a systematic quality assessment and meta-analysis. JAMA 2000;283:1469-75.
14. Gabay C, Medinger-Sadowski C, Gascon D, Kolo F, Finckh A. Synmptomatic effects of chondroitin 4 and chondroitin 6 sulfate on hand osteoarthritis. A randomized, double-blind, placebo-controlled clinical trial at a single center. Arthritis & Rheumatism 2011; 63: 3383-3391.

A FOCUSED APPROACH FOR A BROADER UNDERSTANDING: JOINT HEALTH IN HEMOPHILIA PATIENTS

M. Denne[1], **L. Yamamoto[1]**
[1]Hemophilia – Medical Affairs, Baxter Bioscience, USA

The most common complication in patients with severe hemophilia is recurrent hemarthrosis, which can result in the development of target joints. Target joints are defined as joints with frequent and recurrent bleeding, commonly defined as a joint in which there have been ≥ 4 or more bleeds in a consecutive 6 month period.[1] This recurrent bleeding is thought to be the result of synovial inflammation and increased friability that results in an increased propensity to bleed. The eventual clinical outcome of these continual hemarthroses are well documented and include chronic arthropathy, disability, reduced quality of life and potentially the need for joint repair or replacement.[2] It has been shown, in children that the use of primary prophylaxis to prevent hemarthrosis results in preservation of joint function. The hallmark study evaluated boys < 30 months of age treated with prophylactic vs. on-demand factor replacement therapy. The study found significantly decreased bleeding events in this population and 93% of subjects in the prophylactic group had normal index-joint structure by MRI as compared to 55% of those on episodic therapy.[3] There is a paucity of data, however, evaluating secondary prophylaxis in adults.

Interestingly, little is known regarding the pathogenesis of hemophilic arthropathy, and local evaluation of synovial fluid, synovium, cartilage and bone is limited due to the increased risk of bleeding following invasive evaluation in this patient population.

In addition to arthropathy resulting from bleeding events, osteoporosis is another issue facing the adult hemophilia population. The hemophilia population, as a result of improved diagnosis and treatment over recent years, has a life span approaching that of the normal population, which places these patients at an increased risk for development of age related osteoporosis.[4] In addition to traditional risk factors for bone loss as seen in the general population, hemophilia patients have prolonged periods of immobility and may have additional risk factors resulting from chronic joint bleeding events. An existing pool of data suggests that the low bone mass is more prevalent in the hemophilia population compared to the general population and that a number of factors, including the degree of joint damage, correlate with low bone mass.[5] Further research directions are needed to understand the pathologic changes that are occurring in the adult hemophilic joint. Validated tools for measuring quantitative and semi-quantitative changes in knee cartilage using MRI and ultrasound are needed. Additionally, peripheral markers of bone, cartilage and synovial turnover need to be investigated to evaluate correlations with current and ongoing bone and joint damage.

Future directions include preclinical modeling of joint damage (e.g. mouse and rat models of hemophilic arthropathy and osteoporosis), longitudinal measures of biomarkers following bleeding events, further investigation of the role of inflammation (both localized and systemic) resulting from recurrent joint bleeding and ties to other inflammatory disease states (e.g. cardiovascular disease) and finally, points of clinical intervention.

References:

1. Centers for Disease Control and Prevention. The Universal Data Collection Program. July 2006/Vol8/No. 1. Available at: http://www.cdc.gov/ncbddd/hbd/documents/UDC8(1)Fc.pdf
2. Carcao M, Chambost H and Ljung R. Devising a best practice approach to prophylaxis in boys with severe haemophilia: evaluation of current treatment strategies. Haemophilia 2010;16:4-9.
3. Manco-Johnson MJ, Abshire TC, Shapiro AD et al. Prophylaxis versus episodic treatment to prevent joint disease in boys with severe hemophilia. N Engl J Med 2007;357:535-44.
4. Soucie JM, Nuss R, Evatt B et al. Mortality among males with hemophilia: relations with source of medical care. Blood. 2000;96:437-442.
5. Brown-Glaberman U, Cordoba Kissee M, Damiano ML, Roe DJ, Stopeck AT. Decreased bone mineral density in adult patients with hemophilia: Clinical significance, prevalence and risk factors. JCD 2011;3:27-33.

JOF/JOS SESSION ABSTRACTS

Japanese Osteoporosis Foundation/Japanese Osteoporosis Society (JOF/JOS)

FRACTURE RISK REDUCTION BY THE COMBINATION THERAPY OF ALENDRONATE WITH ALFACALCIDOL IN OSTEOPOROSIS PATIENTS: THE JAPANESE OSTEOPOROSIS INTERVENTION TRIAL (JOINT)-02

T. Hosoi
Department of Clinical Research and Development, National Center for Geriatrics and Gerontology, Obu City, Aichi, Japan

The A-TOP research group was established within the Japan Osteoporosis Society to confirm the clinical significance of concurrent use of osteoporotic drugs. A-TOP stands for adequate treatment of osteoporosis and the group is chaired by Dr. Hajime Orimo. JOINT-02, the second protocol of A-TOP was started in 2003 and conducted to evaluate the effectiveness of the most frequent combination therapy at that time in Japan which is the combination of alendronate and alfacalcidol. Subjects were postmenopausal osteoporosis patients nationwide with a high risk of fractures, randomly allocated between the monotherapy group (alendronate, 5mg/day) and the combination therapy group (alendronate, 5mg/day; alfacalcidol, 1μg/day). They were observed at baseline and at 6-month intervals for 2 years at each site. The primary endpoint was the incidence of new vertebral fractures identified radiographically using semi-quantitative morphometry criterion. Twenty one hundred and sixty four subjects were enrolled onto the trial and 2.022 (combination therapy group: 995; monotherapy group: 1,027) were primarily analyzed. The combination therapy group showed a statistically significant reduction of new vertebral fractures in the early phase of the intervention, and greater effectiveness than monotherapy for subgroups with several backgrounds such as the severer deformity of vertebral fractures or the multiplicity of vertebral fractures. In addition, the incidence of new non-vertebral fractures in weight-bearing bones was lower in the combination therapy group than in the monotherapy group. Combination therapy (alendronate plus alfacalcidol) should be an option for the treatment of postmenopausal osteoporosis in the clinical practice.

INFLUENCE OF CHRONIC KIDNEY DISEASE (CKD) ON THE MEASUREMENT OF SERUM BONE METABOLIC MARKERS

M. Inaba
Osaka City University Graduate School of Medicine, Osaka, Japan

It is increasingly recognized that elderly people suffer from CKD despite normal serum creatinine. The aim of the study was to evaluate the effect of renal dysfunction on the serum level of each bone metabolic marker and thus to assess its usefulness in CKD patients. Serum bone resorption markers, tartrate-resistant acid phosphatase (TRACP)-5b and N-terminal cross-linking telopeptide of type I collagen (NTX) and bone formation markers, bone alkaline phosphatase (BAP) and intact osteocalcin (OC) were measured. All 4 bone markers were significantly negatively correlated with glomerular filtration rate (eGFR) and positively correlated with log serum PTH, suggesting an increase in serum bone markers with development of secondary hyperparathyroidism, although the rates of increase in NTX and OC induced by eGFR reduction appeared steeper than those of TRACP-5b and BAP. Multiple regression analysis including age, gender, BMI, the presence of diabetes, eGFR, and log serum PTH showed an association of log serum PTH with all 4 bone markers. Of importance, eGFR was associated with serum NTX and OC, but not with serum TRACP5b or BAP. In conclusion, this data shows that renal dysfunction does not influence serum TRACP-5b and BAP, but has a significant influence on NTX and OC, resulting in false increase of NTX and OC in CKD patients.

PRESENT STATUS OF BONE TURNOVER MARKERS WITH TREATMENT OF OSTEOPOROSIS IN JAPAN –THE JAPANESE GUIDELINES FOR THE USE OF BONE TURNOVER MARKERS (2011 EDITION)

M. Miura
Pharmaceutical Sciences, Hokuriku University, Kanazawa, Japan

In the NIH consensus development conference 2000, osteoporosis was defined as a skeletal disease with compromised bone strength, which is attributed to integrated bone mineral density (BMD), and bone strength. Bone quality is composed of microarchitecture of bone, bone turnover, accumulation of micro damage, mineralization and properties of collagen in bone matrix. Currently, measurements of biochemical markers for bone turnover are considered a useful clinical measure of monitoring bone response to treatment and a surrogate marker of bone quality. Although originally clinical significance of bone metabolic marker (BTM) has been regarded as surrogate of BMD, recently BTM has been accepted as a noninvasive measurement useful in assessing bone quality and predicting future fracture risk. According to 2010 surveys conducted in Japan, 58.1% of doctors who see osteoporotic patients measure BTMs irrespective of their specialty (BAP 45.3%, uDPD 15.3%, uNTX 60.9%, sNTX 35.0%, uCTX 5.5%, sCTX 3.3%, TRACP-5b 15.0%, ucOC 8.4%). On the other hand, although BMD measurements are widely spread in Japan, sites and methods of BMD measurements installed depend on clinics or hospitals. Since newly developed anti-resorptive agents strongly suppress BTMs, measurements of BTMs provide useful information on efficacy of these agents. In 2001, the BMTs Guidelines Working Group was organized in Japan and has developed “Guidelines for the use of biochemical markers of bone turnover in osteoporosis 2001”. We reviewed the issues involved in creating the past guidelines. In particular, we focused on those topics related to the changes in BMTs and BMD, as identified in the guidelines of 2002 and 2004. Very recently 2011 Guideline on the adequate use of BTMs in daily osteoporosis clinics has been proposed by the Japan Osteoporosis Society which is characterized by the description that BTMs are independent measures to observe different aspects for the prevention and treatment of osteoporosis. Updates and changes in the 2011 guidelines: 1) To compare predictive value / responder rate between commonly markers and new markers (ex. P1NP, TRACP-5b, ucOC); 2) To assess the value of new markers to measure proportion of individual patients reaching and staying within reference range of premenopausal women; 3) To assess the value of combining minimum significant change (MSC).

SERUM 25 HYDROXY VITAMIN D LEVEL ASSOCIATES WITH QUALITY OF LIFE IN OSTEOPOROSIS: THE JAPANESE OSTEOPOROSIS INTERVENTION TRIAL (JOINT)-02

S. Mori
Bone and Joint Surgery, Seirei Hamamatsu General Hospital, Shizuoka, Japan

Deterioration of activity of daily living (ADL) is one of the major problems in osteoporosis with fractures. However, little has been known about the factors contributing to the deterioration of ADL in osteoporosis. We have assessed ADL level using a disease specific Health-Related Quality of Life (HRQOL) questionnaire in 1710 osteoporotic women (mean 76.5 years old) with high fracture risk of A-TOP JOINT-02 study (comparison of Alendronate monotherapy and Alendronate +alfacalcidol combination therapy in postmenopausal osteoporotic patients with a high fracture risk) . Japanese Osteoporosis Quality of Life Questionnaire (JOQOL)

consisting of 6 domains and 38 items. BMD was measured by dual energy x-ray absorptiometry (DXA) and radiological density assessment at axial bones and peripheral bones, respectively. Serum 25 hydroxy vitamin D (25(OH)D) was measured by immunoassay. Means 25(OH)D level was 23.7 ng/ml. Total score of JOQOL was 65.8 ± 15.3 at baseline. Association of the eight parameters (BMD, number of prevalent vertebral fractures, serum 25(OH)D level, history of fall, CKD grade, complications and prior treatment of osteoporosis) with QOL were calculated using multi-regression analysis. The age, number of prevalent vertebral fractures, 25(OH)D, fall and complications were significantly associated with the total score of JOQOL. Serum level of 25(OH)D was significantly associated with three domains after adjustment of confounding factors. These results clearly indicated that serum level of 25(OH)D is a significant predictor of patient's QOL in addition to the traditional risk to reduce QOL. The maintenance of serum 25(OH)D may be required to keep patient's QOL.

BONE METABOLISM MARKERS AND VERTEBRAL FRACTURE RISK IN TYPE 2 DIABETES MELLITUS

T. Yamaguchi[1], T. Sugimoto[1]
[1]*Internal Medicine 1, Shimane University Faculty of Medicine, Izumo, Japan*

Osteoporosis and type 2 diabetes mellitus (T2DM) are now prevalent in aging and westernized societies, and adversely affect the health of the elderly people by causing fractures and vascular complications, respectively. Recent experimental and clinical studies show that both disorders are etiologically related to each other through the actions of osteocalcin and adiponectin. Meta-analyses of multiple clinical studies show that hip fracture risk of T2DM patients is increased to 1.4 to 1.7-folds, although BMD of the patients is not diminished. Vertebral fracture risk of T2DM patients is also increased, and BMD is not useful for assessing its risk. These findings suggest that bone fragility in T2DM depends on bone quality deterioration rather than bone mass reduction. Thus, surrogate markers are needed to replace the insensitivity of BMD in assessing fracture risks of T2DM patients. Markers related to advanced glycation end products as well as insulin-like growth factor-I may be such candidates, because these substances were experimentally shown to modulate bone quality in DM. In practice, it is important for physicians to assess fracture risk in T2DM patients by evaluating prior VFs and fracture histories using spine X-ray and interview, respectively, until the usefulness of surrogate markers is established.

SPODOM SESSION ABSTRACTS

Portuguese Society of Osteoporosis and Bone Metabolic Diseases (SPODOM)

EFFECTS OF THYROID DYSFUNCTION IN BONE

A.P. Barbosa[1], M.R. Mascarenhas[1], A. Gonçalves[1], V. Simões[1], J. Monteiro[1], M. Bicho[1], I. do Carmo[1]
[1]*Endocrinology and Metabolic Diseases, Lisbon's Faculty of Medicine, Endocrinology, Diabetes and Metabolism Department, Orthopedics Department, Santa Maria University Hospital, CHLN-EPE, Lisboa, Portugal*

The thyroid hormones (***T_3*** and ***T_4***) are known to be very important in bone metabolism, not only in skeletal development but also in the preservation of the adult bone mass. However, the mechanisms involved in their skeletal action are far from totally clarified. While ***T_3*** is considered an important regulator of the bone tissue integrity and of the bone formation, ***T_4*** can stimulate directly or indirectly the activity of osteoclasts. More recently, studies of the TSH receptor, suggest that ***TSH*** can protect bone, because it can act as a direct negative regulator of bone remodeling, inhibiting both formation and survival of osteoclasts and inhibiting the differentiation of osteoblasts. So, it has been proposed that low TSH levels, *per se*, as it happens in hyperthyroidism, can predispose to reduced bone mineral density, osteoporosis and fractures. HYPERTHYROIDISM: Hyperthyroidism is a clinical or a subclinical condition caused by exaggerated levels of circulating T_3 and T_4 and may have as etiologic factors the hyperfunction of the thyroid gland (toxic goiter or autoimmune disease) or the ministration of drugs such as L-thyroxine and amiodarone. Some studies have shown that the prevalence of hyperthyroidism in women aged 65 or more, varies between 5 and 15%. In subclinical hyperthyroidism, free T_3 and T_4 levels are in the normal range, but TSH circulating levels are reduced; it is observed in toxic nodular goiter, in autoimmune thyroid diseases, and in the ministration of supraphysiological doses of L-thyroxine (T_4) after thyroidectomy for differentiated thyroid carcinoma. Regarding the mechanisms of this condition, the excess of circulating thyroid hormones can cause in adult life (after the acquisition of peak bone mass) an increase of bone resorption. Bone remodeling accelerates, with increases in both osteoblastic and osteoclastic activities, but originating a decrease in the duration of the bone formation phase and consequently an incomplete substitution of the resorbed bone by a new bone tissue. It is estimated that about 10% of mineralized bone is loss per cycle. More recently, data have shown that also TSH alone seems to be a negative regulator of bone metabolism. So, it is possible that even subclinical hyperthyroidism (normal free T_3 and T_4 levels but reduced TSH) can already cause negative effects in bone mineral density (BMD) as well as to increase the risk of osteoporotic fractures. We studied a group of subclinical hyperthyroid postmenopausal women, and found already significant correlations not only in bone turnover markers but also in some of the hormones implicated in bone metabolism. Hyperthyroidism is a frequent cause of secondary osteoporosis. Osteoporosis and hyperthyroidism have an elevated prevalence in elderly women and are associated to a precocious mortality risk. Besides the changes in BMD and in bone turnover markers, there is an increase in osteoporotic fracture risk, especially at the proximal femur. The weight loss and the gastrointestinal changes (decrease in intestinal calcium absorption and modified vitamin D metabolism) are also associated to the reduction of the body lean mass, thus inducing a higher risk of fragility fractures. Regarding silent vertebral fractures detected by VFA-DXA, our group found a higher prevalence of those fractures in young hyperthyroid men. In patients with differentiated thyroid carcinoma, iatrogenic subclinical hyperthyroidism can originate several degrees of reduction in BMD, but data are contradictory; in postmenopausal women there is risk of reduced BMD, while that risk does not seems to exist in men and in premenopausal women; also, the prevalence of fractures is incompletely documented. A more recent study in 213511 aged 70 or more prevalent L-thyroxine users, showed that it was associated with a significantly increased risk of fragility fractures. We studied a group of hyperthyroid men compared to a control group identical in terms of age, stature, weight and body mass index and found that the prevalence of reduced BMD in whole body and in femoral neck and of osteoporosis was significantly higher in the hyperthyroid group; in another study, in a group of postmenopausal women with hyperthyroidism compared to a control group, we detected a significantly higher prevalence of reduced BMD at all skeletal sites and as well as of osteoporosis, in the hyperthyroid group (Table 1).*Table 1*. Means (±SD) of the total body lean mass and of the BMD at several skeletal sites, in the hyperthyroid postmenopausal and in the control group.

Groups Variables	**CONTROL**	**HYPERTHYROIDISM**	*P*
Total Lean Mass *kg*	**37.9** *(±5.2)*	**37.6** *(±4.1)*	*NS*
BMD *g/cm²* Lumbar	**0.940** *(±0.1)*	**0.770** *(±0.1)*	*0.0000*

Spine			
Hip	**0.700** *(±0.1)*	**0.636** *(±0.1)*	*0.0251*
Distal Radius	**0.646** *(±0.07)*	**0.478** *(±0.1)*	*0.0000*
Whole Body	**1.048** *(±0.1)*	**0.982** *(±0.1)*	*0.0000*

HYPOTHYROIDISM: Hypothyroidism is a clinical or a subclinical condition caused by low levels of circulating T_4 and may have as etiologic factors the hypofunction of the thyroid gland (usually autoimmune disease) or the ministration of drugs such as lithium. The juvenile-acquired hypothyroidism is known to cause growth arrest, delayed bone maturation and short stature, related to the duration of the thyroid hormones deficiency. Hypothyroidism reduces bone turnover and lengthens the remodeling cycle. Also, the increase in the mineralization during the bone formation phase, can, on the opposite, contribute to an increase in bone mineral density. Clinical data concerning bone mineral density and osteoporosis in hypothyroidism are scarce. A prospective study of a cohort of 3567 US community adults, found that men with subclinical hyper or hypothyroidism are at increased risk for hip fracture. Other studies found that the fracture risk was significantly increased both before and after diagnosis of hypothyroidism with a peak around the time of diagnosis. IN CONCLUSION, thyroid hormones are known to be major intervenient in bone metabolism. As thyroid dysfunction is among the most prevalent endocrine diseases and hyperthyroidism is clearly defined as one of the most important causes of secondary osteoporosis, it is far important to diagnose it precociously, in order to reduce the future fracture risk.

BIBLIOGRAFIA

-Barbosa AP, Osteop Int 2011
-Barbosa AP, J Bone Min Res 2011
-Lee JS, Arch Int Med 2010
-Heemstra KA, Thyroid 2006
-Vestergaard P, Thyroid 2002
-Turner MR, Br Med J 2011

MALE HYPOGONADISM AND BONE

M.R. Mascarenhas[1], A.P. Barbosa[1], A. Gonçalves[1], V. Simões[1], M. Bicho[1], J. Monteiro[1], I. do Carmo[1]
[1]*Endocrinology and Metabolic Diseases, Lisbon's Faculty of Medicine, Endocrinology, Diabetes and Metabolism Department, Orthopedics Department, Santa Maria University Hospital, CHLN-EPE, Lisboa, Portugal*

Androgens are synthesized from cholesterol through a cascade of enzymatic pathways and the testes produce and secrete almost all testosterone in men. Male hypogonadism is a clinical condition in which there is not enough testosterone synthesis by the testes, sperm or both. Normal sex steroids levels are important to maximize the peak bone mass and sex steroid hormones deficiencies during adulthood may cause bone loss by an increased bone resorption and may be associated with a low BMD, osteoporosis or/and fragility fractures. Whether androgens have estrogen-like direct actions on bone or indirect effects, via aromatase and/or maintenance of muscle mass, remains to be clarified. Testosterone treatment in men with hypogonadism may affect positively the bone mass, in most osteoporotic patients. EFFECTS OF ANDROGENS ON BONE FORMATION: Androgen receptors were detected in human osteoblasts and may mediate proliferation, growth, production of cytokines and protein synthesis of bone matrix (osteocalcin, type I collagen, osteopontin). In aging male the interaction between decreased testosterone levels and IGF-1 leads to diminished bone formation rate and increase in bone fragility. EFFECTS OF ANDROGENS ON BONE RESORPTION: Androgens may exert a moderate and similar estrogen effect on the resorption of the trabecular bone. A large variety of endocrine causes of failure of the gonads can cause osteopenia. HYPOGONADISM AND BONE TISSUE IN MEN: Male hypogonadism may have several causes (Table 1). The SHBG levels increase and the free testosterone levels are more reduced than total testosterone concentrations with ageing. The threshold below which androgen levels are related to the bone loss onset is not yet established. Male hypogonadism is a major risk factor for osteoporosis in adults, one of the most important secondary causes of osteoporosis and osteoporotic fractures. The BMD is lower in trabecular than in cortical bone. The trabecular bone score (TBS) is also reduced in men with hypogonadism. Hypogonadism in males is also characterized by the lack of estrogen (and unequivocally androgen): the bone disease of men with hypogonadism is also associated with the absence of action of estrogen. Estrogen receptor gene mutations (very high estrogen levels) delays epiphyses closure thus resulting in great stature, but the aromatase deficiency can originate short stature and osteoporosis. Glucocorticoid therapy can induce low testosterone levels, thus contributing to the bone mass loss. Male hypogonadism may modify iPTH and vitamin D, interfering with the calcium metabolism and causing bone mass loss. HYPOGONADOTROPIC or SECONDARY HYPOGONADISM: In the congenital and prepubertal male hypogonadotropic hypogonadism, the BMD is low at the cortical and cancellous bone. In adults, the LHRH analogues therapy is associated with a marked bone mass loss and osteoporotic fractures. In hyperprolactinemia, low BMD at the lumbar spine and at the hip were also detected. *Table 1*. Etiology of male hypogonadism.

Hypergonadotropic hypogonadism or primary gonadal failure	***Hypogonadotropic or secondary hypogonadism***	***Drugs and agents that may cause low testosterone levels***
Testes agenesia	Hypothalamic disorders	Spironolactone
Klinefelter syndrome	LHRH deficiency	Corticosteroids, ketoconazole, ethanol, aminoglutethimide.
Cryptorchidism	Kallmann syndrome	Anticonvulsants, psychotropic drugs, hepatic microsomal enzyme inducers
Bilateral testes torsion	Craniopharyngioma	LHRH agonists, estrogens, anabolic steroids, post-transplant immunosuppressants.
Gonadal dysgenesis	Prader–Willi syndrome	
Hemochromatosis	Lawrence–Moon–Bardet–Biedl syndrome	
Leydig cell dysfunction	Alström syndrome	
Congenital errors of testosterone synthesis; androgen-resistant state and enzyme defects	Fertile-eunuch syndrome	
Leydig cell hypoplasia	Hyperprolactinemia	
LH receptor failure	Prolactinoma	
Absence of androgen receptors: testicular feminization	Tuberculosis, Hypophysitis	
5α-Reductase deficiency	Hemochromatosis	
Reifenstein syndrome: incomplete androgen insensitivity	Sarcoidosis	
Trauma, Radiation	Pituitary disorders (LH and/or FSH deficiency)	
Chemotherapy	Isolated LH deficiency	
Sertoli-cell only syndrome	Tumors, apoplexy	
	Empty sella syndrome	
	Cranial trauma with or without pituitary-stalk transection	
	Irradiation	

HYPERGONADOTROPIC OR PRIMARY HYPOGONADISM: In men with primary hypogonadism, 1 to 3 years after bilateral orchiectomy, a rapid loss of vertebral bone mass (about 7% per year) and increased bone turnover were observed. EFFECTS OF ACUTE HYPOGONADISM: Bilateral orchiectomy leads at once to an increased osteoclast activity, which is inhibited by non-aromatizable androgens. EFFECTS OF CHRONIC HYPOGONADISM: Studies in chronic male hypogonadism revealed decreased rates of bone formation and an increase in average of bone remodeling rates. Our group detected a significant low BMD at several sites of the skeleton in hypogonadal men (Table 2). The BMD is correlated with free testosterone plasma levels in old men. *Table 2*. Mean (±SD) BMD at several skeletal sites in men with hypogonadism and in a control group with normal testicular function.

BMD g/cm^2	**Hypogonadism without therapy**	**Control group**	**P**
L_1-L_4	**0.919** (±0.17)	**1.033** (±0.16)	0.0353
Femural neck	**0.927** (±0.15)	**1.015** (±0.13)	0.0000
Distal forearm	**0.595** (±0.08)	**0.626** (±0.06)	0.0000
Whole body	**1.096** (±0.11)	**1.161** (±0.10)	0.0000

COMPLICATIONS OF OSTEOPOROSIS IN HYPOGONADAL MALES: Hypogonadism may contribute to severe osteoporosis in about 15% of men and androgen deficiency is associated with 30% of the osteoporotic vertebral fractures (increased in iatrogenic hypogonadism of the elderly induced by surgery or LHRH analogues therapy in prostate cancer). THE EFFECTS OF THERAPY ON BONE MASS: The testosterone therapy of adult males with hypogonadism, during 18 months, induces an increase of 5 to 6% in trabecular BMD, but most studies showed a modest increase in the BMD. Further studies are needed to determine whether BMD normalizes with long-term therapy of isolated male hypogonadism. Testosterone therapy inhibits osteoclast activity and increases bone formation. The effects of the treatment of male hypogonadotropic hypogonadism with gonadotropins or androgen therapy are similar. Finally, no data were published about osteoporotic fractures and androgen therapy in men.

References:

Behre HM et al. *JCEM*, 1997;82:2386-90
Bhasin S et al. *JCEM, 2006;* 91:1995–2010
Eriksen EF et al. *Science*, 1988;241:84-6
Khosla S et al. *Endocr Rev*, 2008;29:441-64
Mascarenhas MR et al. *Osteoporosis International*, 2002;13 (supp 1):S136
Mascarenhas MR et al. *Calcified Tissue International*, 2003; 72(4):378-9
Meier C et al. *Arch Intern Med*, 2008;168:47-54
Meier C et al. In: Orwoll ES, Bilezikian JP, Vanderschueren D (Eds): *Osteoporosis in men. The effects of gender on skeletal health*, Amsterdam, Elsevier, 2010; pp 423-34
Rucker D et al. *Clin Endocrinol (Oxford)*, 2004; 60:491-9
Valimaki VV et al. *JCEM,* 2004; 89:3785–9

EFFECTS OF BREAST CANCER ON BONE

R. Sousa
Department of Gynecology, IPOFG-Coimbra, Portugal

Breast cancer (BC) affects skeleton in multiple ways. Between 70% and 100% of women with advanced BC have bone metastasis, being this involvement a major cause of morbidity. Furthermore, osteoporosis and osteopenia are growing concerns among breast cancer survivors and their physicians, and are often attributed to treatment. Osteoporosis increases the risk of bone fractures, leading to pain and disability, need for major surgery, high morbidity and mortality, increased cost of disease management and reduced quality of life for patients. Several mechanisms contribute to bone loss in BC patients – this condition itself might interfere directly with bone metabolism by increasing osteoclastic activity. A variety of hormonal and nonhormonal treatments have the potential to promote bone loss by inducing hypogonadism, which accentuates bone resorption and bone turnover. Chemotherapy is associated with bone loss and increased fracture risk in premenopausal women with BC, for it induces ovarian failure, leading to low estrogen levels. It may also have direct toxic effects on bone cells. Endocrine-based adjuvant therapy has mixed actions on the bone mineral density (BMC). Hormonal therapy includes aromatase inhibitors (AI), estrogen receptor antagonists, gonadotropin-releasing hormone (GnRH) analogs and selective estrogen receptor modulators (SERMs). AI cause low plasma estradiol levels, exceeding the BMD loss observed in postmenopausal osteoporosis, and is therefore likely to need proactive management in order to preserve BMD and prevent fractures. GnRH analogs, such as goserelin, cause ovarian suppression in premenopausal women by lowering plasma estradiol, estrone, and estrone sulfate concentrations up to 98%. They have a negative impact on bone remodeling with a decrease BMD by 6% to 10% within the first 2 years. Surgical induced menopause also causes a large reduction of total bone mass of up to 20% within 18 months in some studies, and BMD appears to continue decreasing thereafter. Tamoxifen treatment is associated with significant bone loss in patients remaining premenopausal after adjuvant chemotherapy for breast cancer. However, tamoxifen offers some protection against bone loss in patients with chemotherapy induced early menopause. Fulvestrant is an estrogen receptor antagonist. It is currently used in advanced breast cancer, usually as second line after anastrozole. Although it has similar side effects to anastrozole, it has no detrimental effect on bones, as levels of circulating estrogen are not affected. In addition to established risk factors such as BMD, women with BC may be exposed to several factors that reduce bone strength and structural integrity. These fracture risk factors include advanced age, low body-mass index, family history of hip fracture, personal history of fragility fracture after age 50, corticosteroid use, excessive alcohol consumption, and smoking. The combination of these genetic, environmental, and cancer treatment related factors contributes to the increased fracture risk observed in women with BC, especially women receiving AI therapy. Interventions to reduce bone loss as well as long-term follow-up studies are a high priority in women who develop chemotherapy-induced ovarian failure or are receiving treatment for BC. The most common therapies used to treat the BMD loss observed in women with postmenopausal osteoporosis, such as oral biphosphonates, calcium and vitamin D supplements, may be insufficient to prevent accelerated BMD loss secondary to chemotherapy-induced menopause and the use of GnRH analogues in premenopausal women, or AI therapy in postmenopausal women. Biphosphonates are considered a first line approach to prevent accelerated BMD loss. They act through inhibition of osteoclast-mediated bone resorption, disrupting the cycle of abnormal bone remodeling associated to osteoporosis or bone metastases. They also reduce skeletal metastases associated pain, improving quality of life. There is emerging evidence of direct and indirect effects on cancer cells, and possible synergy with antineoplastic agents. Zoledronic acid prevents loss of bone density in premenopausal women undergoing ovarian suppression in combination with tamoxifen or anastrozole and in postmenopausal women receiving adjuvant AI. Its addition to adjuvant endocrine therapy may also improve clinical outcomes, in comparison to endocrine therapy alone in pre and postmenopausal women with early stage hormone responsive tumors. Besides pharmacologic therapy, adequate calcium and vitamin D intake, weight-bearing exercise and non-smoking habits are basic healthy lifestyle recommendations which contribute to BMD preservation. Bone health assessment in women undergoing adjuvant therapy for breast cancer should include BMD T-score measurement at baseline and at least every 1 to 2 years during treatment, along with assessment of established risk factors for fracture.

ORAL ABSTRACTS

Joint Biology

BONE MINERAL DENSITY AND LEAN BODY MASS IN YOUNG HYPERTHYROID MEN

A.P. Barbosa[1], M.R. Mascarenhas[1], A. Goncalves[1], V. Simoes[1], A.G. Oliveira[1], D. Santos Pinto[1], M. Bicho[1], I. do Carmo[1]
[1]*Santa Maria Hospital, Lisbon, Portugal*

Hyperthyroidism may contribute to a low peak bone mass and after the third decade of life is one of the most important causes of bone loss. Also, the changes in both lean and fat masses that occur in this disease can contribute to the fragility fractures. AIMS: To evaluate the body composition changes in hyperthyroid young men. MATERIAL AND METHODS: A group of 38 men aged < 40 years were divided and paired in hyperthyroid (n=19) and control (n=19) groups, the lean and fat masses (Kg) and the BMD (g/cm^2) at the lumbar spine (L_1-L_4), proximal femur, distal radius and whole body were evaluated by DXA. No patient was previously treated for hyperthyroidism and/or OP. In the controls, the BMD was qualified by Z-score, according to the ISCD recommendations. Descriptive and comparative tests were used and statistical significance was considered for P < 0.05. RESULTS: The mean total body lean mass and the mean BMD at the hip and at the whole body were significantly reduced in the hyperthyroidism group (Table 1). *Table 1*. The means (±SD) of the body composition components.

GROUPS Variables	CONTROL	HYPER-THYROIDISM	*P*
Age *(years)*	31.9*(±6.0)*	31.6*(±6.2)*	*NS*
Height *(cm)*	176.2*(±.4)*	175.5*(±5.6)*	*NS*
Total Lean Mass *(kg)*	62.5*(±7.5)*	54.9*(±7.1)*	*0.0035*
BMD femoral neck *(g/cm^2)*	0.934*(±0.1)*	0.843*(±0.2)*	*0.0487*
BMD whole body *(g/cm^2)*	1.230*(±0.1)*	1.111*(±0.1)*	*0.0008*

CONCLUSIONS: These results suggest that hyperthyroidism in young adult men can reduce both lean and bone masses, thus predisposing them to an increased risk of future bone fragility fractures.

A PROTOCOL FOR MANAGEMENT OF PERIPROSTHETIC WOUND INFECTION AND SOFT TISSUE COVER FOLLOWING TOTAL KNEE ARTHROPLASTY

M.A.A. Khan[1], **L. Gwozdziewicz**[1], R. Sehgal[1], B. Haughton[1]
[1]*Plastic Surgery Dept., Castle Hill Hospital, Hull, UK*

Introduction: Peri-prosthetic infections can complicate total knee arthroplasty in 1-1.5% of cases. Failure in management may lead to excision arthroplasty, arthrodesis or even limb amputation, with its associated morbidity. We present an audit to investigate our peri-prosthetic infection/wound breakdown following knee arthroplasty and a literature review of current best practice. Methods: A retrospective 11 year review of total knee arthroplasty patients was undertaken, in a single unit. Data was collected on a proforma and patient demographics were identified by case note analysis and theatre logbook study. Incidence of peri-prosthetic knee infection and/or wound complications were investigated. Details of co-morbidities, infections, initial surgical management, plastic surgical involvement and final outcome were recorded. Results: 33 out of 56 patients were available for analysis. The male:female ratio 1:0.7 with a mean age of 70 years(range: 32-88 years). From these 33 patients 5 (15%) showed superficial infections, 14 (42%) with superficial wound dehiscence and 2 (6%) required washout of the prosthesis with long term antibiotic therapy. From the remaining cases: 4 (12%) were managed without plastics involvement, one leading to arthrodesis and 4 (12%) had plastic surgical input, with one leading to arthrodesis. The mean time before plastic surgical review after initial suspicion of infection was 13 weeks. Discussion and Conclusion: A combined ortho-plastic multidisciplinary approach has application in the management of wound and peri-prosthetic total knee infections. Early plastic surgical involvement in compromised knee arthroplasty can improve long-term function. An algorithm of management is presented.

VOLAR LOCKING PLATE VERSUS K-WIRING FIXATION OF DISTAL RADIUS FRACTURES IN 20-65 YEAR OLDS

C. Kiernan
Orthopaedics Dept., University College Hospital Galway, Galway, Republic of Ireland

Introduction: Fractures of the distal radius are one of the most common injuries encountered in orthopaedics. Optimal management remains controversial. Radiographic reconstruction does not correlate with functional outcome in the elderly but remains unclear regarding younger higher demand patients. This study aims to compare outcomes of treatment with volar locking plate versus MUA& K-wire fixation in the 20-65 year population. Methods: A retrospective comparative study of 321 distal radius fractures over a 4 year period was conducted. 151 patients were treated with volar plating and 170 with MUA&k-wire fixation. Radiographic parameters: radial inclination, radial length, volar tilt, ulnar variance and osteoarthritic changes were compared. Functional outcome was assessed using the Disabilities of the arm, shoulder and hand (DASH) score and patient rated wrist evaluation (PRWE) score. Results: Mean age 46.6 years; mean follow up 31.3 months. OTA classification system showed 160 type A, 118 type B and 43 type C fractures. Mean age, sex and fracture pattern were matched between groups. Radiological reconstruction was significantly better in the volar plate group: radial inclination 22.1° v 21.3°(p=0.09), volar tilt 4.2°v1.7 °(p=0.07), ulnar variance -0.5mm v 0.1mm(p=0.03), radial length 10.9mm v 10.4mm(p=0.01). 4%(6/151) of the volar plate group were radiologically unacceptable versus 13%(22/170) in the k-wire group(p=0.03). Mean DASH/PRWE scores showed no difference between the two groups: DASH 12.8v12; PRWE pain 12v8.8; PRWE function 9.9v10.6; PRWE total 21.9v19.4. Conclusion: Volar plating results in superior reconstruction versus k-wires. This does not translate to better functional outcomes or less pain at 2.5 years follow up.

CONDYLAR VOLUME AND SURFACE IN CAUCASIAN ADULT SUBJECTS

S. Tecco[1], **E. Marchetti**[1], L. Tettamanti[2], S. Mummolo[1], F. Festa[3], G. Marzo[1]
[1]*Department of Health Science, University of L'Aquila, L'Aquila;* [2]*Department of Reconstructive Surgery and and Advanced Technologies, University of Insubria, Varese;* [3]*Department of Oral Science, Nano and Biotechnology, University G. D'Annunzio, Chieti, Italy*

Background: Osteoarthritis is the most frequent chronic joint disease causing pain and disability. Besides biomechanical mechanisms, the pathogenesis of osteoarthritis may involve inflammation, vascular alterations and dysregulation of lipid metabolism. As statins are able to modulate many of these processes, this study examines whether statin use is associated with a decreased incidence and/or progression of osteoarthritis. Methods: Participants in a prospective

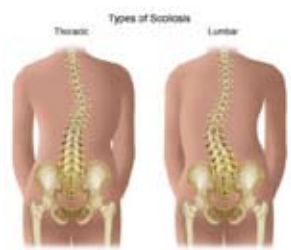
population-based cohort study aged ≥55 years (n=2921) were included. X-rays of the knee/hip were obtained at baseline and after on average 6.5 years, and scored with the Kellgren & Lawrence score for osteoarthritis. Any increase in score was defined as overall progression (incidence and progression). Data on co-variables were collected at baseline. Information on statin use during follow-up was obtained from computerized pharmacy databases. The overall progression of osteoarthritis was compared between users and non-users of statins. Using a multivariate logistic regression model with generalized estimated equation, odd ratios and 95% confidence intervals were calculated after adjusting for confounding variables. Results: Overall progression of knee and hip osteoarthritis occurred in 6.9% and 4.7% of the cases, respectively. The adjusted odds ratio for overall progression of knee osteoarthritis in statin users was 0.43 (95% CI 0.25-0.77, p=0.01). The use of statins was not associated with overall progression of hip osteoarthritis. Conclusions: Statin use is associated with more than 50% reduction in overall progression of osteoarthritis of the knee, but not of the hip.

SCOLIOSIS AND DENTAL OCCLUSION

S. Tecco[1], **S. Mummolo[1]**, L. Tettamanti[2], E. Marchetti[1], A. Monaco[1], G. Marzo[1]

[1]Department of Health Science, University of L'Aquila, L'Aquila; [2]Department of Reconstructive Surgery and Advanced Technologies, University of Insubria, Varese, Italy

Background: Idiopathic scoliosis is a deformity without clear etiology. It is unclear whether there is an association between malocclusion and scoliosis. Several types of occlusion were described in subjects with scoliosis, mostly case-reports. Objectives: The aim of this review was to evaluate the type of occlusions more prevalent in subjects with scoliosis. Search strategy. All randomized and controlled clinical trials identified from the Cochrane Oral Health Group Trials Register, a MEDLINE search using the Mesh term scoliosis, malocclusion, and relevant free text words, and the bibliographies of papers and review articles which reported the outcome of orthodontic treatment in subjects with scoliosis that were published as abstracts or papers between 1970 and 2010. Selection criteria: All randomized and controlled clinical trials published as full papers or abstracts which reported quantitative data on the outcomes malocclusion in subjects with scoliosis. Data collection and analysis. Data were extracted without blinding to the authors, age of patients or type of occlusion. Main results: Using the search strategy eleven observational longitudinal studies were identified. No randomized clinical trials were recorded. Twenty-three cross-sectional studies were recorded, and the others studies were reviews, editorials, case-reports, or opinions. The clinical trials were often not controlled and were about the cephalometric evaluation after treatment with the modified Milwaukee brace, followed by the orthodontic treatment of the class II relationship with a functional appliance. Clinical trials also included the study of the associations between scoliosis and unilateral crossbite, in children with asymmetry of the upper cervical spine. This association was also investigated in rats, pigs and rabbits in clinical trials. The other associations between scoliosis and occlusion seem to be based only on cross-sectional studies, case-reports, opinions. Authors' conclusions: Based on selected studies, this review concludes that there is plausible evidence for an increased prevalence of unilateral Angle Class II malocclusions associated with scoliosis, and an increased risk of lateral crossbite, midline deviation in children affected by scoliosis. Also, documentation of associations between reduced range of lateral movements and scoliosis seem convincing. Data are also mentioned about the association between plagiocephaly and scoliosis.



KEY ENZYMES INVOLVED INTO STEROID METABOLISM AND IDIOPATHIC SCOLIOSIS: A POSSIBLE GENETIC LINKAGE

T. Esposito[1], **B. Varriale[1]**, G.F. Di Martino[2], M. Chierchia[2], D. Ronca[2]

[1]Department of Experimental Medicine; [2]Department of Orthopaedics & Traumatology, Second University of Naples, Naples, Italy

Idiopathic Scoliosis (IS) pathogenesis is still unknown. There is a ratio of 50% in childhood. The genetic inheritance of IS remains still unclear although evidences claim for a recessive multi-factorial inheritance. Being IS as a sex-conditioned disease, we found a linkage between the estrogen content and IS in a girls population of southern of Italy. The 17β-estradiol, progesterone and testosterone contents in affected teens is lower with respect to unaffected girls ($p<0.01$, $p<0.01$ and $p<0.05$). It has been claimed for a linkage between the IS and some chromosomal regions (chromosome 6 and 10) by diverse authors. Thus we have undertaken a study having as a target the linkage between the IS phenotype and polymorphisms for loci on both chromosome 6 and 10. The genetic loci we have studied were 6p21.3 (17β-HSD), 6p21 (3β-HSD), 6q25.1 (ERα), 10q24.3 (17α-hydroxylase), 10q24.31 (21α-hydroxylase) and 10q24.32 (17,20 lyase). Polymorphisms in the coding regions of all genes studied have been found in IS girls (not in the control). It is conceivable that those polymorphisms may have a linkage between the steroidogenetic enzymes and IS, although more functional study on the effect of such polymorphisms are needed to better understand the role may have. Among the ERα we identified four polymorphisms in the exons encoding for the steroid binding domain and two other in the trans-activation domain that could have an effect on the receptor efficiency. The overall data indicate a clear linkage between the endocrine status and the IS phenotype.

Muscles

OSTEOPATHIC TREATMENT METHOD ACCORDING TO THE FASCIAL DISTORTION MODEL (FDM) IN THE MANAGEMENT OF 'FROZEN' SHOULDER

M. Fink

Department of Rehabilitation Medicine, Hannover Medical School, Hannover, Germany

Background: Painful stiffness of the shoulder is a common ailment and notoriously difficult to treat. The present prospective controlled randomized single-blind controlled trial evaluates the efficacy of the 'Fascial Distortion Model' according to Typaldos as a remedy for the 'frozen shoulder'. Materials and methods: A total of 60 patients were randomized to receive either the FDM-guided treatment (FDM, n=30) or a 'conventional' manual therapy (MT, n=30). The primary endpoint for the treatment effect was the shoulder mobility, and secondary endpoints were pain (measured on a VAS), raw force and function as expressed by the Constant-Murley and DASH scores. Results: Before therapy, groups were well comparable in terms of all outcome parameters. All endpoints showed a substantial and significant improvement in both treatment groups. Improvement was significantly more marked in the FDM group as compared to the MT group, and the effect occurred significantly faster. During post-treatment observation, there was no further improvement and the achieved benefit in mobility in the FDM group was even partly lost. However, the abduction ability of 150.2±37.2° continued to be substantially better than in control patients (124,1±38,6°), and the ultimate improvement in maneuverability was 71% as opposed to 39% in controls. Secondary outcome parameters (raw force, functional handicap, and pain) showed a significant improvement in both groups but a significantly better result in patients treated according to FDM guidelines. However, patients in this group rated the treatment as significantly more unpleasant.

ACTIVATION OF THE TRANSVERSUS ABDOMINIS, PAIN, AND FUNCTIONAL DISABILITY IN PATIENTS WITH CHRONIC NONSPECIFIC LOW BACK PAIN AND LUMBAR DISC HERNIATION

A. Marques[1], **F. França[1]**, L. Ramos[1], T. Burke[1]
[1]Department of Physical Therapy, Speech Therapy and Occupational Therapy Universidade de São Paulo, São Paulo, Brazil

Introduction: Chronic low back pain (cLBP) is defined as back pain lasting more than 12 weeks, and it affects more than 50% of the population. Changes in motor control of abdominal muscles such as transversus abdominis (TrA) have been reported in subjects with nonspecific LBP, however it was not observed in individuals with lumbar disc herniation (LDH). This study aimed to contrast pain, functional disability, and TrA activation in subjects with cLBP and HLD. Method: This study examined 60 subjects divided into three groups: Lumbar disc herniation (HL) n=20, Mean age 44.6 (6.42), BMI 25.81 (2.88); Nonspecific LBP (LB) n=20, Mean age 42.75 (4.56), BMI 24.86(2.96); Control (CG) n=20, Mean age 43.35(7.37), BMI 24.43(2.35). Pain was evaluated with Visual Analogue Scale, functional disability with Oswestry disability questionnaire and the ability to contract the TrA muscle with Pressure Biofeedback Unit – PBU. Intergroup statistical analysis was performed using the one-way ANOVA and Kruskal-Wallis for data with normal and without normal distribution respectively and the Tukey test for multiple comparisons. A significance level was α=0.05. Results: Pain and functional disability were similar in HL and LB groups (p>0.05) and the ability to contract TrA was similar in HL and LB groups, however different from the CG (p<0.05). Conclusion: The results indicate that individuals with cLBP and LDH have the same level of pain, functional disability and ability to contract the TrA, different from the individuals without low back pain who had better activation of TrA. Table 1. Intergroup analysis of pain, functional disability and activation of TrA

Variables	LB(n=20)	HL(n=20)	CG(n=20)	p
Pain (0-10cm)	6.35(1.53)	6.25(1.94)	-	0.855*
Functional disability (0-45)	17.25(3.72)	15.9(3.54)	-	0.072**
Activation of TrA (2 to -10 mmHg)	-0.65(1.43)[1]	-1.55(0.85)[1]	-4.02(2.17)[2]	< 0.05***

p value for t Test*
Mann Whitney**
Tukey***
Difference statistically significant[1,2]

DEFINING SARCOPENIA: THE IMPACT OF DIFFERENT DIAGNOSTIC CRITERIA ON THE PREVALENCE OF SARCOPENIA IN A LARGE MIDDLE AGED COHORT

A.Y. Bijlsma[1], C.G.M. Meskers[2], C.H.Y. Ling[1,3], M. Narici[4], S.E. Kurrle[5], I.D. Cameron[6], R.G.J. Westendorp[1,7], **A.B. Maier[1,7]**
[1]Department of Gerontology and Geriatrics; [2]Department of Rehabilitation Medicine, Leiden University Medical Centre, Leiden, The Netherlands; [3]Geriatric Department, Prince Charles Hospital, Brisbane, Australia; [4]Institute for Biomedical Research into Human Movement and Health, Manchester Metropolitan University, Manchester, UK; [5]Northern Clinical School, Faculty of Medicine; [6]Rehabilitation Studies Unit, Faculty of Medicine, University of Sydney, Australia; [7]Netherlands Consortium for Healthy Aging, Leiden University Medical Centre, Leiden, Netherlands

Sarcopenia, low muscle mass, is an increasing problem in our aging society. The prevalence of sarcopenia varies extremely between elderly cohorts ranging from 7 to over 50%. Without consensus on the definition of sarcopenia, a variety of diagnostic criteria are being used. We assessed the degree of agreement between seven different diagnostic criteria for sarcopenia based on muscle mass and handgrip strength, described in literature. In this cross-sectional study, we included men (n=325) and women (n=329) with complete measurements of handgrip strength and body composition values as measured by bioimpedance analysis within the Leiden Longevity Study. Prevalence of sarcopenia was stratified by gender and age. In men (mean age 64.5 years) the prevalence of sarcopenia with the different diagnostic criteria ranged from 0% to 20.8% in the lowest age category (below 60 years), from 0% to 31.2% in the middle (60 to 69 years) and from 0% to 45.2% in the highest age category (above 70 years). In women (mean age 61.8 years) the prevalence of sarcopenia ranged from 0% to 15.6%, 0% to 21.8% and 0% to 25.8% in the lowest, middle and highest age category respectively. One participant (0.3%) was identified having sarcopenia according to all diagnostic criteria that marked prevalence above 0% (Figure 1). We conclude that the prevalence of sarcopenia is highly dependent on the applied diagnostic criteria. It is necessary to reach a consensus on the definition of sarcopenia in order to make studies comparable and for implementation in clinical care.

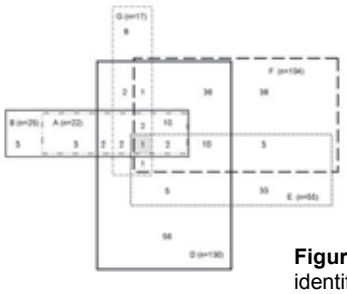


Figure 1: Number of participants identified as having sarcopenia according to various definitions, represented by letter codes

SEMG ACTIVITY OF MASTICATORY, NECK, AND TRUNK MUSCLES DURING THE TREATMENT OF SCOLIOSIS WITH FUNCTIONAL BRACES

S. Tecco[1], S. Mummolo[1], E. Marchetti[1], R. Gatto[1], L. Tettamenti[2], **G. Marzo[1]**
[1]Department of Health Science, University of L'Aquila, L'Aquila; [2]Department of Reconstructive Surgery and and Advanced Technologies, University of Insubria, Varese, Italy

Background: Studies on the relationship between occlusal problems and the spine are of increasing interest. In this study, we monitored the sEMG activity of masticatory, neck, and trunk muscles during the treatment of scoliosis in young patients, and compared the data with a control of untreated group. Methods: Twelve white Caucasian patients (9 males and 3 females; mean age of 8.0 ± 1.5 years) with scoliosis and Class I occlusion (without crowding) were included in this study (study group). Fifteen healthy subjects (9 males and 6 females; mean age of 9.5 ± 0.8 years) were recruited as control group. The subjects were visited before they underwent the treatment of scoliosis, as well as after 3 (T1) and 6 months (T2) of their treatment for scoliosis. The patients were instructed to wear the device during sleep and during the day, according to the protocol given by their orthopedic. Result: The treated group showed statistically significant changes in the sEMG activity of masticatory, neck, and trunk muscles, both at rest and during MVC of the mandible with respect to T0. The masseter and the anterior temporalis showed a significant improvement in the asymmetry index from T0 to T2. On the other hand, subjects in the control group did not register much change. Conclusion: Our findings suggest that the use of a functional device for the treatment of scoliosis induces a significant reduction in the asymmetry index of the trunk muscles, as well as a significant increase in the contractility of masticatory muscles.

MYOFASCIAL TRIGGER POINT AND PLANTAR HEEL PAIN: OVERLY COMMON BUT UNDR-TREATED

B. Nguyen
Podiatry Dept., Darebin Community Health Service, East Reservoir, Australia

The cause of plantar heel pain has been a diagnostic challenge even though it is one of the most common musculoskeletal disorders of the foot and ankle. Its resistance to contemporary interventions has frustrated clinicians and researchers. The pathogeneses and hypotheses proposed are many and diverse. Myofascial trigger point (MTrP) as an intervention for plantar heel pain (PHP) has been inconspicuous. MTrP offers an alternative explanation of the aetiology of PHP and could be the basis for musculoskeletal disorders of the entire body. The full extent of its significance and potential is largely unexplored in podiatric literature and medicine. The diagnosis of PHP has undergone several evolutions since the day the preconceived notion of the pathogenesis was presumed to be isolated to the plantar surface of the heel bone and fascia. Medical imaging places importance on heel spurs and are still being used by clinicians as diagnostic success, experts have recognized heel spurs are incidental rather than diagnostic. Not long ago, the pathogenesis of PHP was believed to be repetitive trauma to the plantar fascia causing microtears and inflammation (fasciitis), when inflammation was not evident, a degenerative process (fasciosis) was proposed. The current nomenclature is fasciopathy. The same parallel can be drawn for Achilles enthesopathy, Achilles tendonitis, Achilles tendinosis and Achilles tendinopathy. Some of the current indications for foot surgeries for non-osseous structures of the foot and ankle need to be re-evaluated in light of the characteristics of MTrP. Having a good understanding of MTrP is an essential skill for musculoskeletal therapists.

THE EFFECTS OF A PHYSICAL THERAPY INTERVENTION ON FUNCTIONAL OUTCOME MEASURES IN FRAIL PATIENTS ON HEMODIALYSIS

J. Nussbaum[1], R.K. Garcia[1]
ProHealth & Fitness, PT, OT, PLLC, NY, NY, USA

Background: Frailty is highly correlated with increased disability, falls, morbidity, and mortality. The literature describes patients “diagnosed” with frailty as having three (3) or more of the following criteria: 1) poor gross handgrip strength, 2) unintentional weight loss of more than 4.5 kg within a year, 3) exhaustion, 4) slow normal walking speed, and 5) physical inactivity. The literature also reports that patients with end stage renal disease (ESRD) on hemodialysis (HD) often present with the above criteria, along with many other co-morbidities, that contribute to physiological, psychological, and functional impairments. A recent literature review revealed a limited number of substantial studies that demonstrated a relationship between a decrease in one or more of the five (5) criteria of frailty and a reduction in the negative associated impairments. Therefore, the purpose of this study was to examine the effects of a skilled restorative physical therapy program on functional outcomes in frail patients with ESRD on HD. Methods: The Institutional Review Board of Touro College, New York, NY, approved the study. All eligible participants signed informed consents prior to data collection. One hundred and twenty-three (65 females mean age 65.11 ±11.5 and 52 males mean age 63.19 ±10.96) patients from seven (7) different dialysis facilities participated in this quasi-experimental study. All participants were evaluated by a physical therapist (PT) and non-randomly assigned into either a control (n=62) or an experimental (n=61) group. The following functional outcome measures were then assessed at baseline and at 12 weeks: Sit to Stand 5 repetitions (STS(5), seconds), 6 Minute Walk Test 6MWT, feet), Gross Grip Strength (Grip, lbs./sq. inch), 360° Turn (seconds), Timed Up and Go (TUG, seconds), 20’ Normal Gait Speed (NGS, seconds), and 20’ Fast Gait Speed (FGS, seconds). The experimental group participated in the skilled restorative physical therapy program (RPTP), 2-3x/week for 12 weeks. The RPTP included therapeutic exercise and activities, neuromuscular re-education, and manual techniques. Patients in the experimental group were cued for proper technique and closely monitored for pulse oximetry, blood pressure, heart rate, and rate of perceived exertion during all interventions. Rest periods were timed and utilized for breathing control and patient education. Some innovative, functional mobility treatment techniques such as distracted walking, walking while talking, water carrying, lifting while gripping were utilized during the sessions. Several other complex-resisted, multi-joint movements and activities were also implemented. The control group received standard HD care. Data Analysis: Descriptive statistics were used to summarize all demographic data and functional outcome measures. The Mann-Whitney U Test was used to determine initial group equivalence (pretest) and to determine differences between groups (posttest). All data were analyzed at the 0.05 level of significance using IBM SPSS PASW Statistics© 18.0. Results: Although patients were not randomized into groups, pretest scores between groups for most outcome measures demonstrated group equivalence (p=.163-.903). Significant differences were found between the experimental and control groups for the 6MWT (p=.000), Grip (p=.000), 360° Turn (p=.030), NGS (p=.002), and FGS (p=.000). Conclusions: The findings of this study inferred that a RPTP implemented by skilled PTs on frail patients with ESRD on HD may significantly improve several functional outcome measures. The RPTP also identified effective interventions that may be beneficial in improving physical activity, independent function, and quality of life in this medically complex patient population. A RPTP aimed at increasing physical activity, enhancing grip strength, improving walking speed, and improving overall functionality may reduce the risk factors associated with frailty, thereby decreasing morbidity and mortality in this at risk population. Future studies should examine long-term, multi-center, studies in larger, randomly assigned groups.

RELATION BETWEEN FACIAL MORPHOLOGY AND SEMG ACTIVITY OF HEAD, NECK, AND TRUNK MUSCLES IN CAUCASIAN ADULT FEMALES

S. Tecco[1], L. Tettamanti[2], S. Mummolo[1], E. Marchetti[1], G. Gallusi[3], G. Marzo[1]
[1]Department of Health Science, University of L'Aquila, L'Aquila; [2]Department of Reconstructive Surgery and Advanced Technologies University of Insubria, Varese; [3]Department of Oral Science, Nano and Biotechnology, University of Tor Vergata, Rome, Italy

This study aimed to evaluate whether there is an association between facial morphology on cephalometrics and surface electromyographic (sEMG) recordings of head, neck, and trunk muscles. Forty-seven Caucasian adult females, 18 to 29 years of age (average: 24), underwent lateral skull radiographs in “natural head position”, obtained by having the subject look at a small mirror at eye level, and sEMG recordings for the following muscles: masseter, anterior temporal, digastric, posterior cervicals, sternocleidomastoid, and upper and lower trapezius. All muscles were monitored bilaterally at mandibular rest position and during maximal voluntary clenching (MVC). The maximal bite force was also measured to check MVC. Pearson’s correlation coefficient revealed significant correlations

(P<0.01): (i) between the variables concerning mandibular position and size and the sEMG activity of upper trapezius at mandibular rest position; (ii) between the topographic correlation between the maxillary and mandibular bases (called skeletal class) and the sEMG activity of upper trapezius at MVC; (iii) between the sEMG activity of sternocleidomastoid and the Frankfort to mandibular plane angle; and (iii) between the sEMG activity of masseter and the anterior cranial base to mandibular plane angle. Some associations between cephalometric variables and the sEMG of head, neck, and trunk muscles were observed. No certain conclusion, however, was possible on the mechanism concerning these results. Future longitudinal studies are required.

STRIKING PREVALENCE OF AXIAL SPONDYLOARTHRITIS IN PRIMARY CARE PATIENTS WITH CHRONIC LOW BACK PAIN: A CROSS-SECTIONAL STUDY

A. Weel

Clinical Immunology & Rheumatology Dept., Maasstad Ziekenhuis, Rotterdam, Netherlands

Background: Treatment of axial Spondyloarthritis (aSpA) is most successful in an early stage of the disease.[1] Early treatment requires early recognition in primary care. Until now however, the prevalence of aSpA in primary care is unknown. Moreover 'red flag' symptoms that general practitioners might use to identify patients at risk of aSpA, are missing. Methods: Patients aged 19-45 years with chronic low back pain were identified from general practitioners records. All participants completed Inflammatory back pain questionnaires, underwent an interview and physical examination by rheumatologist. HLAB27 and CRP were assessed. Sacroiliitis was assessed by conventional radiography and MRI. Patients were identified as aSpA when fulfilling the ASAS criteria. Multivariate bootstrap regression and ROC analysis were used to develop a simple referral model. Results: 364 patients (36.3 years old (sd 6.8), mean symptom duration 10.0 years (sd 7.44)) were evaluated. The prevalence of aSpA was 21.5 % (n=77). Ankylosing Spondylitis, the prototype of aSpA, was found in 24 persons (6.6%). Of all potential determinants (Table1) only ASAS-IBP questionnaire, good response on NSAIDs and family history of SpA were related to aSpA with OR (95% CI) of respectively, 2.6 (1.4-4.7), 2.6 (1.2-5.8) and 3.5 (1.9-6.4). The ROC/AUC of the referral model combining these factors was 0.76 (SE 0.03) and showed a sensitivity and specificity of respectively, 79% and 60%. Conclusion: These results indicate a strikingly high prevalence of aSpA in primary care patients with CLBP. Using a simple referral tool might help general practitioners to identify patients at risk for aSpA. 1. Sieper J, Rudwaleit M, Baraliakos X, et al. The Assessment of Spondyloarthritis international Society (ASAS) handbook: a guide to assess Spondyloarthritis. Ann Rheum Dis 2009;68 Suppl 2:ii1-44.

Determinant	Sensitivity (%)	Specificity (%)
History		
Male	36.4	55.8
BMI <=25	31.2	61.3
IBP (rheumatologist opinion)	29.9	86.0
Good response to NSAID's	76.5	52.5
Positive family history	22.1	92.0
Uveitis	3.9	98.6
Crohn's/colitis	3.9	99.0
Peripheral arthritis	13.0	93.7
Dactylitis	5.2	96.9
Enthesitis	10.4	85.0
Psoriasis	6.5	95.5
Diagnostic		
CRP > 10 mg/l	11.7	95.8
HLA-B27 positive	19.5	98.3
X-SIJ	36.4	95.5
IBP Questionnaire		
Calin	85.7	27.2
Berlin	79.2	34.1
ASAS	55.8	67.2
Combined determinants		
ASAS IBP, NSAID, fam history SpA	82	52

Osteoarthritis

ERYTHROCYTE SEDIMENTATION RATE (ESR) AND LEUKOCYTE CHANGES IN CANINE MODEL OF OSTEOARTHRITIS

A. Ajadi

Department of Veterinary Medicine and Surgery, Faculty of Veterinary Medicine, University of Agriculture (Veterinary Medicine and Surgery), Abeokuta, Nigeria

Erythrocyte sedimentation rate (ESR) has been evaluated in humans and was reported to be elevated in osteoarthritis (OA) patients (1). We evaluated changes in ESR and leukocytes following experimental OA in dogs. Ten adult local dogs (Mean weight = 12.4 ± 1.8kg) were used. Dogs were judged free of musculoskeletal abnormalities based on physical examination and preoperative radiographs. Experimental OA was induced on the right knee using the groove model and confirmed by radiographic evidences of joint space narrowing and osteophytes. Gait assessment (GAS) was done subjectively and scores assigned. Blood was obtained for determination of ESR, tWBC, neutrophil and lymphocyte counts and knee radiographs obtained fortnightly up to twelve weeks. GAS and radiographic scores (RAS) were compared at six and twelve weeks using Wilcoxon sign rank test, while ESR and leukocyte parameters were compared with ANOVA. Correlation between parameters was evaluated using Pearson's correlation. A "P" value less than 0.05 was considered significant. Both ESR and neutrophil/lymphocyte (N/L) ratio increased significantly (P<0.05) from week 2 up to week 12 of OA. However, tWBC, neutrophil and lymphocyte counts did not differ significantly. Both GAS and RAS increased up to week 6 of OA and were significantly higher at week 6 than week 12. ESR was significantly (P= 0.033) and positively correlated (n=0.793) with N/L ratio, but negatively correlated (n= -0.843) with GAS. There was no significant correlation between these parameters and RAS. It was concluded that ESR and N/L ratio might be used to monitor progression of OA in dogs. References: Dieppe, P., Lim, K. (1998). Osteoarthritis and Related Problems: Clinical Features and Diagnostic Problems. In Klippel JH, Dieppe PA eds, Rheumatology, 2nd Edition. London: Mosby, 831- 845

CYTOKINE PRODUCTION BY INFRAPATELLAR FAT PAD CAN BE STIMULATED BY INTERLEUKIN 1β AND INHIBITED BY PEROXISOME PROLIFERATOR ACTIVATED RECEPTOR α AGONIST

S. Clockaerts[1,2], **Y. Bastiaansen-Jenniskens[1]**, C. Feijt[1], L. De Clerck[3], J. Verhaar[1], A-M. Zuurmond[4], V. Stojanovic-Susulic[5], J. Somville[6], M. Kloppenburg[7], G. Van Osch[1]

[1]Department of Orthopaedics, Erasmus MC, University Medical Center, Rotterdam, Netherlands; [2]Department of Orthopaedics & Traumatology; [3]Medicine/Rheumatology University of Antwerp, Antwerp, Belgium; [4]TNO Leiden, Leiden, Netherlands; [5]Centocor Research & Development, a division of Johnson & Johnson Pharmaceutical Research & Development, L.L.C. of

Pennsylvania, PA, USA; [6] Department of Orthopaedics and Traumatology, University of Antwerp, Antwerp, Belgium; [7]Rheumatology Dept., Leiden University Medical Center, Leiden, Netherlands

Objective: Infrapatellar fat pad (IPFP) might be involved in osteoarthritis by production of cytokines. We hypothesized that production of cytokines is sensitive to environmental conditions. We evaluated cytokine production by IPFP in response to IL1β and investigated the ability to modulate this response with an agonist for Peroxisome Proliferator Activated Receptor α (PPARα). PPARα is activated by lipid lowering drugs such as fibrates. Methods: Cytokine secretion of IPFP was analyzed in the medium of explants cultures of 29 osteoarthritic patients. IPFP (n=5) and synovium (n=6) were cultured with IL1β and PPARα agonist Wy14643. Gene expression of IL1β, MCP1, IL6, TNFα, leptin, VEGF, IL10, prostaglandin-endoperoxide synthase(PTGS)2 and release of TNFα, MCP1 and PGE2 were compared to unstimulated IPFP and synovium explants. Results: IPFP released large amounts of inflammatory cytokines, adipokines and growth factors. IL1β increased gene expression of PTGS2, TNFα, IL1β, IL6 and VEGF and TNFα release in IPFP. MCP1, leptin, IL10 gene expression and MCP1, leptin and PGE2 release did not increase significantly. Synovium responded similar to IL1β as IPFP, except for VEGF gene expression. Wy14643 decreased gene expression of PTGS2, IL1β, TNFα, MCP1, VEGF and leptin in IPFP explants and IL1β, TNFα, IL6, IL10 and VEGF in synovium that responded to IL1β. Conclusion: IPFP is an active tissue within the joint. IPFP cytokine production increases by IL1β and decreases by a PPARα agonist. Similar effects were observed in synovium. Fibrates could represent a potential disease modifying drug for osteoarthritis by modulating inflammatory properties of IPFP and synovium.

BELIEFS AMONG CANADIAN PHYSIOTHERAPISTS REGARDING THE USE OF THERAPEUTIC ULTRASOUND FOR MANAGEMENT OF MILD TO MODERATE KNEE OSTEOARTHRITIS

N. MacIntyre[2], **M. Bhandari[1]**, J. Busse[3]
[1]Surgery Dept.; [2]McMaster University, Hamilton; [3]Institute for Work and Health, Toronto, Canada

The aim of this study was to describe beliefs and practice patterns regarding the use of therapeutic ultrasound (US) for the management of mild to moderate knee osteoarthritis (OA) in primary care physiotherapy practice in Ontario, Canada. An email invitation to complete an on-line survey was distributed to all members of the Ontario Physiotherapy Association. The survey asked about current use and attitudes towards US for mild to moderate knee OA. The majority of respondents (100 out of 123) reported use of US to manage mild to moderate knee OA: “rarely” by 45, “occasionally” by 39 and “frequently” by 16. Of the 100 respondents who reported at least some use of US for knee OA, most employed this modality to reduce pain in the surrounding soft tissue (n = 66) and/or the knee joint (n = 43). Reasons given by 23 respondents for never using US include the perceived lack of evidence (60%), the belief that time is better spent on active treatments/self-management (27%), and lack of availability or sufficient visits (13%). Endorsement that US is likely to be beneficial for clients with mild to moderate knee OA was divergent (strongly agree = 7, agree = 11, somewhat agree = 38, not sure = 12, somewhat disagree = 15, disagree = 25, strongly disagree = 15). Interestingly, only 56 respondents endorsed belief in US efficacy despite the fact that 100 respondents use it. Future research needs to address this evidence gap and reduce variability in physiotherapy primary care in Ontario.

TRANSFORMING GROWTH FACTOR BETA SIGNALLING AND OSTEOARTHRITIS: REGULATION AND ROLE OF TRANSFORMING GROWTH FACTOR BETA RECEPTOR TYPE II IN ARTICULAR CHONDROCYTES

C. Bauge[1], E. Duval[1], S. Leclercq[1,2], P. Galera[1], K. Boumediene[1]
[1]EA3214 Matrice Extracellulaire et Pathologie, Univ Caen; [2]Département de Chirurgie Orthopédique, Clinique Saint Martin, Caen, France

During osteoarthritis, chondrocytes undergo modifications of their phenotype, which may result from alteration of TGFb signaling. This study investigates the role of TGFß response during chondrocyte dedifferentiation/redifferentiation and inflammation; two processes that mimic, in vitro, some aspects of osteoarthritis, and the expression of TGFb signalling mediators during OA in vivo. Inflammation and chondrocyte dedifferentiation interfere with TGFß signalling by decreasing TßRII mRNA and protein levels and subsequent TGFβ response. At contrary, redifferentiation of passaged chondrocytes permits to restore, at least in part, TßRII expression. Similarly, differentiation of human bone marrow mesenchymal stem cells toward chondrocytes increases TßRII expression. In addition, immunohistological analysis from human OA cartilage shows an important decrease in TGF-beta receptor II in fibrillated cartilage areas. Similar results are obtained using OA rabbit model. Interestingly, TßRII overexpression abolishes the loss of TGFß responsiveness induced by IL-1, whereas in passaged chondrocytes, it permits to increase the expression of aggrecan or type II collagen. Moreover, Sp1 manipulation by silencing or ectopic expression revealed a link between expression levels of this transcriptional factor, which is crucial for constitutive expression of TβRII in cartilage, and TGFß response. Therefore, these data permit us to suggest an important role of TßRII expression during osteoarthritis, and bring new insights in our understanding of chondrogenesis process. These recent insights may contribute to identify therapeutic approaches and new targets to treat osteoarthritis.

HYPOXIA INDUCES CHONDROCYTE PHENOTYPE: MOLECULAR MECHANISM AND APPLICATION IN CARTILAGE TISSUE ENGINEERING

E. Duval[1], C. Bauge[1], R. Andriamanalijaona[1], H. Bénateau[1,2], S. Leclercq[1,3], S. Dutoit[4], L. Poulain[4], P. Galera[1], **K. Boumediene[1]**
[1]Univ Caen - EA3214 Matrice Extracellulaire et Pathologie; [2]Department of Maxillofacial Surgery, CHU; [3]Clinique Saint Martin, Caen; [4]GRECAN, François Baclesse Center, France

The aim of this study was to assess the possibility of cartilage tissue engineering from human bone marrow (hBM) stem cells, as well as human articular chondrocytes (HAC). The ability of these cells to differentiate into chondrocyte-like cells were evaluated *in vitro* and *in vivo*, as well as molecular mechanisms involved in the regulation of aggrecan and type I, II and X collagen. hBM stem cells and dedifferentiated HAC were differentiated into chondrocyte-like cells by culturing them in alginate beads under hypoxia without adding any growth factors or serum. Then, the behaviour of these beads was evaluated *in vivo* in nude mice. We demonstrated that hypoxia associated to alginate beads culture induces chondrogenic differentiation of hBM cells or restores chondrocyte phenotype from dedifferentiated HAC, as mirrors by the increase of type II collagen and aggrecan expression and the decrease of type I and X collagen. This phenotype could be maintained *in vivo*. We also provide evidences that HIF-1a is essential for hypoxic induction of chondrogenesis. This transcriptional factor not only is able to induce the expression of cartilage matrix gene (aggrecan, type II collagen), but also to repress type I and type X collagen expression. We also elucidated the different mechanisms responsible for its effects. Some of them were direct. For instance HIF1a induces aggrecan expression by direct binding on aggrecan promoter. Others were indirect and involved the regulation of other transcription factors, such as Sox9 or Cbfa1. This study demonstrates that culture in alginate beads associated to hypoxia culture or HIF-1a overexpression is effective, simple, fast and safety to induce chondrocyte phenotype from hBM cells or HAC, without using growth factors, and that this phenotype can be maintained in vivo, leading to the formation of a tissue looking like hyaline cartilage. Consequently, this study brings an interesting system for biotechnology of cartilage engineering. *This work was*

supported by EU (GENOSTEM FP6) and by Conseil Régional de Basse-Normandie (France).

OBESITY AND OUTCOME OF LOWER LIMB ARTHROPLASTY PATIENTS ENROLLED IN AN ENHANCED RECOVERY PROGRAMME: A 1000 PATIENT STUDY

P. Buddhdev[1], N. Davies[1], T. Waters[1]
[1]*Trauma & Orthopaedics, Watford General Hospital, Watford, London, UK*

Introduction: Obesity is a direct contributor to degenerative joint disease. As the prevalence of obesity increases globally, more overweight patients will present for lower limb arthroplasty. There are reports that overweight patients in the UK's National Health Service, typically with a Body Mass Index (BMI) over 30 (BMI 30-39 obese, BMI≥40 morbidly obese), are being denied operations on the premise that they are at risk of significant complications. Enhanced Recovery Programmes (ERP) are designed to enable patients to recover quickly and return home safely within a few days. Objectives: The aim of this study was to compare the outcome of obese and non-obese patients enrolled in our ERP. Methods: We prospectively studied 1000 consecutive patients who underwent primary and revision lower limb arthroplasty enrolled in the ERP from March 2010 to July 2011. 454 patients (45%) were considered obese (BMI of >30) with 34 patients (3%) considered morbidly obese (BMI >40). Outcomes measured included: Length of stay, wound complications, VTE and blood transfusion requirements. Data was collected to 42 days following discharge. Results: There was no significant difference in the length of stay between the obese (BMI >30) and non-obese (BMI<30) groups (median stay 4 days). No other significant differences were noted between the two groups. Conclusion: The overwhelming body of evidence in the scientific literature suggests that obese patients have much to gain from lower limb arthroplasty with no significant increase in complications. Our study has demonstrated similar results for patients enrolled in the ERP. The refusal of surgery to these patients based on their weight is discriminatory, unfair and not evidence-based medicine.

STATIN USE IS ASSOCIATED WITH REDUCED INCIDENCE AND PROGRESSION

S. Clockaerts[1,4], G. van Osch[1], Y. Bastiaansen-Jenniskens[1], J. Verhaar[1], F. Van Glabbeek[4], J. Van Meurs[3], H. Kerkhof[3], A. Hofman[2], B. Stricker[2], S. Bierma-Zeinstra[1]
[1]*Orthopaedics Dept.;* [2]*Epidemiology Dept.;* [3]*Internal Medicine Dept., Erasmus MC, University Medical Center, Rotterdam, Netherlands;* [4]*Orthopaedics Dept., University of Antwerp, Antwerp, Belgium*

Background: Osteoarthritis is the most frequent chronic joint disease causing pain and disability. Besides biomechanical mechanisms, the pathogenesis of osteoarthritis may involve inflammation, vascular alterations and dysregulation of lipid metabolism. As statins are able to modulate many of these processes, this study examines whether statin use is associated with a decreased incidence and/or progression of osteoarthritis. Methods: Participants in a prospective population-based cohort study aged ≥55 years (n=2921) were included. X-rays of the knee/hip were obtained at baseline and after on average 6.5 years, and scored with the Kellgren & Lawrence score for osteoarthritis. Any increase in score was defined as overall progression (incidence and progression). Data on co-variables were collected at baseline. Information on statin use during follow-up was obtained from computerized pharmacy databases. The overall progression of osteoarthritis was compared between users and non-users of statins. Using a multivariate logistic regression model with generalized estimated equation, odd ratios and 95% confidence intervals were calculated after adjusting for confounding variables. Results: Overall progression of knee and hip osteoarthritis occurred in 6.9% and 4.7% of the cases, respectively. The adjusted odds ratio for overall progression of knee osteoarthritis in statin users was 0.43 (95% CI 0.25-0.77, p=0.01). The use of statins was not associated with overall progression of hip osteoarthritis. Conclusions: Statin use is associated with more than 50% reduction in overall progression of osteoarthritis of the knee, but not of the hip.

HYALURONIC ACID IN THE TREATMENT OF KNEE OSTEOARTHRITIS, THE CURRENT EVIDENCE WITH A SPECIAL EMPHASIS ON THE DIFFERENCE BETWEEN PRODUCTS

S. Colen[1], M. Van den Bekerom[2] , M. Mulier[1], D. Haverkamp[3]
[1]*Orthopaedic Surgery Dept., University Hospital Leuven, Leuven, Belgium;* [2]*Orthopedic Surgery, Spaarne Hospital, Hoofddorp;* [3]*Orthopaedic Surgery, Slotervaart Hospital, Netherlands*

Although accepted as a conservative treatment option of knee osteoarthritis, the debate about the effectiveness of intra-articular treatment with hyaluronic acid is still going on because of the contrasting outcomes in different studies. Compared to other treatment options or even placebo, hyaluronic acid shows no difference in improvement in several well designed studies. Besides the effectiveness of all hyaluronic acid types, the question whether one brand of hyaluronic acid is better than another is still unanswered. In this systematic review we compare the effects of hyaluronic acid to placebo in general and of different brands of hyaluronic acid separately to placebo. We also compare the efficacy of different brands of hyaluronic acid. Results: hyaluronic acid has an improvement in pain of approximately 40-50% compared to baseline. However, compared to placebo (infiltration of saline) this effect is not that large. Due to a large effect of placebo (30-40% pain reduction for at least 3 months) we conclude that hyaluronic acid has a weighted mean difference of just 10.20 using the VAS pain, which can be discussed if this is reaching the minimum clinically important difference. Does a patient notice the difference in treatment improvement between hyaluronic acid and placebo? Comparing different brands of hyaluronic acid we are not able to conclude that one brand has a better efficacy than another, because of the heterogeneity of the studies and outcomes. Discussion: in the future it is necessary to determine the exact working mechanism of placebo, because this may give us an idea how to treat osteoarthritis more efficient. In contrary it is important to compare different brands of hyaluronic acid to determine if one of the brands or different molecular weights of hyaluronic acid is the best to treat osteoarthritis. Our recommendation is to start large (multicenter) randomized controlled trials to give us more evidence about the efficacy of the different brands of hyaluronic acid.

MANIPULATIONS OF DISULFIDE BONDS IN AN AMYLIN OCTAPEPTIDE: A MECHANISM TO MODIFY BIOACTIVITY

J. Cornish[1], D. Naot[1], R. Kowalczyk[2], M. Watson[1], K.E. Callon[1], P.W. Harris[2], M.A. Brimble[2]
[1]*Department of Medicine;* [2]*School of Chemical Sciences, University of Auckland, New Zealand*

Amylin, a peptide hormone co-secreted with insulin from the þ-pancreatic cells, is active in fuel metabolism. We established amylin is anabolic to osteoblasts, whilst inhibiting osteoclastogenesis in vitro and in vivo thus suggesting a role in therapy of osteoporosis; although because of the peptide size and its non-osteogenic effects, it is not an ideal therapeutic agent. Previous structure-activity relationships demonstrated that an octapeptide fragment of amylin, amylin-(1-8) a ring-peptide, is inactive on fuel metabolism, but still anabolic to osteoblasts in vivo and in vitro. This small ring-peptide has thus been used as a model for the creation of orally active, non-peptide analogues, as potential candidates for the therapy of osteoporosis. The disulfide bond in novel amylin-(1-8) analogues was modified either *via* macrocyclization or bridging reagent to increase potency and/or stability. A dibromomaleimide linker -analogue 1 (A1), a thiobenzyl linker (A2, A3), a thioalkyl chain of variable length (A5, A6), and a thiol-Michael modification (A7) were used to generate bridged analogues of amylin-(1-8)-NH_2. "Click chemistry" was also used to afford a triazole-linked analogue. Importantly, a Nobel Prize-winning Ring Closing Metathesis (RCM) technology was used to afford chemically inert stapled analogues (A8-16). The analogues were

screened for proliferative activity in osteoblasts at physiological concentrations. Six analogues (A2, A8, A12, A13, A15, A16) significantly stimulated increases in mitogenesis at a similar level to the native peptide with improved stability. These novel entities could lead to development of stable therapeutic compounds for use in osteoporosis treatment or for promotion of healing fractures. Further chemical syntheses are needed to optimize these promising analogues. Subsequent synthetic modifications may further improve activity and stability.

INVESTIGATING GASTROINTESTINAL FUNCTION AND MICROBIOTA PROFILES IN PATIENTS WITH OSTEOARTHRITIS – A ROLE FOR GLUCOSAMINE AND GREEN-LIPPED MUSSEL

S. Coulson[1], P. Masci[1], P. Vecchio[2], L. Vitetta[1]
[1]*School of Medicine, The University of Queensland, Brisbane;* [2]*Rheumatology Dept., The Princess Alexandra Hospital, Australia*

Aim: Investigate gastrointestinal (GI) dysfunction and microbiota profiles in patients with knee OA. Further, to consider if clinical efficacy of Glucosamine (GlcN) and Green-lipped mussel (GLM) supplementation for OA symptoms could also improve GI function. Introduction: Efficacy of GlcN and GLM for OA remains controversial. Analyses of discrepancies have failed to consider inefficient GI function and irregular GI flora as confounders against effective metabolism and utilization of OA-specific nutraceuticals. Acetaminophen and NSAIDs prescribed for OA symptomology are largely responsible for this confounding effect. Previous clinical data demonstrated GLM (3000mg/day) concurrently and significantly improved symptoms of GI dysfunction and knee OA. It is hypothesized that improvement in GI function and microbiota profiles will correlate to greater knee OA symptom relief in patients when supplementing with GlcN and GLM. Methodology: Forty knee OA patients have been randomized (open-label) to GlcN or GLM (3000mg/day) for 12 weeks. Assessments are T_0, T_6 and T_{12} weeks using Lequesne Index, WOMAC; Gastrointestinal Symptom Rating Scale (GSRS), Faecal Microbial Analysis and SF-12. Pain severity and analgesic mediation intake are recorded daily. Discussion: Baseline data was indicative of an altered microbiota profile and elevated GSRS scores compared to a healthy population group. GlcN and GLM demonstrated efficacy in treating knee OA symptoms. By $T_{12,}$ WOMAC and Lequesne scores improved concurrently with GSRS scores. It is hence biological plausible to conclude that GlcN and GLM at increased doses not previously reported, improved GI function, integrity and microbiota profile as well as knee OA symptoms (pain, stiffness, function).

CLINICAL CHARACTERISTICS AND MEDICATION USE OF PATIENTS WITH KNEE OSTEOARTHRITIS SELECTED FOR TOTAL JOINT REPLACEMENT SURGERY

T de Boer[1], M. Stukstette[1], P. Welsing[1], M. Huisman[2], A. Polak[3], J. Bijlsma[1], S. Mastbergen[1], F. Lafeber[1]
[1]*Rheumatology & Clinical Immunology Dept., University Medical Center Utrech, Utrecht;* [2]*Rheumatology Dept.;* [3]*Orthopaedics Dept., Sint Franciscus Gasthuis Rotterdam, Netherlands*

Introduction: Specific indications for total knee replacement (TKR) surgery are not clearly defined or evidence based. Generally accepted are pain and restrictions in performance despite the use of (non-) pharmacological interventions. The aim of this study is obtaining insight in characteristics and previous pharmacological management of end-stage knee OA patients, and to explore whether patients without adequate pain medication still benefit from pain medication. Method: From 172 successive TKR patients, those not using adequate analgesics were randomized to an NSAID (celecoxib, 2dd200mg daily or naproxen, 3dd250mg) or no medication for 6 weeks prior to surgery. Patient characteristics, severity of symptoms (WOMAC pain, stiffness and physical function), medication use and radiological features (K&L and Altman score) were collected. Modified OMERACT/OARSI responder criteria were used to calculate the percentage responders. Results: The year prior TKR, 26% (n=44) of patients used NSAIDs daily, 27% (n=47) used PCM daily, or occasional NSAID, and nearly half (47%; n=81) used PCM occasionally or no medication at all. Of 81 patients not using adequate analgesics, 46 were randomized to NSAID treatment and 35 to no treatment. Patients treated 6 weeks with an NSAID improved significantly in pain and stiffness (-5.7 [-10.9; -0.5] and -9.6 [-16.4; -2.8], resp. both $p<0.05$). 27% of patients could be classified as an actual responder. Conclusions: Most patients awaiting TKR experienced significant levels of pain and limitations in activities, but surprisingly did not take daily NSAIDs. Patients with inadequate medication, starting NSAIDs daily, improved clinically significantly.

SELF-REPAIR IN DEGENERATIVE JOINT DISEASE

V. Di Nicola
Interbion, Gordola, Switzerland

Introduction: This study presents a method for treating and structurally improving articulations affected by Degenerative Joint Disease (DJD). Scholars including Davis JW, Filatov VP and Cerletti U have been studying and using the regenerative properties of placenta, amnios and other non-vital tissues since the early 1900s. These pioneering studies have opened new avenues for tissue renewal. More recently, the new biological knowledge about extra cellular nucleic acids, growth factors (GF)-as by-products of trauma response- and heat shock proteins (Hsp) has helped to advance research even further. Building on those experiences, we have developed a regenerative gel obtained with distressed, processed blood, Polydeoxyribonucleotides (Pdrn), and a thickening substance. The objective was to stimulate the local innate stem-cells with our gel in order induce tissue repair. Methods: The focus of this analysis is on two groups of patients: the first one composed of over-eighties and the second group was from 45 to 55 year old patients.Treated patients have been clinically and radiologically evaluated with a follow-up of 6 to 48 months. Results: Data show a statistically significant improvement in terms of pain and joint mobility, sometimes coupled with a clear radiological improvement. Follow-up shows encouraging data in terms of clinical stability over time. During the study we encountered virtually no side effects, adverse reactions, or toxicity. Conclusion: This study suggests a new methodological approach and treatment of DJD based on tissue regeneration and restoration resulting in clinical resolution.

PLOWING IN A CARTILAGE MODEL OF DIARTHRODIAL JOINTS COULD INDUCE CATABOLISM

L. Gallo[1], V. Colombo[1], M.R. Correro-Shahgaldian[1]
[1]*Center of Dental Medicine, University of Zurich, Zurich, Switzerland*

Purpose: Human diarthrodial joints undergo complex rolling/plowing loading patterns scarcely investigated in live tissue. Yet, joint breakdown could be partially explained by mechanobiological effects also due to plowing. Objective of this study was to investigate the biological response of cartilage tissue models to plowing with *in vivo* data on strains, forces, stresses, and work density. Methods: Cartilage plowing was performed by means of an explant test system previously developed and validated. Cartilage specimens were kept in a tank filled with DMEM solution. Adequate sensors measured force and displacement in relevant directions. Live cartilage strips from bovine nasal septum of one year old calves were submitted to plowing for 2 hours at 37°C in DMEM solution by using a cylindrical aluminum indenter (Æ 25 mm) moving tangentially at 10 mm/sec and simultaneously applying normal forces of 25, 50 or 100 N respectively. Analyses were performed 0, 2, 4 and 24 hours post loading. Results: Overall cell viability exceeded 95% for all applied forces, although superficial zones of dead chondrocytes were observed, increasing with the applied normal force. qRT-PCR showed that plowing induces MMP-3 upregulation dependent on the applied force (peaks of 2.3x, 4.7x and 6.3x for 25, 50 and 100 N respectively). Other genes involved in cartilage turnover were shown not to be significantly affected by plowing. Conclusions: This study shows that plowing of cartilage appears to induce significant dose-dependent

mechanobiological effects, and the loading parameters studied would promote the production of catabolic enzymes tending to degrade the extracellular matrix.

HOW WIDESPREAD ARE OUTCOMES MEASURES AND INSTRUMENTS FOR OSTEOARTHRITIS AND HOW VALID ARE THEY?

B. Hanson[1], M. Suk[2], D. Helfet[3], D. De Faoite[1]
[1]AO Clinical Investigation and Documentation, AO Foundation, Duebendorf, Switzerland; [2]Orthopedics Dept., University of Florida - Shands Jacksonville, FL, USA; [3]Orthopedic Surgery Dept., Hospital for Special Surgery, NY, USA

INTRODUCTION: This paper investigates if outcomes measures in the literature were designed for use in an osteoarthritic group and validated in a subsequent study. METHODS: A total of 296 outcomes measures and instruments were identified from a previously assembled database and checked for the presence of the word "osteoarthritis" in the title to ensure relevance. The validity of an outcome measure (ie, it measures what it was designed to measure) was examined across three elements: - *Content*: the content was developed by a team of professionals or through statistical modeling; - *Construct*: the instrument was validated against a generic instrument or correlated with hypothesized subscales from another instrument; - *Criterion*: the instrument was validated against a “gold standard” instrument or is predictive of a future outcome. RESULTS: 3% of outcome measurements (10/296) are specifically designed for use on osteoarthritic patient groups based upon their title. Two outcome measurements are double counted as they are employed for use in both hip and knee patients. The body part and number of identified outcome measures are as follows: knee (4), hip (3), ankle (1), hand (1), and shoulder (1). 90% are patient-reported (9/10), with a single outcome measure being clinician-based (1/10). All of the outcome measures (10/10) are validated for use. 60% of these (6/10) are validated for all 3 elements of validity. SUMMARY: Only a small amount of outcomes measures specifically designed for osteoarthritis are available. However, those that are available are generally patient-reported, and display a high degree of validity.

JOINT-PAIN COMORBIDITY IS ASSOCIATED WITH UNFAVORABLE HEALTH STATUS AND MEDICATION USE IN HIP AND KNEE OSTEOARTHRITIS: A CROSS-SECTIONAL STUDY

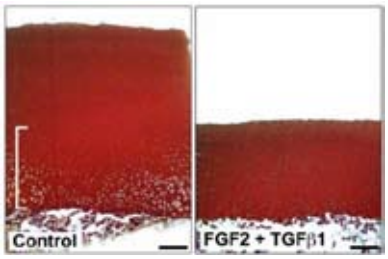
T. Hoogeboom[1,3], A. den Broeder[1], B. Swierstra[2], R. de Bie[3], C. van den Ende[1]
[1]Department of Rheumatology; [2]Department of Orthopaedics, Sint Maartenskliniek, Nijmegen; [3]Department of Epidemiology, Maastricht UMC, Maastricht, Netherlands

Objective: To determine the prevalence of joint-pain comorbidities (JPCs) in hip or knee osteoarthritis (OA) and to assess differences in characteristics of individuals with and without JPCs. Methods: In this cross-sectional study, individuals referred to secondary care for treatment of hip/knee OA completed questionnaires to determine socio-demographic characteristics, disease-related outcomes, and JPCs. We defined JPC as pain perceived in a joint, other than the index joint, for more than half of the days in the preceding month. Differences in patient- and disease-related characteristics between participants with and without JPCs were compared using analyses of covariance and logistic regression. Results: 401 individuals, 117 with hip OA and 284 with knee OA, returned the questionnaire (82% response rate); the mean (SD) age was 58 (13) years and 58% of the responders were women. Fifty-eight percent of the participants reported symptoms in ≥1 joint other than the index joint. Participants with JPCs were more likely to be women, less educated, and had more medical comorbidities. Individuals with joint-pain comorbidities reported unfavorable outcomes on pain, functioning, fatigue, distress, and health-related quality of life compared with patients without JPCs (p<0.001 for all). Moreover, use of NSAIDs (p<0.038), opioids (p<0.010), and supplements (p<0.019) was higher in the group with JPCs. Conclusion: Our results indicate that individuals with JPCs represent a clinically relevant and large subgroup of people with OA of the knee or hip. We recommend to address JPCs in both research and clinical practice.

FGF2 AND TGFβ1 INDUCE PRECOCIOUS MATURATION OF ARTICULAR CARTILAGE: IMPLICATIONS FOR REPAIR OF OSTEOARTHRITIC LESIONS

I. Khan[1], C. Archer[1]
[1]Pathophysiology & Repair Dept., Cardiff School of Biosciences, Cardiff, UK

Post-natal maturation of articular cartilage is a key developmental process that allows joint-specific adaptation of tissues to their local biochemical and biomechanical environment. Immature cartilage, a thick and relatively undifferentiated tissue undergoes a radical morphological transformation to generate a stiff and highly structured tissue that can potentially last a lifetime. Cartilage in osteoarthritic lesions can be viewed as undergoing a reversal of maturation, in that molecular, cellular and extracellular features found in immature cartilage are re-expressed. Whilst it is known that the presence of articular cartilage-derived stem cells in normal and osteoarthritic cartilage indicates that there is an inherent and viable cellular basis for tissue repair, the extent of repair is partially dependent upon recapitulation of post-natal developmental cues that induce maturation, and therefore, functional repair of cartilage. We have discovered that FGF2 and TGFβ1 induce precocious maturation of articular cartilage[1], rapidly restructuring immature cartilage in morphology, phenotype and function such that it is thinner, more differentiated and stiff, see Figure (cartilage explants were cultured for 21 days). Maturation proceeds as a process of synchronized growth and resorption, with articular cartilage stem cells generating growth and the highly regulated activity of matrix metallopeptidases stimulating resorption. Significant changes in collagen gene expression and collagen structure through crosslinking correlate with a 200% increase ($P<0.05$) in tissue stiffness. Understanding how articular cartilage maturation is initiated and regulated will allow us to control this process in order to enhance intrinsic repair i*n vivo* and grow high quality cartilage *in vitro*. 1. Khan, IM *et al* (2011) Arthritis Rheum *Epub.*



EVALUATION OF SEPARATE QUANTITATIVE RADIOGRAPHIC FEATURES ADDS TO THE PREDICTION OF INCIDENT RADIOGRAPHIC OSTEOARTHRITIS IN INDIVIDUALS WITH RECENT ONSET OF KNEE PAIN: FIVE-YEAR FOLLOW-UP IN THE CHECK COHORT

M.B. Kinds[1,2], A.C.A.Marijnissen[1], K.L. Vincken[2], M.A. Viergever[2], K.W. Drossaers-Bakker[3], J.W.J. Bijlsma[1], S.M.A. Bierma-Zeinstra[4,5], P.M.J. Welsing[1,6], F.P.J.G. Lafeber[1]
[1]Department of Rheumatology & Clinical Immunology Dept.; [2]Image Sciences Institute, University Medical Center Utrecht; [3]Arthritis Center Twente, University Arthritis Center Twente, University Twente & Medisch Spectrum Twente, Enschede; [4]General Practice; [5]Orthopaedics, University Medical Center Rotterdam; [6]Julius Center for Health Sciences & Primary Care, University Medical Center Utrecht, Utrecht, Netherlands

Introduction: Detailed radiographic evaluation might enable the identification of osteoarthritis (OA) earlier in the disease. This study evaluated whether and which separate quantitative features on knee radiographs of individuals with recent onset knee pain are associated with incidence of radiographic OA and persistence and/or progression of clinical OA during five-year follow-up. Methods: From the Cohort

Hip & Cohort Knee study participants with knee pain at baseline were evaluated. Radiographic OA development was defined as Kellgren & Lawrence (K&L) grade ≥II at five-year follow-up. Clinical OA was defined as persistent knee pain and as progression of WOMAC pain and function during follow-up. At baseline radiographic damage was determined by quantitative measurement of separate features using Knee Images Digital Analysis, and by K&L-grading. Results: Measuring osteophyte area (odds ratio (OR)=7.0) and minimum joint space width (OR=0.7), in addition to demographic and clinical characteristics, improved the prediction of radiographic OA five years later (area under curve (AUC)=0.74 *vs.* 0.64 without radiographic features). When the predictive score (based on multivariate regression coefficients) was larger than the cut-off for optimal specificity, the chance of incident radiographic OA was 54% instead of the prior probability of 19%. Evaluating separate quantitative features performed slightly better than K&L-grading (AUC=0.70). Radiographic characteristics hardly added to prediction of clinical OA. Conclusions: In individuals with onset knee pain, radiographic characteristics added to the prediction of radiographic OA development five years later. Quantitative radiographic evaluation in individuals with suspected OA is worthwhile when determining treatment strategies and designing clinical trials. Funding source: Dutch Arthritis Association.

HIGH TIBIAL OPEN-WEDGE OSTEOTOMY: NEW TECHNIQUES AND EARLY RESULTS

W. Kolb
Department of Orthopaedics, Bethesda Krankenhaus Stuttgart, Stuttgart, Germany

High tibial osteotomy is an efficient method to treat the unicondylar osteoarthritis. The combination of locked plate fixators and the minimally plate osteosynthesis (MIPO) technique allows plate osteosynthesis without bone grafts. The aim of the present report is to describe (1) new planning methods (2) and new techniques for opening-wedge high tibial osteotomies. Analysis of knee malalignment includes 5 criteria (Frontal mechanical axis, joint line, sagittal mechanical axis, patellofemoral joint, and malrotation). The post-operative correction is planned with use of the method of Miniaci et al. or the methods of Dugdale et al. or Coventry. The mechanical axis is shifted to the Fujisawa point. An individual correction of various deformities according to the intraarticular disease is also recommended. The post-operative correction can also be planned with an arthroscopy before osteotomy according to the Outerbridge classification. A tool preOp plan was developed by Siemens to support planning deformity corrections with TomoFix. Computer-assisted navigation systems may improve precision and accuracy of the leg axis correction. Barrel-vault (dome) osteotomies, lateral-closing wedge, medial opening wedge high tibial osteotomies or a combined procedure are used to treat various deformities of the knee. Modern open wedge high tibial osteotomy involves sawing and chiselling through the bone and the application of an internal (or external) splint to fix the fragments in the required juxtaposition until bone healing is complete. The open wedge high tibial osteotomy in the MIPO technique with the TomoFix internal fixator obtains significant improved clinical results after a short to medium term follow-up.

JOINT RESURFACING WITH DECELLULARIZED TYPE 1 COLLAGEN AS AN ALTERNATIVE TO REPLACEMENT OR ARTHRODESIS FOR HALLUX RIGIDUS OSTEOARTHRITIS

A. Landsman
Surgery Dept., Harvard Medical School, Cambridge, MA, USA

The first metatarsal phalangeal joint is one of the most common sites for osteoarthritis. This painful condition results in hallux rigidus, and frequently leads to either arthrodesis or joint replacement. As an alternative, we report on a series of 12 cases in which damaged cartilage was resected along with peri-articular osteophytes, and a sleeve fashioned from decellularized collagen was placed over the metatarsal head. We also examine the histologic changes which occur in the knee joint of the New Zealand white rabbit, following abrasion of the femoral cartilage and resurfacing with decellularized collagen. It was hypothesized that when first metatarsal phalangeal joints were resurfaced with decellularized type 1 collagen (either allograft or xenograft), this would result in normal, pain-free gliding motion to that joint. Clinical evaluation included pre- and post-operative pain assessments, radiographic measures, and clinical measurements of range of motion. Data was collected after 1 week, 1 month, 3 months, 6 months, and 1 year after surgery. These results were compared and contrasted to reports in the literature that describe outcomes following fusion and artificial joint arthroplasty. Based on clinical outcomes, the author found that there were fewer complications associated with joint resurfacing, when compared to total and hemi joint replacement. Joint stability and functional range of motion was better following joint resurfacing, as compared to total and hemi joint replacement. When compared to arthrodesis, the healing time was dramatically shorter with joint resurfacing, and early mobility and complication rates were also reduced. Histologic examination of the rabbit knee procedure provided support at the cellular level for our hypothesis that the joint surface became smooth, and that the collagen appears to have been well incorporated. Based on the author's experience, the use of decellularized type 1 collagen to resurface appears to be a highly satisfactory procedure, which restores normal function and reduces pain in treated patients.

CLARIFYING THE ROLE OF ADAMTS4 AND ADAMTS5 IN HUMAN OSTEOARTHRITIS: FULLY SELECTIVE AND NEUTRALIZING MONOCLONAL ANTIBODIES FOR CHARACTERIZATION OF THE DISEASE AND DEVELOPMENT OF A DISEASE MODIFYING THERAPEUTIC

J. Larkin[1], T. Lohr[1], L. Elefante[1], J. Shearin[2], R. Matico[2], J-L. Su[2], J. White[1]
[1]Biopharm R&D; [2]Platform Technology & Science - Biological Reagents & Assay Development, GlaxoSmithKline, King of Prussia, PA, USA

Characterization of the pathologic processes involved in osteoarthritic cartilage degradation have been a significant focus of research over the past few decades with the ultimate goal of identifying key factors and the development of novel treatment strategies. Through the use of knockout mouse strains it has been widely reported that ADAMTS5 is an instrumental protease responsible for driving cartilage loss in preclinical models of arthritis. However, because these studies were performed using systems that may not accurately mimic the human condition and etiology, questions remain about the level of ADAMTS5 involvement in human osteoarthritis, particularly in relation to ADAMTS4. To address these questions, fully selective, high affinity ADAMTS4 and 5 monoclonal antibodies were generated and assessed for their ability to inhibit recombinant and native aggrecanase activity and modulate disease-related endpoints in an *ex vivo* human osteoarthritic cartilage explant system and *in vivo* using the DMM mouse model of osteoarthritis. From these studies it is clear that, as predicted from the knockout mouse studies, ADAMTS5 is a major protease involved in human osteoarthritis. Pharmacokinetic parameters and the ability of these monoclonal antibodies to reach the site of target expression and purported disease activity following systemic administration is also demonstrated, suggesting that large proteins can, in fact, fully penetrate into the dense cartilage matrix making them a viable therapeutic platform for targets within the cartilage. Structural models were also employed to predict the interaction between the target antigen and antibody. As a result of

this work, an ADAMTS5 selective monoclonal antibody was humanized and progressed for development as an osteoarthritis disease modifying drug.

A NEW TOOL FOR MEASURING CUP ORIENTATION IN TOTAL HIP ARTHROPLASTY FROM PLAIN RADIOGRAPH

C-K. Liaw[1], T-Y. Wu[2], R-S. Yang[3], S-M. Hou[4]
[1]Department of Orthopaedics, Tao-Yuan General Hospital, Taoyuan; [2]General Practice, Taipei City Hospital, Renai Branch; [3]Department of Orthopaedics, College of Medicine, National Taiwan University & Hospital; [4]Department of Orthopaedics, Shin Kong Wu Ho-Su Memorial Hospital and Health System, Chinese Taipei

The orientation of the hip joint cup is an important measure of total hip arthroplasty (THA). Orientation includes abduction (inclination) and anteversion. Anteversion can be further considered as true (anatomic) and planar (radiographic) anteversion. We developed a new protractor to measure the orientation of the cup in THA. With this new device, we can measure the true and planar anteversion as well as abduction. In order to verify the protractor's accuracy, we used a software simulator that simulates 45 THA radiographs with 15 different anteversions ranging from 15 to 29 degrees. Then we measured the planar anteversion with ours and Lewinnek method. The median error was 1 degree with ours and 1.23 degrees with the Lewinnek method. Maximum errors are 3 degrees with ours and 2.61 degrees with the Lewinnek method. Mean errors were 0.96 degrees with ours and 1.2 degree with the Lewinnek. The standard deviations are 0.74 with ours and 0.57 with the Lewinnek. By using two-sample student-*t* test, there was no difference between the two methods (p=0.09). We also compared with Pradihan's data on literature. There was also no statistical difference (p=0.57). According to the result, our new method is as good as the Lewinnek and Pradihan methods.

OBESITY INFLUENCE THE CLINICAL OUTCOME AND THE QUALITY OF LIFE FOLLOWING PRIMARY TOTAL KNEE ARTHROPLASTY

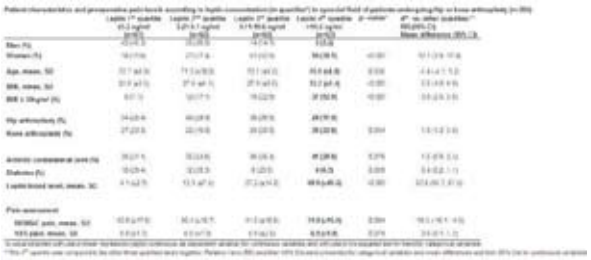
A. Liljensøe[1], I. Mechlenburg[1], J.O. Laursen[2]
[1]Orthopaedic Research Unit, Aarhus University Hospital, Aarhua; [2]Orthopedic Surgery Dept., Hospital Southern Jutland, Denmark

Introduction: In Denmark, there are annually performed between 7-8000 primary total knee arthroplasty (TKA) and there seems in all countries to be a rapid increase in the number of knee replacements. The most frequent indication for TKA is osteoarthritis (80%). Investigations have shown that obesity is a significant factor for the development of arthritis. On the contrary the associations between obesity and outcomes following TKA are ambiguous. The purpose of the study was to investigate whether there is an association between the preoperative BMI in TKA patients and the effect five years postoperative. Method and Material: 197 patients, who had undergone primary TKA in 2005 and 2006, participated in a five years follow-up study. The outcome measures were patient reported outcome (SF-36), which consists of eight strands and two component scores, "physical component score" and "mental component score" and the Knee Society Rating System (KSS) "knee score" and "function score", and improvement of the two KSS scores, from baseline to follow-up. Results: With Ordinal logistic regression (adjusted for gender, age, basic disease and surgical procedure) were found statistically significant association between BMI and nine of the fourteen outcome measures. For all outcome measures were found OR > 1. With a difference in BMI at 1 kg/m^2 increases the risk of lower scores from a minimum of 2% OR 1.02 (0.97-1.07) p = 0.5 ("mental component score") to maximum 14% OR 1.14 (1.08-1.21) p <0.001 (KSS function score). With a difference in BMI at 5 kg/m^2 increases the risk of lower scores from a minimum of 9% OR 1.09 ("mental components scores") to a maximum of 96% OR 1.96 (KSS function scores). With a difference in BMI of 10 kg/m^2 rises risk of worse score with minimum 19% OR 1.19 ("mental component score") to a maximum of 284% OR 3.84 (KSS function score). Discussion: - The association between BMI and the efficacy 5 years following primary TKA is clear. - High BMI increases the risk of poor outcome following TKA.- More than half of the outcome measures are statistically significant.- All the results showed OR > 1.- The estimates can be used as a predictor for the expected efficacy of the treatment for each patient. - Nothing in the analysis suggests random finds.

SYNOVIAL FLUID LEPTIN LEVEL AND JOINT PAIN IN END-STAGE OSTEOARTHRITIS: A POTENTIAL EXPLANATION FOR INCREASED PAIN IN WOMEN AND IN OBESE PATIENTS

A. Lübbeke[1], A. Finckh[2], G. Puskas[1], D. Suva[1], A. Lädermann[1], S. Bas[2], D. Fritschy[1], C.Gabay[2], P. Hoffmeyer[1]
[1]Orthopaedic Surgery Dept.; [2]Rheumatology Dept., Geneva University Hospitals, Geneva, Switzerland

Synovial leptin levels are increased in osteoarthritis (OA), particularly in women and in obese patients. Furthermore, in these two patients groups higher pain levels before joint replacement have been described. We hypothesized that synovial fluid (SF) leptin concentrations correlate with pain severity, and thus mediate the association between increased joint pain and (1) female gender and (2) obesity. Cross-sectional study including all patients with primary hip and knee OA undergoing total joint arthroplasty in a large orthopaedic center, between January and December 2010. On the day of intervention, SF and serum were sampled and leptin concentrations were assessed using an ELISA kit. Main outcome was severity of joint pain measured preoperatively with WOMAC and VAS pain scale. 250 patients were included, 134 patients underwent hip and 116 knee arthroplasties. Mean (±SD) age was 72 (±9) years, 62% were women. Mean SF leptin levels were 22.5 (± 25.3) ng/ml in women and 5.3 (±5.5) ng/ml in men (p<0.001). SF leptin concentrations >19.6 ng/ml (highest quartile) were significantly associated with increased pain levels on both WOMAC and VAS pain scale. The association remained unchanged after adjusting for presence of contra-lateral arthritic joints and diabetes. Significant associations between increased joint pain and (1) female gender and (2) BMI observed in univariate analyses disappeared after adjusting for SF leptin concentrations, suggesting that these associations are mediated by leptin levels. Joint pain is significantly associated with SF leptin concentrations. Increased pain observed in women and in obese patients may be related to high leptin levels.



IMPLEMENTATION OF CLINICAL PRACTICE GUIDELINES FOR MANAGEMENT OF NONSURGICAL KNEE OSTEOARTHRITIS: A SURVEY OF PHYSIOTHERAPISTS IN DIRECT ACCESS PRACTICE SETTINGS IN ONTARIO, CANADA

N. MacIntyre[1], B. Hale[3], M. Bhandari[2], J. Busse[4]
[1]Rehabilitation Science Dept.; [2]Surgery Dept., McMaster University, Hamilton; [3]University of Guelph, Guelph; [4]Institute for Work and Health, Toronto, Canada

The aim of this study was to explore facilitators and barriers towards implementation of Clinical Practice Guidelines (CPGs) for management of nonsurgical knee osteoarthritis (OA) for physiotherapists in primary care settings in Ontario, Canada. We invited all members of the Ontario Physiotherapy Association (OPA) to complete an electronic questionnaire in order to access the physiotherapists treating people with nonsurgical knee OA in primary care. The total score for 17 statements regarding nonsurgical knee OA CPGs of which the physiotherapist was aware could vary from 0

to 85 as previously described by Larson, 2004 (with higher scores indicating more perceived facilitators to implementation). Respondents were also asked to identify the main facilitator and barrier to implementation. The CPGs survey was accessed by 121 OPA members. Partial data was provided by 26 respondents and these were not included in the analyses, for a completed survey response rate of 78.5% (n = 95, 25 men). The mean total score was 45.5 (standard deviation=19; minimum=0, maximum=76). The main facilitator for implementing CPGs was the ability to spend sufficient time with the client and the main barrier was the lack of awareness/access in their specific practice setting. Strategies for practical translation of CPGs for nonsurgical knee OA into physiotherapy management of nonsurgical knee OA in primary care are needed.

PREVALENCE OF LOW BMD AND OSTEOPOROSIS IN MALE HYPOGONADISM

M.R. Mascarenhas[1], A.P. Barbosa[1], A.G. Oliveira[1], A. Goncalves[1], V. Simoes[1], D. Santos Pinto[1], M. Bicho[1], I. do Carmo[1]
[1]*Santa Maria Hospital, Lisbon, Portugal*

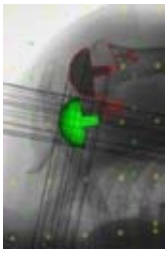
AIMS: To evaluate the bone mineral density (BMD) in hypogonadal males without therapy as compared with a group of normal men. MATERIALS AND METHODS: A group 73 hypogonadal men without treatment (eugonadotropic, hypergonadotropic and hypogonadotropic hypogonadism subgroups) were compared to a control group. The BMD at the L1-L4, at the hip, at the distal forearm and at the whole body were accessed by DXA, as well as the total body fat and lean masses. The LH, FSH, PRL, estradiol and testosterone blood levels were measured. The weight, height and BMI were also determined. Descriptive, Anova and regression analysis statistical tests were used; statistical significance was considered for P<0.05. RESULTS: The mean BMD, T-scores and Z-scores and the total lean mass were lower, while the mean total fat mass was higher, in the hypogonadism group. Low BMD and osteoporosis prevalence were higher in the hypogonadism group and also in the hypogonadotropic hypogonadism subgroup. The normal BMD was associated to an increased mean height and BMI. CONCLUSIONS: In male hypogonadism, the prevalence of low bone mass was elevated (>65%) as well as that of osteoporosis (almost 40%). BMD was influenced positively by the height, body fat mass and BMI; so, the shortest height and lowest corpulence hypogonadal patients may indicate a worse bone disease. *TABLE 1.* Prevalence of low BMD and osteoporosis in hypogonadal men.

GROUP	HYPOGONADISM n = 73*(100%)*	CONTROL
BMD		n = 73*(100%)*
Normal	25*(34.2%)*	65*(89.0%)*
Low	19*(26.0%)*	7*(9.6%)*
Osteoporosis	29*(39.8%)*	1*(1.4%)*

PRECISION OF RADIOLOGICAL METHODS NOVEL IN RELATION TO RESURFACING HUMERAL HEAD IMPLANTS: ASSESSMENT BY RADIOSTEREOMETRIC ANALYSIS, DXA, AND GEOMETRICAL ANALYSIS

I. Mechlenburg[1], M. Stilling[1], A. Amstrup[2], K. Soballe[1], T. Klebe[3]
[1]*Orthopaedic Research Unit, Aarhus University Hospital, Aarhua;* [2]*Radiology Dept., Holstebro Regional Hospital;* [3]*Orthopaedics Dept., Silkeborg Regional Hospital, Denmark*

Background and purpose: Resurfacing humeral head implants (RHHI) are used to preserve bone stock and restore normal anatomy in the osteoarthritic shoulder joint. The purpose of this study was 1) to describe novel methods in relation to RHHI 2) to estimate the precision of the radiological methods, 3) to present preliminary clinical and radiological results at 6 months follow-up after Copeland and Global Cap RHHI. Methods: 21 patients (10 females) at a mean age of 64 (39-82) years and with shoulder osteoarthritis were included and randomized to a Copeland (n=11) or Global C.A.P (n=10) RHHI. The patients were followed clinically with Constant Shoulder Score (CSS) and Western Ontario Osteoarthritis of the Shoulder Index (WOOS). Conventional radiographs were obtained for measurement of Length of Glenohumeral Offset (LGHO). Migration of the RHHI was analyzed with RSA and the periprosthetic bone mineral density (BMD) was measured with DXA. Results: The precision of the radiological methods was high for the LGHO and acceptable for RSA and for DXA. At 6 months, shoulder function had improved significantly for both RHHI groups. The median difference in LGHO pre- to postoperative for the Copeland increased significantly whereas the median difference for the Global C.A.P. was slightly reduced. The migration and BMD was comparable for both RHHI. Interpretation: The protocol for RSA and DXA used in relation to RHHI in this study should be improved in order to enhance the precision of the methods. Based on these preliminary radiological and clinical results, the performance of the 2 RHHI is comparable.



THE ACTIVITY OF CATHEPSIN D AND ALPHA-1-ANTITRYPSIN IN SYNOVIAL FLUID AND BLOOD SERUM OF PATIENTS WITH OSTEOARTHRITIS

D. Olszewska-Słonina[1], D. Mątewski[2], K. Olszewski[2], A. Woźniak[1], B. Kowaliszyn[3]
[1]*Department of Medical Biology;* [2]*Department of Orthopaedics and Traumatology, Collegium Medicum of Nicolaus Copernicus University;* [3]*Department of Genetics and General Animal Breeding, Faculty of Animal Breeding and Biology, University of Technology and Life Sciences, Poland*

The first signs of joint degeneration are clinical and the progress of cartilage deterioration is not well monitored with biochemical methods. The role of lysosomal enzymes in articular cartilage remains unclear. The aim of this study was to assess the level of cathepsin D and its antiprotease alpha-1-antitrypsin in synovial fluid and blood in 43 patients (32 women and 11 men) with hip or knee osteoarthritis before total arthroplasty and on tenth day after surgery and also to find out if these biomarkers might be helpful in cartilage degeneration assessment. There was no significant statistical difference between cathepsin D activity before the surgery and its activity on the tenth day after it in the analyzed group. Its preoperative activity in patients with osteoarthritis was lower by 12.4% in synovial fluid and by 51.9% in blood while after arthroplasty lower by 89.8% than in the reference group. Simultaneously the preoperative activity of alpha-1-antitrypsin in the study group was by 23.0% higher in synovial fluid and 20.3% in blood while postoperative was by 63.5% higher than in the reference group. 26.4% increase in the alpha-1-antitrypsin activity in blood serum after surgical treatment was statistically significant. The low cathepsin D activity in osteoarthritis of big joints may result from the decrease of cartilage cells during the degenerative process. The level of alpha-1-antitrypsin strongly suggests the existence of local acute phase response in the joint. Thus, the level of cathepsin D and its antiprotease in patients' synovial fluid and blood may be helpful in monitoring the osteoarthritis treatment.

EXTENSOR MECHANISM RUPTURE FOLLOWING TKA: SHOULD WE FIX IT?

L. Delasotta[1,2], A. Rangavajjula[3], M. Porat[2], F. Orozco[2], **A. Ong**[2]
[1]Surgery, Temple University; [2]Orthopaedic Surgery, Rothman Institute; [3]School of Medicine, Thomas Jefferson University, Philadelphia, PA, USA

Background: Extensor mechanism reconstruction following TKA is a very debilitating condition; however, surgical management of this condition remains controversial. Our hypothesis is that Achilles allograft improves extensor function following rupture. Methods: We retrospectively reviewed approximately 1200 patients who underwent revision total knee arthroplasty from Jan, 2004 to June, 2009. A total of 21 patients underwent extensor mechanism reconstruction utilizing fresh-frozen Achilles allograft; eight had both knees replaced prior to extensor disruption. Five patients had a preoperative infection. Twelve patients had a patella rupture; six, patellar comminution; three, Quadriceps rupture. The mean age (yrs), ASA (median), BMI, and follow-up (mo) were 70.05yo, 36.9, 3, and 54.4, respectively. Patient satisfaction and validated outcome scores were obtained. Controls were patient-matched. Results: Satisfaction data: overall satisfaction with surgery>extent of pain relief>ability to perform home or yard work>ability to perform recreational activities; Control>Case patients. KOOS/UCLA scores were greater in control patients. Active extension improved in 90%; extensor lag, 86%; range-of-motion, 90%; flexion, 57%. Complications include: extensor revision (19%); high-riding patella (14%); hip fracture d/t fall (5%); periprosthetic infection (10%); postop renal failure (5%); and mental status changes (10%). Conclusion: We recommend the use of Achilles allograft for this debilitating condition. Patients preoperative expectations should be realigned to improve overall patient satisfaction. Patients demonstrate good postoperative function, but preventing this complication is critical. New risk factors may be bilateral TKA, significant medical comorbidities, ORIF for patellar comminution, joint infection, and elevated BMI.

INTRAOPERATIVE PERIPROSTHETIC FRACTURES DURING TOTAL KNEE ARTHROPLASTY: THE BOX CUT

L. Delasotta[1,2], A. Rangavajjula[3], **F. Orozco**[2], A. Ong[2]
[1]Surgery, Temple University; [2]Orthopaedic Surgery, Rothman Institute; [3]School of Medicine, Thomas Jefferson University, Philadelphia, PA, USA

Introduction: Intraoperative incidence of distal femur fractures during TKA are unknown. Our hypothesis is that the box cut increases the risk of intraoperative fractures. Methods: From 2008-2010, 1,469 primary TKAs were performed. A descriptive study and two sawbone analyses were performed. Five different fracture reduction treatment options were utilized. KOOS/UCLA/Satisfaction scores were collected. One sawbone analysis compared cruciate retaining to posterior stabilized; the other, five different manufacturers posterior stabilized box cut sizes in three bone sizes. Results: Five females and one male, 73.3yoa (± 7.2), experienced an intraoperative fracture during primary TKA. BMI was 31.55(± 9.577;range:50.1-23.7). Follow-up was 12.33 months (Range 2-39months). Posterior stabilized fractures occurred 0.323%; for total-stabilized, 3.13%. Females fractured 0.414% during posterior-stabilized total knee arthroplasty and 5.1% during total-stabilized knee arthroplasty. There were no fractures during cruciate-retaining prostheses with deep tibial polyethylene inserts. Relative risk for a female fracture was 5.68 relative to men. Postoperative patient satisfaction and outcome scores were similar. The average medial-lateral and anterior-posterior measurements for condyle size for large, medium, and small sawbones were 3.1cm and 4.3cm, 2.6cm and 4.1cm, 2.1cm and 3.9cm, respectively. Conclusions: Distal femur fractures can occur with posterior and/or total-stabilized TKA systems that require box cuts. Prostheses that preserve femur bone are likely to reduce the risk of intraoperative fractures; we recommend preserving distal femur bone to decrease the incidence of femoral condyle fractures for the small, old, osteopenic/porotic, female.

INTRA-ARTICULAR GIANT CELL TUMOR OF THE TENDON SHEATH (GCT-TS) OF THE KNEE, A REPORT OF SEVEN CASES AND REVIEW OF THE LITERATURE

D. Schrander[1], M. Schotanus[3], N. Kort[3], P. Theunissen[2], E. van de Bogert[1], I. Heyligers[1]
[1]Orthopedic Surgery Dept.; [2]Pathology Dept., Atrium MC Heerlen, Heerlen; [3]Orthopedic Surgery, Orbis Medical Centre, Sittard, Netherlands

The giant cell tumor of the tendon sheath (GCT-TS) is a benign tumor, rarely occurring intra-articular. In this report we describe seven cases of an intra-articular GCT-TS in the knee joint. Clinically, the patients presented in our orthopedic clinic with medial pain and locking of the knee or an extension deficit. In arthroscopy the masses were seen intra-articularly, originating from different parts of the knee, mostly the intercondylar area. Giant cell tumor of the tendon sheath (GCT-TS) is also known as nodular tenosynovitis. It is a benign growth of histiocyte-like cells associated with multinucleated giant cells. It is the second most seen benign tumor of the hand, after the ganglion. Most lesions involve the tendon sheath or the small joints of the fingers, while involvement of large joints is less common. Intra-articular GCT-TS of large joints is rare and often misdiagnosed. Intra-articular GCT-TS of the knee should be differentiated from pigmented villonodular synovitis (PVNS), which more frequently involves the knee joint. Even though histological features are similar, intra-articular GCT-TS and PVNS are distinguished by differences in clinical and arthroscopic manifestations. We describe a 23-year-old male and a 50-year old female who presented with intra-articular GCT-TS in the left knee, near the anterior cruciate ligament. The final diagnosis was made from evidence of typical histological findings revealing giant cells and numerous ovoid and polygonal cells. In total we found seven patients with an intra-articular GCT-TS of the knee

"BEATING OSTEOARTHRITIS": DEVELOPMENT OF A STEPPED CARE STRATEGY TO OPTIMIZE UTILIZATION AND TIMING OF CONSERVATIVE TREATMENT MODALITIES FOR PATIENTS WITH HIP OR KNEE OSTEOARTHRITIS

A. Smink[1], C. van den Ende[1], T. Vliet Vlieland[3], B. Swierstra[2], J. Kortland[4], J. Bijlsma[5], T. Voorn[6], H. Schers[6], S. Bierma-Zeinstra[7], J. Dekker[8]
[1]Rheumatology Dept., Sint Maartenskliniek; [2]Orthopaedics Dept., Sint Maartenskliniek, Nijmegen; [3]Rheumatology Dept., Leiden University Medical Center; [4]Dutch Patient Organization for Rheumatic Diseases; [5]Rheumatology and Clinical Immunology Dept., University Medical Center Utrecht; [6]General Practice Dept., Radboud University Nijmegen Medical Center; [7]Orthopaedics Dept., Erasmus MC, University Medical Center, Rotterdam; [8]Rehabilitation Medicine Dept., VU University Medical Center, Netherlands

Inadequacies in health care practices have been reported despite existing guidelines to manage hip or knee osteoarthritis. To facilitate guideline implementation and improve utilization of conservative treatment options a care strategy should be developed. This study describes the development of an evidence-based, multidisciplinary, patient-centered, stepped care strategy. A national, multidisciplinary, steering group developed the strategy in three phases: 1) consensus among steering group members (first draft); 2) written consultation of 23 representatives of patient organizations and professional associations involved in osteoarthritis care (second draft); 3) consensus of the final draft after discussion in two rounds during a conference with representatives from the different disciplines. The final stepped-care strategy presents, in three tiers, the optimal order for conservative treatment modalities. It recommends that more advanced options should only be considered if options listed in previous steps failed to produce satisfactory results. Hence, the first step treatment options can be offered to all patients but may also be provided through self-care (education, life style advice, and acetaminophen). The second step (exercise therapy, dietary therapy, and Non-Steroidal Anti Inflammatory Drugs) and third step treatment options (multidisciplinary care, intra-articular injections, and transcutaneous electrical nerve stimulation) can be considered for people with persisting complaints. Through a consensus procedure, we succeeded to develop a multidisciplinary, patient-centered,

stepped care strategy based on national guidelines. This strategy provides a framework for health care providers and patients with hip or knee osteoarthritis to discuss the optimal timing of the various treatment options.

EVALUATION OF FREQUENCY OF OSTEOARTICULAR COMPLICATIONS OF BRUCELLOSIS IN PATIENT ADMITTED TO BEHESHTI HOSPITAL, KASHAN

Z. Soleimani
Department of Adolescent Medicine, Kashan University of Medical Sciences, Kashan, Islamic Republic of Iran

Background and Aim: Regarding the high prevalence of brucellosis and frequency of osteoarticular complications of brucellosis and abnormal physical examination due to it, this study was conducted on hospitalized brucellosis patients in Kashan Beheshti Hospital. We conducted this study due to updating our formation and determination of frequency of osteoarticular complications in admitted brucellosis patients. Materials and Methods: This study was performed through existing data in 248 admitted brucellosis patients demographic, osteoarticular complications were extracted and collected data were analyzed. Results: The most common osteoarticular symptom was low back pain (38.3%), and after that respectively knee pain (14.1%), hip pain (9.3%), ankle pain (9.3%) and elbow pain (1.2%), were osteoarticular symptoms of patients. Low back pain got a growing path with increasing age and ankle pain had a decreasing process. Hip pain was more common in the less than 20 years old group. Abnormal physical examination had been detected in sacroiliac (32.2% of patients), knee (14.1%), hip (9.3%), vertebra (6.0%), ankle (3.6%) and elbows (1.2%) and in sacroiliac and vertebra got a growing path with increasing age. Abnormal physical examination in hip and ankle, were more common in the less than 20 years old group. Abnormality of physical examination of knee was the only complication that had a noticeable difference in different sexes (28.1% in males in compare of 11.2% in females). The most common arthritis was in knee (7.7%), and then hip arthritis (3.6%) and ankle arthritis (1.2%). elbow arthritis had seen in only 1 patient (0.4%). Conclusion: Our research reviled that the most common osteoarticular symptom was low back pain, abnormal physical examination was regnant in sacroiliac and knee arthritis was the most common arthritis in brucellosis patients. Because of high frequency of low back pain and other joints pain, brucellosis must be considering in deferential diagnosis in any patients with back pain and arthralgia (especially with prolonged fever). Further because of the high frequency of abnormal physical examination especially in sacroiliac and knee, careful osteoarticular exam in all of the patients with general complaints and osteoarticular symptoms was suggested. Vice versa if abnormal physical examination in joints or arthritis was detected, brucellosis must be considering the head of deferential diagnosis.

HIP REVISION SURGERY USING THE BIPOLAR CUP AVANTAGE

W. Steens[1], C. Götze[2]
[1]Orthopedic Surgery Dept., Orthopaedisch-Neurochirurgisches Zentrum, Datteln; [2]Orthopaedic Surgery Dept., Auguste-Viktoria-Klinik, Germany

INTRODUCTION: Luxations in revision arthroplasty are a serious complication with an incidence of up to 30 percent. In particular in patients with previous operation and resection of bone and soft tissue, the instability increases significantly. OBJECTIVES: The use of the bipolar revision cup Advantage® has to be proven valuable to avoid recurrent luxation. METHODS: 27 consecutive revisions of the bipolar acetabular component were performed. The mean age at the time of revision was sixty-seven years (range, forty to ninety-one years). The mean rate of previous operations was 5.1 cases (range, one to fourteen). In eleven hips (40.7%) the acetabular cup was revised, in 16 hips (59.3%) an additional stem revision was performed. In ten cases the revision was performed by a proximal femur reconstruction, in one patient by a total femur reconstruction. The follow-up was short-term, at a mean of twenty months (range, thirteen to twenty-nine months). The clinical results were evaluated prospectively by the Harris hip score (HHS) and the activity score according to Sutherland (aSL). The migration of the cup and the change of the inclination angle were calculated radiographically. RESULTS: There has been one dislocation of the polyethylene liner in the recent follow-up, which could be treated conservatively by closed reduction. No patients required reoperation because of technical errors or loosening of the bipolar acetabular implant. The HHS improved from a mean of 40.5 (range 7 - 77.4) to 66.8 points (range 17.4 - 89.9). The modified Sutherland score improved to 5.9 (range 3 to 9) of ten possible points. Radiographic follow-up revealed neither evidence of component loosening nor migration or polyethylene wear. CONCLUSION: Use of this bipolar unconstrained component was successful in restoring stability in hip revision arthroplasty, e.g., in patients with severely unstable hips. It has to be observed carefully if there are any disadvantages of these devices because of higher polyethylene wear in the mid- or long-term follow-up. The possible disadvantages of dissociations between the inner liner from the outer liner or damage of the polyethylene liner limits the indication of this device to serious revision cases. REFERENCES: 1. Blom AW, Rogers M, Taylor AH, Pattison G, Whitehouse S, Bannister GC. Dislocation following total hip replacement: the Avon Orthopaedic Centre experience. Ann R Coll Surg Engl 2008;90:658-62. 2. Sah AP, Estok DM. Dislocation rate after conversion from hip hemiarthroplasty to total hip arthroplasty. J Bone Joint Surg Am 2008;90-A:506-16

CEMENTED OR UNCEMENTED FIXATION OF PROXIMAL INTERPHALANGEAL JOINT IMPLANTS? A 2 YEAR RCT OF IMPLANT FIXATION, PERIPROSTHETIC BONE DENSITY AND FINGER FUNCTION

M. Stilling[1], K. Krøner[1], B. Munk[1], I. Helleberg[2], K. Ulstrup[2], O. Rahbek[1], L. Rømer[3], K. Soballe[2]
[1]Orthopaedics Dept.; [2]Occupational Therapy Dept.; [3]Radiology Dept., Aarhus University Hospital, Aarhua, Denmark

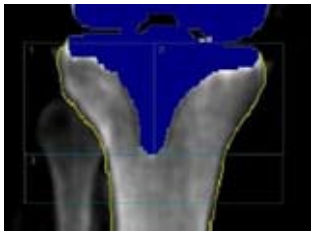
Background: Relatively few surgical options exist for the painful arthritic proximal interphalangeal (PIP) joint. Arthroplasty provides pain relief and stability and is the only treatment to preserve motion. The Avanta SR implant is a newer anatomically-shaped semi-constrained soft-on-hard bearing design that requires little bone resection, and allows for preservation of the collateral ligaments and stability. Purpose: The purpose of this study was to evaluate cemented or uncemented fixation of the Avanta PIP implant. Methods: 30 patients (7 males) were randomly treated with either cemented (C) or press-fit (PF) fixation of the Avanta SR PIP implant in one of the 4 ulnar fingers. Chamay approach with detachment of the extensor-tendon was used. Patients were seen for follow-up 6 times during 2 years. Outcome was evaluated by 1) implant migration, 2) periprosthetic BMD changes around and below the stem, and 3) clinical assessment of pain (VAS), ROM, pulpa-vola distance (PVA) and strength-measures.

Results: PF fixation of the proximal component resulted in less Total Rotation (TR) ($p<0.05$) at 6 months and 1 year. Total translation and Maximum Total Point Motion was similar. At 2 years BMD in the AP plane was reduced ($p<0.05$) by 8-12% below the stem in both groups, and by 6-7% around the stem in the C group. At 2 years: 5/13 and 1/13 patients with C and PF fixation, respectively, reported pain (VAS$\geq$4) with motion at 2 years. Active flexion and extension was 61˚and -6˚, respectively. Average PVA was 4mm. 2 patients (1 in each group) were amputated because of poor function. Grip and Pinch was similar. Conclusion: Cementless fixation appears to be superior in terms of better stability of the implant, better preservation of periprosthetic bone, and less pain 2 years follow-up.

INCREASED PERIPROSTHETIC STRESS SHIELDING WITH AN I-BEAM COMPARED WITH A FINNED TIBIAL COMPONENT STEM DESIGN. A 2-YEAR DXA AND RSA RCT

M. Stilling[1], A. Odgaard[1], F. Madsen[1], L. Rømer[2], O. Rahbek[1], N. Trolle Andersen[3], K. Soballe[1]
[1]Orthopaedics Dept.; [2]Radiology Dept.; [3]Biostatistics Dept., Aarhus University, Aarhus, Denmark

Background: The tibial component often has a stem to aid fixation in the tibia. Purpose: The purpose of this study was to compare implant fixation, periprosthetic bone change, and clinical outcome of tibial components with different stem design. Methods: 54 patients/knees (15 males) with knee osteoarthritis at a mean age of 77 years (70 – 90) were randomly allocated to receive tibial components with either an I-Beam stem (n=27) or a finned stem (n=27) (CoCr modular Tibial Tray Interlock, Biomet Inc). The tibial component was cemented on the cut surface (Palacos R bone cement) but not around the stems. Five patients (I-Beam stems) were lost to follow-up. Implant migration (Model-Based RSA), periprosthetic bone mineral density (BMD), and American Knee Society Score (AKSS) was evaluated through 2 years follow-up. Results: At 2 years follow-up, total translation (p=0.24) was 0.70mm (SD 0.66) and 0.47mm (SD 0.42), and total rotation (p=0.45) was 1.11˚ (SD 0.85) and 0.88˚ (SD 0.52), for the I-beam stem and the finned stem tibial components, respectively. Migration (MTPM) between 1 and 2 years was less than 0.2 mm and all implants were considered stable. Between baseline and 1 year the peri-prosthetic BMD on AP scans decreased 10% (0.09 g/cm^2) around I-beam and 2% (0.02 g/cm^2) around the finned stem components (p=0.02). In the tibia below the stem BMD decreased by 6% and increased by 3% (p=0.01) at 1 year for the I-beam and finned stem components, respectively. At 2 years BMD loss progressed in general in both groups. Knee score, function score, pain, and satisfaction were similar. Conclusion: RSA showed similar stability of the tibial components with I-Beam and finned stems at 1 and 2 years follow-up. The heterogeneous BMD changes raise concerns for potential component subsidence or loosening for the I-Beam stem at longer-term.



LARGE-SCALE ASSESSMENT OF BIOCHEMICAL MARKERS FOR OSTEOARTHRITIS: AN ANALYSIS IN CHECK

E. van Spil[1], J. Wesseling[1], F. Lafeber[1]
[1]Rheumatology & Clinical Immunology Dept., University Medical Center Utrecht, Utrecht, Netherlands

Introduction: Small-scale studies on only one or a few simultaneously assessed biomarkers in end-stage osteoarthritis (OA) are discordant with the concept of OA as a complex joint disease. Instead, CHECK (Cohort Hip & Cohort Knee) is a large-scale study on multiple biomarkers in early-stage OA. Method: CHECK consists of 1002 individuals with early symptomatic, primary knee and/or hip OA. Clinical as well as radiographical parameters are recorded during 10-year follow-up. Data up to 5-year follow-up are available now. Serum, plasma and urine samples are collected at baseline and 2, 5, 8 and 10 years. At present, 14 biomarkers have been assessed in all baseline samples: uCTX-II, uCTX-I, uNTX-I, sCOMP, sPIIANP, sCS846, sC1,2C, sOC, sPINP, sHA, sPIIINP, pLeptin, pAdiponectin, and pResistin (commercially available ELISA's or RIA's). Results: Participants showed clinical joint complaints, but no or only minimal radiographic OA signs at baseline. Analyses already showed several correlations among biomarkers, especially within the cluster of bone metabolism and between this cluster and uCTX-II. Low-grade correlations between biomarkers and age, BMI, gender, and menopausal status were noted. Interestingly, uCTX-I, uNTX-I, sPINP, but also uCTX-II, showed a quite abrupt increase around the age of 50-55 yrs, more pronounced in women than in men. At present, extensive analysis of relationships between biomarkers and demographic, clinical, and radiographic parameters is performed. Conclusions: CHECK is unique worldwide. It provides a unique opportunity for future analyses and a valuable contribution to our knowledge of OA biomarkers. Funding: Dutch Arthritis Association.

MINIMAL INVASIVE PROCEDURES FOR THE TREATMENT OF HIP AND KNEE OSTEOARTHRITIS

S. Ventura[1], A. Musolino[1], M. Cancelli[2], M. Beatric[i2], V. Verna[3], A. Borré[3], G. Massazza[1]
[1]Department of Physical Medicine and Rehabilitation; [2]School of Physical and Rehabilitation Medicine, University of Torino, Torino; [3]Department of Rehabilitation Medicine; [4]Department of Radiology, CTO/M. Adelaide Hospital, Italy

The incidence of the osteoarthritis (OA) of the hip and of the knee is constantly increasing. Despite the good results achieved by prosthetic surgery, it is not risk-free. Alternative and less invasive therapies have been developed. In our hospital we started to use two different approaches: intra-articular hyaluronic acid (HA) injections and pulsed radiofrequency (pRF) nerve blockade. Both the techniques are used in hip and knee OA. HA has proven actions in increasing the synovial fluid viscosity, in modulating the nociceptive stimuli and in acting as a local anti-inflammatory. We studied particularly hip HA injections. We treated patients affected by hip OA with a single, ultra-sound guided intra-articular injection of high molecular weight HA, repeated yearly, for a total of more than 150 procedures. We observed good results both in pain and function, evaluated with WOMAC scale, with no major complications. Similar results have been observed with knee osteoarthritis. An alternative method for relieving pain is to interrupt the nerve transmission. Several methods of neurolysis are available: surgical, chemical, and pRF thermocoagulation. In conventional RF neurolysis, irreversible nerve damage is associated with several major problems. Short pulses of RF energy produce central and peripheral neuromodulatory effects. The risks of complications are minimal. In this case, our studies are still in the first phases. We performed, at the moment, 5 procedures on the knee and 4 on the hip. The first results are encouraging, based on a follow up between 3 weeks and 4 months. In conclusion, between the pharmacological treatment and the surgery, there are many minimal invasive, reversible, safe procedures that can be considered for treatment of OA.

SERUM CARTILAGE OLIGOMERIC MATRIX PROTEIN (COMP) LEVELS IN KNEE OSTEOARTHRITIS IN AN INDIAN POPULATION

P. Verma[1], K. Dalal[1]
[1]Biophysics Dept., All India Institute of Medical Sciences, New Delhi, India

Objective: To investigate the role of Cartilage Oligomeric matrix protein as biomarker in predicting knee OA progression in Indian Population. Methods: One hundred patients were evaluated for the presence of Cartilage Oligomeric matrix protein in blood serum after recording their clinical history. All patients with clinical isolated knee OA according to the American College of Rheumatology (ACR) criteria and without other causes of pain in the knee were included. Fifty individuals were selected, matched for age and sex, and used as controls. Blood samples were taken from all participants and serum COMP levels were measured by Enzyme linked Immuno Sorbent assay (ELISA). Results: The serum COMP levels in the patients with knee OA were positively correlated with disease duration and patient's age. The level of COMP was significantly higher in patients as compared to Controls. It was also observed that patients having BMI more than 30 have higher COMP levels. Meanwhile no gender differentiation was seen in level of COMP but it was observed that OA occurs more commonly in female. Conclusion: Increased amounts of COMP fragments are released into serum only in early stage osteoarthritis. The amount of COMP in blood

serum varies with duration of disease and with osteoarthritis disease stage. Although COMP is sensitive to the agent's active in matrix breakdown in joint disease, differences may thus exist in the release mechanisms and attempted repair. Based on the study result, we can say that the concentrations of the COMP in body fluid may serve to monitor treatment efficacy, disease progression and repair in osteoarthritis and other joint diseases.

EARLY OA COHORT OF HIP AND KNEE: THE CHECK STUDY

J. Wesseling[1], J. Bijlsma[1]
[1]*Rheumatology & Clin Immunology Dept., University Medical Center Utrecht, Utrecht, Netherlands*

Purpose: CHECK is a 10- year follow-up study with early symptomatic OA of knee or hip. The first objective is to follow the course of functional status of patients to identify prognostic factors to predict and explain the course of OA in an early stage. The second is to study the mechanisms that cause joint damage and to identify markers for diagnosis and course of joint damage. Methods: Inclusion criteria are: participants with pain of knee and/or hip, aged 45- 65 years. They had not yet consulted their physician for these symptoms, or the first consultation was within 6 months before entry. The visits at the study centre include an intake, physical examination, questionnaires standardized radiography and blood and urine analysis (0, 2, 5, and 8 years). On entry multiple serum (8x 750µl), mononuclear cell DNA, plasma (12x 750µl) and urine (3x15 ml) are centrally stored. After 2, 5 and 8 years again serum (4x 750µl), plasma (4x 750µl) and urine (6x 7.5 ml) are taken. Results: The data of baseline and follow-up until 5 years is now available. 1002 participants are included with a mean age of 56 years, mean BMI of 26kg/m^2 and 79% are female. On baseline mean WOMAC pain is 74,7; stiffness is 66,8 and functional activities is 76,5 (100 representing the best health status). Only 120 participants had presence of Kellgren & Lawrence grade > 1. Conclusion: We were able to form a unique cohort of 1002 participants with complaints of early symptomatic OA.

STRUCTURAL TISSUE REPAIR AND PROLONGED CLINICAL IMPROVEMENT BY JOINT DISTRACTION IN TREATMENT OF END-STAGE KNEE OSTEOARTHRITIS: THE TWO YEARS FOLLOW-UP

K. Wiegant[1], F. Intema[2], P. Roermund[2], A.K. Marijnissen[1], S. Cotofana[3], F. Eckstein[3], S. Mastbergen[1], F. Lafeber[1]
[1]*Department of Rheumatology & Clinical Immunology Dept.,* [2]*Department of Orthopaedics, University Medical Center Utrecht, Utrecht, Netherlands;* [3]*Department of Musculoskeletal Anatomy, Paracelcus Medical University, Salzburg, Austria*

INTRODUCTION: Knee joint distraction (KJD) is a treatment for end-stage knee osteoarthritis (OA) that temporarily unloads the femorotibial cartilage and subchondral bone. METHODS: Twenty patients considered for a TKP were included and treated with KJD for 2 months. KJD was performed by placing two monotubes with internal coil springs bridging the knee joint, creating a distance of 5 mm. Primary clinical outcome was pain and function by WOMAC questionnaire and secondary the VAS pain score. Primary structural outcome was minimal joint space width (JSW) on standardized weight bearing radiographs. Secondary structural outcomes were quantitative MRI cartilage morphology parameters. Biomarkers for collagen type II turnover (PIIANP/CTXII) were evaluated. The study was approved by the medical ethical committee (METC) of the University of Utrecht and all patients gave written informed consent. RESULTS: Total WOMAC score increased from 45%±3.6 at baseline to 78%±4.8 at 2 years ($p<0.000$) and VAS pain score decreased from 73±2.1 to 28±6.0 mm ($p<0.000$). Clinical improvement coincided with structural tissue changes: minimum JSW increased from 1.0±0.3 to 1.8±0.3 mm ($p<0.03$); the cartilage thickness over total subchondral bone area (ThCtAB) increased (2.4±0.1 to 2.8±0.1 mm; $p<0.05$) and the percentage of denuded subchondral bone area decreased (dABp:22±5 to 8±2 %; $p<0.004$). MRI and X-ray changes correlated ($r=0.67$ $p<0.000$). Ratio of collagen type II turnover changed in favor of synthesis ($p<0.003$). CONCLUSION: At present, distraction therapy appears to be the first treatment that can reverse cartilage damage in end-stage knee OA accompanied by significant clinical improvement sustaining at least two years.

A SIMPLE MATHEMATICAL STANDARDIZED MEASUREMENT OF ACETABULUM ANTEVERSION AFTER TOTAL HIP ARTHROPLASTY

C-K. Liaw[1], **T-Y. Wu**[2], R-S. Yang[3], S-M. Hou[4]
[1]*Department of Orthopaedics, Tao-Yuan General Hospital, Taoyuan;* [2]*General Practice, Taipei City Hospital, Renai Branch;* [3]*Department of Orthopaedics, College of Medicine, National Taiwan University & Hospital;* [4]*Department of Orthopaedics, Shin Kong Wu Ho-Su Memorial Hospital and Health System, Chinese Taipei*

We invented a standardization method to measure the cup's anteversion after total hip arthroplasty without the influence of patient's position. We measured 68 radiographs of 10 patients after THR and calculated the error of each measurement, defined as difference with the average of the same measuring method on the same patient. We also calculated the repeatability standard deviation (RSD) of each method according to the ASTM E691. Mean absolute inter-examination angle error, defined as the average of the absolute deviations, was 0.75o for standardized anteversion (range 0.03 – 2.51o), as compared with those without standardization, 2.30o (range 0.04 – 13.04o). The inter-examination measurement reliability (precision), defined as one RSD, was 0.99o for standardized anteversion, as compared with those without standardization, 3.50o. There was no difference between patient #4 and #5 without ($p=0.097$). There is significantly difference with standardization ($p<0.0001$). Our study demonstrated that this mathematical method is a precise tool to measure the anteversion of the acetabular cup. We hope it can be used widely in the future.

THE EFFECT OF LOW-FREQUENCY PULSED ELECTROMAGNETIC FIELDS ON OSTEOPOROSIS: A SYSTEMATIC REVIEW

L. Xia
Rehabilitation Medicine Dept., Huaxi Hospital, Sichuan University, Chengdu, China

Objective: To assess the efficacy and safety of low-frequency pulsed electromagnetic fields (PEMFs) on osteoporosis. Methods: According to the inclusion criteria, all randomized controlled trials of PEMFs on osteoporosis were performed. All of the clinical trials were searched from the Cochrane Controlled Trials Registered Medline, Embase, Medline, and Chinese National Knowledge Infrastructure Database. The selection of studies, assessment of methodological quality and data extraction were performed by two reviewers independently according to predefined inclusion and exclusion criteria. Results: Ten randomized controlled trials including 814 patients of osteoporosis met the inclusion criteria, which has 426 treated patients and 388 controlled patients. But most included trials were of low quality and small sample. A "Funnel plot" showed asymmetry, which indicated possible publication bias and low quality in methodology. And publication bias showed that the trials with negative results might not be published. The results of meta-analysis indicated that: The treatment of PEMFs on osteoporosis can increase BMD; the treatment of PEMFs combined with drug therapy can increase more BMD than patients treated drug therapy alone; The treatment of PEMFs and drug therapy has the similar efficacy on increasing BMD; The treatment of PEMFs can effectively relieve pain caused by osteoporosis. No significant adverse effects were reported. Conclusion PEMFs shows some effects and relatively safe on osteoporosis according to the resent researches. However, the evidence is not strong enough because of the low-quality trials and publications bias. Large sample, rigorous designs, randomized controlled trials of PEMFs for osteoporosis are needed to further assess the effect.

Osteoporosis

INDUCTION OF AN OSTEOPOROTIC PHENOTYPE WITH NELL-1 DEFICIENCY

J. Zara[1], **J. Aaron[1]**, M. Chiang[1], A. Askarinam[1], A. Nguyen[1], X. Zhang[1], K. Ting[1], C. Soo[1]
[1]*University of California, Los Angeles, Los Angeles, CA, USA*

Introduction: Higher incidences of pathologic bone fractures are reported in osteoporotic patients including long bone and hip fractures, making it a serious public health concern. Polymorphism of the Nell-1 gene, first identified as upregulated in craniosynostosis patients, was recently found to be associated with osteoporosis. Previous studies have shown that Nell-1 overexpression induces osteogenesis in multiple in vivo models. In this study, we examined the consequences of deficiency of Nell-1 in mice. METHODS: E-nitrosourea (ENU) mutagenesis was used to induce Nell-1 deficiency in mice, and verified by PCR and western blot. Aged female mice heterozygous for the ENU-induced Nell-1 mutation (ENU +/-) were examined by DEXA, live micro CT, fluoride ion incorporation, serum TRAP5b, standard histology, and histomorphometry to determine changes in skeletal phenotype. RESULTS: DEXA and micro CT analysis showed that ENU +/- mice exhibit an osteopenic phenotype, with decreased bone mineral density and altered trabecular bone formation compared to wild type littermates. In addition, F18 ion incorporation showed reduced bone formation in the ENU +/- mice. Increased osteoclast activity was observed by serum TRAP5b. Bone marrow mesenchymal cells (BMSCs) isolated from ENU +/- mice showed reduced osteoblast differentiation in vitro. CONCLUSION: Nell-1 is an osteogenic growth factor important for bone maintenance. Nell-1 may be one of many causative factors in the pathoetiology of osteoporosis, modulating both osteoblast and osteoclast activity. It has potential to be a useful tool in its prevention and/or treatment of osteoporosis.

THE EFFECTS OF THE OBSTRUCTIVE SLEEP APNOE SYNDROME (OSAS) ON BONE METABOLIC PARAMETERS

B. Acs
5. Department of Endocrinology and Diabetes, Semmelweis University School of Ph.D. Studies, Budapest, Hungary

Objective(s): The prevalence of the OSAS among Hungarians is between 2-4% and it has been associated with metabolic diseases, hypertension, type 2 diabetes mellitus and hyperlipidaemia. The aim of our study was to compare the bone metabolic parameters of male patients suffering from metabolic diseases with or without OSAS in order to answer the question whether the presence of OSAS has an effect on bone mineral density (BMD) and bone fragility. Materials and methods: Age-matched 68 male patients with metabolic diseases with OSAS and without OSAS (mean age: 54.9 vs. 56.2 years) were evaluated. To evaluate OSAS we used the ”Berlin Sleepiness Scale” and “Epworth Sleepiness Scale”. Patients identified by these tests were sent to a sleep laboratory for further examination and confirmation of diagnosis. BMD and prevalence of bone fractures were measured. Results: The BMD, measured at the left femoral neck and lumbar spine was lower in patients with OSAS than in patients without OSAS (femoral neck: Z-sc: -1.07± 0.11 vs. –0.61 ± 0.1 p< 0,05 and T-sc: -2.45 ± 0.16 vs. -1.98 ±0.15, lumbar spine: Z-sc: -1.11±0.15 vs. -0.48 ± 0.15, p<0,05 and T-sc: -2.53±0.20 vs. –1.91±0.20, p<0,05). Also the prevalence of the bone fractures was higher among patients with OSAS than in patients without it (35% vs. 20%). Conclusion: Screening OSAS and starting it’s treatment in time not only lowers the frequency and severity of the metabolic diseases and bone fractures but it also increases the quality of life.

OSTEOPOROSIS IN THALASSEMIA PATIENTS OF NORTH INDIA: STATUS OF 25-HYDROXYVITAMIN D DEFICIENCY AND EFFECT OF VITAMIN D RECEPTOR GENE POLYMORPHISMS

S. Agarwal[1], R. Kumar[1], K. Singh[1], A. Shukla[1], S. Phadke[1]
[1]*Genetics Dept., Sanjay Gandhi Post Graduate Institute of Medical Sciences, Lucknow, India*

Background: Bone disease comprising of low bone mineral density, bone pain and fractures is a characteristic feature of thalassemia. Vitamin D receptors (*FokI*, *TaqI* and *BsmI*) polymorphisms are closely related to low bone mineral density (BMD) at the lumbar spine and hips which can be used as a useful genetic marker in predicting bone disease in these patients. Aim: To find out the status of Vitamin D receptors gene polymorphisms and its effect on osteoporosis in thalassemia patients. Material and Methods: BMD was measured in 40 beta thalassemia major patients by Dual Energy X ray Densitometry (DEXA). Serum 25(OH) vitamin D levels were estimated by ELISA. VDR gene polymorphisms (*FokI*, *TaqI* and *BsmI*) were analyzed by PCR-RFLP method. Results: 80.6% cases were found to be 25(OH) Vitamin D deficient. Z score of BMD of lumbar spine and hips were -2.31±1.18 and -2.09±0.89.Osteoporotic lumbar spine was observed in 42.5% cases of thalassemia. A positive correlation of vitamin D level was found with Z score of BMD of lumbar spine (r= 0.398, p value=0.027). Polymorphisms of *FokI* and *BsmI* were found significantly correlated with BMD of lumbar spine. However, no association of BMD was observed with *TaqI* polymorphism. Conclusion: The present study showed a high prevalence of low BMD in thalassemia, suggesting that they should be targeted for DEXA screening and osteoporosis prevention before permanent end organ bone damage occurs. The VDR genotyping can be used as additional test in individuals who are susceptible to osteoporosis so that early preventive measurements can be taken.

ASSESSMENT OF OSTEOPOROSIS BY DXA AND QUS IN THALASSEMIC PATIENTS

A. Argentiero[1], C. Neglia[1], A. Peluso[2], S. Di Rosa[2], V. Caiaffa[2], N. Agnello[1], A. Cozma[1], G. Chitano[1], D. Paladini[1], E. D'alò[1], M. Benvenuto[1], P. Piscitelli[1], A. Distante[1]
[1]*Istituto Scientifico Biomedico Euro Mediterraneo - ISBEM, Brindisi;* [2]*ASL TA - Health Local Autority Taranto, Italy*

Aims: As osteoporosis is a leading cause of morbidity in patients affected by major or intermediate beta-thalassemia, we aimed to assess the association between *T*-scores values obtained by Dual-Energy X-ray Absorptiometry (DXA) and Quantitative Ultra-Sounds (proximal phalanges) with the effects of age, hormonal factors and previous fractures in thalassemic patients. Methods: 88 patients with beta thalassemia (males:42; females:46) were recruited at Microcitemia Center of Taranto Hospital. The patients were screened from 2008 to 2010 with both techniques and *T*-score values were obtained for each subject. Three categories were identified: a) Normal (whenever any T-score >-1.0SD); b) Osteopenia (*T*-score between -1.0SD and -2.5SD for DXA or between -1.0 and -3.2SD for QUS); c) Osteoporosis (T-score values <-2.5SD for DXA or <-3.2SD for QUS). Results: The overall prevalence of osteoporosis was 52% with DXA and 10% with QUS, whereas osteopenia was found in 32% of patients screened with DXA and in 60% of cases with QUS. We observed an inverse correlation between age and T-score values only when analyzing QUS measurements (*P<0.05*). Hypogonadism, hypothyroidism and hepatitis-*b* were significantly associated with lower *T*-score values with both methods. Previous fractures were associated with T-scores <-2.5SD only in patients screened with DXA. Conclusions: These data confirm that hormonal deficiency is the most important factor associated with osteopenia and osteoporosis in beta thalassemia. Both DXA and QUS are useful in discriminating subjects at higher risk of osteoporosis, while only DXA is able to provide information on risk of fracture in thalassemic patients.

CAN AN INTEGRATED APPROACH BE A BETTER CHOICE IN THE MANAGEMENT OF OSTEOPOROSIS? A PILOT STUDY

Y. Bali
Shalya Tantra (Ayurvedic Surgery), Ebnezar Orthopedic Center, Bangalore, India

Background: Osteoporosis is a disease characterized by low bone mass. This loss of bone mass is caused because of several reasons including lifestyle and heredity. Currently 1.6 million hip fractures occur worldwide each year; which could go up to 4.5 million and 6.3 million 2050. Osteoporosis causes bone degeneration which leads to loss of height over time and also back pain, hence, early on prevention is to be kept in mind as the treatment. Aim: To assess the effectiveness of integrated approach of yoga therapy (IAYT) and to evaluate the quality of life and anxiety levels of the people afflicted with osteoporosis. Methods and Materials: Total of 20 subjects, randomized to study (n=10) and control (n=10) groups. Yoga group was given IAYT with the routine conventional treatment and control group with only the conventional treatment. Assessments were made at the 1st and the 21st day using Short Form 36 (SF-36) and self-evaluation questionnaires (STAI). Results: Yoga group has shown a significant difference in all domains of SF-36 and STAI compared to control group. This study hints that yoga can be a good tool to handle the quality of life and anxiety levels which forms an important part of management of this particular disease. Conclusion: This was an exploratory study that needs further research by application on large sample size to determine the effects of IAYT.

DIAGNOSTIC CRITERIA FOR THE PATIENTS WITH PRIMARY HYPERPARATHYROIDISM

I. Boulytcheva
Pathology Dept., Hospital # 62, Moscow, Russian Federation

Primary hyperparathyroidism (PHPT) is a common endocrinopathy seen today all over the world. Most frequently it affects older people in the 6th to 7th decade of life and is commonly caused by parathyroid adenoma or carcinoma. In a 8 year period, 32 cases of PHPT were identified in Hospital 62, Moscow area, Russia, 14 patients developed "brown" tumors in different locations and were first admitted to the hospital as patients with metastatic disease, 12 patients had characteristic radiologic features and 6 patients were "asymptomatic" with the diagnosis being made incidentally with the initial findings of hypercalcemia on routine laboratory studies, leading to further investigation. Surgical treatment was performed in 18 cases with the diagnosis of parathyroid ademona (14 cases), parathyroid hyperplasia (2 cases) and parathyroid carcinoma (2 cases). Overall, treatment options included parathyroidectomy, bisphosphonates, calcitonin and calcimimetics. In our review we discuss PHPT in detail with focus on differential diagnosis and clinical manifestations. We highlight the indications for surgical and medical management.

DOES LEAD EXPOSURE CONTRIBUTE TO THE UNCOUPLING OF BONE RESORPTION AND BONE FORMATION?

J. Brito[1], L. Gonçalves[1], I. Costa[1], A. Maia e Silva[1], I. Cavaleiro[1], J. Marques[1]
[1]*Instituto Superior de Ciências da Saúde Egas Moniz, Monte de Caparica, Portugal*

So far, it is not clear whether lead (Pb) is a causative agent of osteoporosis or if its concentration in blood and bones varies as a result of increased bone turnover rates characteristic of this disease. In current metabolic modeling of Pb in humans, Pb is incorporated in bone as new bone is formed, being removed from the tissue as a result of bone resorption by osteoclasts. Further, it is assumed that both the incorporation and removal of Pb in bone are independent from age and level of exposure, which has been contradicted by previous research conducted in vivo in large populations occupationally exposed to Pb. Here, we report the preliminary results obtained in an animal study which aims were to: - assess the distribution of Pb in organs of animals under increasing lead exposures, by Wavelength Dispersive X Ray Fluorescence spectrometry; - assess the impact of exposure to Pb on biochemical markers of bone formation and resorption, namely osteocalcin (OC) and C-terminal peptide-bound crosslinks of Type I collagen (CTX-I);- perform genetic analysis of studied groups to study the potential mutagenic effects of Pb. Conclusion: Pb exposure seems to induce a significant increase in bone resorption rates as expressed by CTX-I, with no effect on OC serum levels; however, genetic analysis revealed that higher Pb exposure may result in higher number of CA dinucleotide repeat amplifications of the Insulin-like growth factor-I gene, thus benefiting bone formation. How these differential effects impact on bone strength is currently being investigated.

SHOULD DXA T-SCORES OR Z-SCORES BE USED FOR DIAGNOSING AND MANAGING OSTEOPOROSIS IN PREMENOPAUSAL WOMEN AND MEN AGED 20 TO 50 YEARS?

J. Carey[1], M. Delaney[2], B. Richmond[3], T. Love[6], B. Cromer[5], A. Licata[4], P. Miller[7]
[1]*Rheumatology Dept.;* [2]*University College Hospital Galway, Galway, Republic of Ireland;* [3]*Radiology Dept.;* [4]*Endocrinology Dept., Cleveland Clinic;* [5]*Adolescent Medicine Dept.;* [6]*Epidemiology and Biostatistics Dept., Case Western Reserve University, Cleveland, OH;* [7]*Department of Medicine, Colorado Centre for Bone Research, CO, USA*

Osteoporosis is endemic in elderly Western populations. DXA measures bone mineral density (BMD) in g/cm^2. DXA manufacturer's software then calculates T-scores and Z-scores based on this measurement, subject demographics and a reference population. National and international guidelines for the diagnosis and management of osteoporosis are generally based on T-scores and Z-scores. DXA criteria using T-scores are the accepted international standard for diagnosis in postmenopausal women and men aged 50 years and older. Diagnostic criteria for DXA diagnosis in premenopausal women and men aged 20-49 years have been proposed based on DXA Z-scores and additional clinical problems. Recommendations for additional investigations and treatment of osteoporosis are often based on T-scores and Z-scores. Conceptually these values should be identical or similar in young men and women but our studies show this is not always the case. We have previously shown definitions and calculation methods for both T-scores and Z-scores vary. We have established the variance in T-scores and Z-scores that can be seen for any given BMD measurement in adults aged 20 to 50 years. We have also shown how this can result in significant differences between T-scores and Z-scores in these populations, and diagnostic discordance. The lack of standardization, and resultant variation which may occur in obtaining these values, undermine the validity of new and established osteoporosis guidelines. The differences in how these values are obtained, and whether they should be used in premenopausal women, young adult men and other populations will be discussed.

TIME-DEPENDENT EFFECT OF BISPHOSPHONATE ON OSTEOPOROTIC RAT SPINE FUSION

C.K. Chug[1], S.B. Park[2]
[1]Neurosurgery Dept., Seoul National University Hospital; [2]Neurosurgery Dept., Seoul Paik Hospital, Seoul, Republic of Korea

Bone grafting is a common procedure in spinal arthrodesis. In osteoporotic patients with spinal arthrodesis, it is important to use anti-resorptive therapy to reduce bone resorption and bone fragility. However, there is no sufficient knowledge about the appropriate time in using bisphosphonate for patient with osteoporosis who underwent spinal arthrodesis. Therefore, we studied the effect of bisphosphonate on osteoporotic spinal arthrodesis according to the different administration times of bisphosphonate. Female Sprague-Dawley rats (n=100) were ovariectomized (OVX) or sham-operated, and randomized into five groups: Group I (sham-operated + arthrodesis alone), Group II (OVX + arthrodesis alone), Group III (OVX + arthrodesis +the simultaneous injection of ibandronate, 25 ㎍/kg/25 days), Group IV (OVX+ the early injection of ibandronate, 25 ㎍/kg/25 days +arthrodesis) and Group V (OVX + arthrodesis + the delayed injection of ibandronate, 25 ㎍/kg/25 days). Eight weeks after ovariectomy, surgery as lumbar spinal arthrodesis was performed using autologous tail bones. Animals were killed 4 and 8 weeks after arthrodesis and bone formation assessment was performed using bone mineral density, manual palpation, and radiological evaluation through micro-computed tomography, histomorphometry and mRNA expression. The early injection of ibandronate increased BMD of femur in OVX rats and did not hinder bone fusion rate as compared to the delayed injection of ibandronate. In radiological analysis, GIV with the early injection had the increased bone volume in grafted site at 8 weeks after surgery. The exposure period of ibandronate positively affected endochondral and intramembranous ossifications in histomorphometric analysis. Ibandronate changed the activities of bone turnover in OVX groups as similar to that of sham group. The early administration of ibandronate did not inhibit osteogenesis including endochondral and intramembranous ossification and fusion rate. That means that bisphosphonate should be administered early in osteoporotic patient who need a spinal arthrodesis.

CEMENTLESS ARTHROPLASTY FOR OSTEOPOROTIC INTERTROCHANTERIC FRACTURE IN THE ELDERLY

Y.Y. Chung
Department of Orthopaedics, Kwangju Christian Hospital, Gwangju, Republic of Korea

Purpose: To evaluate the positive effects and problems through clinical and radiological results of cementless bipolar hemiarthroplasty for osteoporotic unstable intertrochanteric fractures in the elderly. Materials and Methods: From December 2006 to June 2009, 54 bipolar hemiarthroplasties were performed in 54 patients in our hospital. The mean age was 78.8 (67-93) years. Of these cases, 13 were males and 41 were females. The fractures were of type A2.1in 17cases, type A2.2 in 23 cases and type A2.3 in 14 cases. There was no waling limitation in 45 patients, but 4 of the remaining 9 patients had walking limitations and used walking aids at their residence. A posterolateral approach as well as cementless femoral stems was used in all the patients. Clinical results were evaluated according to operation time, amount of bleeding, time to resume walking, duration of hospital stay, recovery of walking ability, and complications. Prostheses loss was evaluated on the follow-up radiographs. Results: Twenty-two of 39 patients who had medical co-morbidity had more than two medical co-morbidities. Operations were performed at a mean time of 5.5 days after the fracture. The mean operation time was 95 minutes. The average total amount of bleeding was of 715cc. Patients began walking at an average of 5.9 days after operation and the average duration of hospital stay was 19.2 days. 16 patients (29.6%) died at an average period of 1.6 years after their operation. At the time of discharge, 32 patients (59 %) had recovered walking ability, but at the last follow-up compared to the pre-injury status, the recovery rate of walking had decreased to 46% (25 patients). Complications included a deep infection in one case, dislocation in 2 cases and hematoma in 2 cases. The cause of revision was deep infection. There were no revisions due to prosthesis loosening. Conclusion: Cementless bipolar hemiarthroplasty for osteoporotic intertrochanteric fractures in the elderly had some problems due to the prolonged operation time and increased amount of bleeding, but it also had advantages including the early return to walking after the operation and decreased hospital stay. It is one of the treatment options for the elderly with osteoporotic unstable intertrochanteric fractures.

EVALUATION OF OXIDATIVE STATUS IN OSTEOPENIC AND OSTEOPOROTIC POSTMENOPAUSAL WOMEN

R. De Giuseppe[1], F. de Liso[1], C. Novembrino[1], P. Bonara[2], F. Bamonti[1]
[1]Dipartimento di Scienze Mediche, Università degli studi di Milano, Milano; [2]Department of Internal Medicine, Fondazione IRCCS, Cà Granda Ospedale Maggiore Policlinico, Italy

Osteopenia is a condition where bone mineral density is lower than normal and it is considered to be a precursor to osteoporosis, a systemic skeletal disease characterized by a decreased bone mineral density leading to a consequent increase in bone fragility and a susceptibility to fractures. After menopause, bone turnover acceleration induces an imbalance between bone resorption and formation, leading to a final bone loss. It has been suggested that oxidative stress, an unbalance between oxidants and antioxidants, is associated with the pathogenesis of osteoporosis. To study oxidative status in osteopenia and osteoporosis, 61 consecutive women (61.01±7.82years; BMI 25.39±3.71Kg/m^2) were evaluated by ultrasonographic examination of bone tissue (DBM Sonic Bone Profiler, IGEA, Italy) and divided into: Group A: forty-four osteopenic subjects (59.63±7.14years); Group B: seventeen osteoporotic subjects (66±6.88years). Subjects were evaluated for serum oxidized LDL (oxLDL, competitive ELISA method, Mercodia, Sweden), Reactive Oxygen Species concentrations (ROS) and Total Antioxidant Capacity (TAC) both by spectrophotometric methods (Diacron International, Italy). ROS concentrations were significantly higher in group A than in B (393±61.89 *vs* 359.76±46.94UCarr; $p<0.05$, respectively) while oxLDL levels were higher in osteopenic than osteoporotic subjects but not significantly (81±35.04 *vs* 76.81±28.31U/L); no significant difference in TAC was found between the groups. Our preliminary results showed an increased oxidative stress condition in osteopenia more than in osteoporosis, possibly due to osteoclastic activity which is probably higher. A balance between oxidants and antioxidants is important for maintaining a correct equilibrium between osteoblast and osteoclast activities and, therefore, regulating bone resorption.

OXIDATIVE STRESS IN BONE REMODELLING

E. Filaire
CTI, Orleans, France

Reactive oxygen species (ROS) are well recognised for playing a dual role as both deleterious and beneficial species. They are normally generated by tightly regulated enzymes. ROS overproduction arises either from mitochondrial electron transport chain or excessive stimulation of NAD(P)H resulting in oxidative stress, a deleterious process that can be an important mediator of damaging to cell structures (lipids, membranes, proteins, and DNA). However, ROS/RNS (e.g. superoxide radical and nitric oxide) could have a beneficial effect at low/moderate concentrations. Physiological roles in cellular responses to noxia have been reported, in defence against infectious agents, in the function of a number of cellular signalling pathways, and the induction of a mitogenic response. The role of ROS in bone metabolism is dual. It is a key modulator of bone cell function and also implicated in the pathophysiology of mineral tissues. In fact, the development of osteoporosis has been associated with increased levels of oxidative stress in osteoblasts, suggesting that

this may be one critical component of the pathophysiology of bone loss. Thus, the ultime mechanism behind ROS contribution to bone metabolism is still controversial. To explore this further, the aim of the present review is to examine the bone remodelling and metabolism in relation to oxidative stress and exercise.

2 YEAR TREATMENT EFFECTS OF THE CATHEPSIN K INHIBITOR, ONO-5334, ON BMD AS MEASURED BY 3D QCT IN THE HIP AND THE SPINE

K. Engelke[1], S. Nagase[2], T. Fuerst[1], M. Small[2], T. Kuwayama[2], S. Deacon[2], R. Eastell[3], **H. Genant[4]**
[1]Synarc, Hamburg, Germany; [2]Ono Pharma UK LTD, London; [3]University of Sheffield, UK; [4]UCSF, San Francisco, CA, USA

The purpose of this study was to evaluate the efficacy of the Cathepsin K inhibitor, ONO-5334 in a randomized, double-blind, parallel-group study with QCT (exploratory endpoint). 285 post-menopausal female subjects (age: 55-75) with osteoporosis (with no fragility fractures) or osteopenia (with a fragility vertebral fracture) were equally randomized to five study arms: three doses of ONO-5334 (50mg bd, 100 or 300mg qd), placebo (PBO) or Alendronate (ALN, 70mg qw). A subset of 120 subjects had baseline and 2 year follow-up QCT femur scans, 118 subjects had baseline and follow-up QCT spine scans. Analysis was performed in integral, cortical and trabecular VOIs. Percentage BMD changes after 24 months relative to baseline are shown in the table. 24 month QCT results of ONO-5334 treatment showed persistent BMD increases in integral, trabecular and cortical compartments of spine and the hip for all treatment groups, although the effect was greater for trabecular than for cortical BMD. Sub VOIs of the spine and femur, e.g. the neck showed similar results. In the spine all ONO-5334 doses showed similar changes in trabecular BMD but cortical changes numerically favored 300 mg qd. In the femur, ONO-5334 300 mg qd produced higher BMD increase than other doses, particularly for trabecular BMD. Compared to ALN, ONO-5334 50 mg bd and 300 mg qd appeared to show equivalent increases in integral & cortical BMD and numerically superior increases in trabecular BMD.

Table: ANCOVA of percentage change from baseline in volumetric BMD
LSMean +/- SE, Full Analysis Set was used, *<0.05, **<0.01, ***<0.001 vs. placebo

VOI		PBO	ONO-5334 50mg bd	ONO-5334 100mg qd	ONO-5334 300mg qd	ALN 70mg qw
Total vertebral body	Int BMD	1.6± 1.3	9.9± 1.2***	9.6± 1.1***	12.1± 1.2***	10.8± 1.2***
	Trab BMD	-0.4± 2.0	12.4± 1.9***	12.3± 1.8***	13.0± 1.8***	12.6± 1.9***
	Cort BMD	0.8± 1.1	6.5± 1.1***	5.3± 1.0**	7.9± 1.0***	7.9± 1.0***
Total femur	Int BMD	-0.9± 0.8	4.6± 0.7***	2.7± 0.7***	5.4± 0.7***	4.6± 0.7***
	Trab BMD	0.1± 2.2	13.0± 2.0***	9.8± 1.8***	14.7± 1.8***	11.5± 2.0***
	Cort BMD	0.0± 0.7	2.9± 0.6**	1.3± 0.6	3.4± 0.6***	2.5± 0.6**

ANCOVA: Analysis of Covariance

PHARMACOLOGICAL CHARACTERIZATION OF THE POTENT, SELECTIVE AND ORALLY ACTIVE CATHEPSIN K INHIBITOR MIV-711

U. Grabowska
[1]Medivi, Cambridge, UK

Cathepsin K is highly expressed in osteoclasts where it plays a key role in resorbing bone and therefore an attractive target in bone-related disorders. Herein, we summarize the preclinical pharmacology of the cathepsin K inhibitor MIV-711. MIV-711 displayed a K_i of 1 nM against human cathepsin K while being more than 1,000-fold selective vs. other related cathepsin enzymes such as B, F, H, L, S and V. In human osteoclasts *in vitro*, MIV-711 inhibited bone resorption in a concentration-dependent manner with an IC_{50} of 40 nM. Washout experiments demonstrated that MIV-711 efficacy in osteoclasts lasted longer when compared to the non-basic inhibitor odanacatib, most likely due to prolonged residence time in the osteoclast. Additionally, *in vivo*, MIV-711 reduced plasma CTX-I levels in healthy, young male cynomolgus monkeys in a dose-dependent manner (range: 3-30 µmol/kg p.o.). Anti-resorptive efficacy outlasted compound exposure – most likely due to prolonged inhibition of osteoclasts. Repeated administration of MIV-711 (30 µmol/kg, p.o. once daily for 5 days) to cynomolgus monkeys evoked daily increases in plasma parathyroid hormone, a peptide hormone known to exert anabolic effects on bone. In dogs subjected to partial medial meniscectomy, an experimental model of osteoarthritis, daily dosing of MIV-711 for 28 days reduced biomarkers of bone resorption. In contrast to approved anti-resorptive therapy, markers of bone formation remained unchanged. In summary, MIV-711 is a potent, selective and orally active cathepsin K inhibitor which inhibits bone and cartilage resorption, and is likely to provide therapeutic opportunities in bone-related disorders such as osteoporosis and osteoarthritis.

A STUDY OF PROPRANOLOL AND SKZD ON CENTRAL DEPRESSANT AND ANTI-OSTEOPOROSIC ACTIONS IN OVARIECTOMIZED RATS

T. Ishida[1], W. Zhang[1], H. Fujieda[1], N. Nagaoka[1], N. Tanahashi[2]
[1]Acupuncture Department; [2]Suzuka University of Medical Science, Suzuka, Japan

Objective: The study was originally designed to determine the effects of a β-blocker (propranolol) and an analogous action of Shakanzou Decoction (SKZD) on bone mass in ovariectomized rats. Methods: Thirty-eight female Sprague-Dawley rats were divided into four groups initially, a sham-operated group (Sham, n=7), a model ovariectomized (OVX) group (Model, n=7), an OVX treated with propranolol group (Pro, n=12) and a SKZD group (SKZD, n=12). After 15 weeks of treatment, the expected effects were not found. In order to verify the situations of our experiment, we modified the study by administering calcitonin to a subgroup of tested Pro and SKZD rats. Results: The Pro and SKZD treatments showed decreased heart rate and plasma norepinephrine, but neither an increased bone mass nor any bone metabolism difference from the model rats was found. However, the same OVX-induced bone loss was prevented by the sequent treatment of calcitonin. Conclusion: Our results provide no evidence that β-blocker drugs stimulate bone formation and do not justify its use for treatment of osteoporosis.

TWO UNUSUAL CASES OF MALE IDIOPATHIC OSTEOPOROSIS

I. Jamall[1], M.C. Ullrey[2], M. Rocchietti[3], V. Rochira[4], E. Pignetti[5]
[1]Risk-Based Decisions, Inc.; [2]Sacramento Heart and Vascular Medical Associates, Sacramento, CA, USA; [3]Internal Medicine Unit, Second Faculty of Medicine, University of Rome La Sapienza, Rome; [4]Universita degli Studi di Modena e Reggio Emilia, Cattedra e Servizio di Endocrinologia, Metabolismo e Geriatria, Nuovo Ospedale S. Agostino-Estense di Baggiovara, Ricercatore Universitario; [5]Departimento di Medicina, Endocrinologia, Metabolismo e Geriatria, Policlinico, Lab universitario di Endocrinologia e Malattie Metaboliche, Italy

In 2007, an otherwise athletic male patient, then aged 41, years presented with chronic lower back pain for approximately 20 years. On examination, the patient appeared healthy and all routine blood tests were unremarkable. In November 2008, the patient underwent a complete body scan which showed osteoporosis (T-score -2.2, Z-score -1.5. This was confirmed by a DXA scan in January 2009 and in 2010 showing osteoporosis of the lower spine and hip. After ruling out multiple myeloma, hypogonadism, and marfanoid syndrome, initial attempts to treat the patient with Fosamax and Actonel were quickly abandoned due to severe gastrointestinal distress and jaw pain. In April 2009, a tentative diagnosis of idiopathic osteoporosis was advanced when serum tests revealed normal testosterone but an estradiol level of 15 pg/mL. In 2010, the patient was examined by one of us in Rome and the osteopenia was confirmed. At this time, the patient's maternal first cousin, a 47-year old male, had a DXA scan which also showed osteopenia/osteoporosis. Subsequent blood tests confirmed normal testosterone in the presence of 17 pg/mL of estradiol. A genetic defect in aromatase, the enzyme responsible for conversion of testosterone to estradiol, was postulated. Blood samples from both patients were analyzed in Modena. No known mutation in the aromatase gene was found but both patients exhibited the same single nucleotide polymorphisms (SNPs) pattern in the aromatase gene. The follow up and treatment of these unusual cases

will be discussed in greater detail along with the role of estradiol in bone health in males.

DEFEROXAMINE INCREASE BONE MINERALIZATION DENSITY OF POSTMENOPAUSAL OVARIECTOMY MODEL AND PROMOTE BIOLOGICAL ACTIVITY OF OSTEOBLAST IN VITRO

Y. Ma

Orthopaedics Dept., The Second People's Hospital of Changzhou, Changzhou, China

Objective: To investigate improvement of bone mineral density (BMD) by deferoxamine (DFO) intervention for osteoporotic model and its possible mechanism for osteoblast in vitro. Methods: 40 SD rats were divided into four groups, as ovariectomized model, ovariectomized model with DFO (100mg/kg, twice a week) intervention, sham group and control group. After 12 weeks research, serum ferritin, serum iron and BMD were detect. Osteoblasts (hFOB1.19) were cultured with different concentrations of DFO (0uM, 5uM, 10uM, 20uM), respectively. MTT assay was used to detect osteoblast activity after 24h. Alkaline phosphatase (ALP) activity was measured by ALP kit after 10 days. Von Kossa staining was used to counted calcium nodules after 15 days. Type I collagen (COL1) mRNA and protein expression were detected by RT-PCP and western blot after 72h. Results: The sham group and control group showed no significant difference. Compared with control, bone mineral density of model group was significantly lower, meanwhile serum iron and ferritin increased significantly ($P<0.05$). Compared with model group, bone mineral density of DFO intervention group increased significantly, and with serum iron and ferritin significant decrease ($P<0.05$). In vitro, cell proliferation viability was stimulated at 5uM, but depressed at 10uM and 20uM ($P < 0.05$). The ALP activity was promoted by DFO with concentration dependently ($P < 0.05$). The number of mineralized nodules were increased significantly with DFO treatment at 5uM, 10uM and decreased at 20uM ($P < 0.05$). The mRNA expression of COL1 was promoted significantly by DFO (5-20uM) ($P < 0.05$). The protein expression of COL1 was promoted by DFO treatment at 5uM, 10uM and inhibited at 20uM ($P < 0.05$). Conclusion: The model of osteoporosis existed iron overload, which improved by DFO treatment. DFO had effects on cell culture in vitro, with low-dose stimulation and with high-dose inhibition on osteoblasts activity. DFO might be used as a new type of osteoporosis treatment; further research needs to be carried out.

THE INFLUENCE OF CONCOMITANT ADMINISTRATION OF PREDNISOLONE WITH ALENDRONATE ON THE INCIDENCE OF OSTEONECROSIS OF THE JAWS: OBSERVATIONS FROM A CASE CONTROLLED STUDY FROM THE SOUTH EAST OF SCOTLAND

N. Malden[1], V. Lopes[2]

[1]*Oral Surgery Dept.; Edinburgh Dental Institute, Edinburgh, UK*

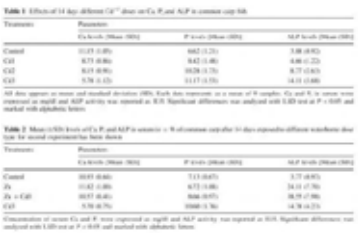
Aim: To examine the characteristics of alendronate related osteonecrosis of the jaw (AONJ) in the population of the south-east of Scotland (SES) comparing those receiving alendronate alone and with prednisolone. Method: A prospective case series of patients presenting from the SES, over a seven year period from June 2004 to July 2011, were studied in relation to the known drug patient years (DPYs) administered to this population. Results: The cumulative alendronate prescribed to the population of the SES was 73,848 DPYs. A total of 26 cases of alendronate ONJ were diagnosed from this population suggesting an incidence of 1:2840 DPYs of which 16 had received alendronate alone mean age 77.4yrs (SD 8.5) and 10 had received alendronate to counteract the osteoporotic effects of prednisolone mean age 69yrs (SD 12.1). In considering age there was no statistical significance between the two groups ($p = 0.73$). The period of drug administration to the first presentation of ONJ, for the alendronate alone group was a mean period of 59.25 months (SD 42.47) compared to those also receiving prednisolone where the mean period was 34.6 months (SD 35.3). In considering drug administration period, there was statistical significance demonstrated between the two groups ($p = 0.030$).Conclusion: The concomitant use of alendronate with prednisolone significantly reduced the period of administration to first presentation of AONJ, suggesting prednisolone was a significant co-risk factor. Routinely limiting initial courses of alendronate to 5 years could dramatically reduce the incidence of this rare but debilitating disease.

PROTECTIVE EFFECT OF ZINC ON RELATED PARAMETERS TO BONE METABOLISM IN COMMON CARP FISH (CYPRINUS CARPIO L.) INTOXIFIED WITH CADMIUM

P. Malekpouri[1], A.A. Moshtaghie[2]

[1]*Young Researchers Club, Science and Research Branch, Islamic Azad University, Tehran;* [2]*Department of Biochemistry, School of Basic Science, Falavarjan Branch, Islamic Azad University, Isfahan, Islamic Republic of Iran*

The short term effects of waterborne cadmium (Cd^{+2}) on the levels of serum parameters related to bone metabolism including calcium (Ca), inorganic phosphorus (Pi) and alkaline phosphatase (ALP) in common carp fish (Cyprinus carpio L.) were studied. Fish were treated with varying concentrations of Cd^{+2} (0.22, 1.1 and 2.2 mg l^{-1}) daily for 14 days. The results obtained show that serum Pi and ALP concentrations were elevated by increasing Cd^{+2} concentrations in water containing fish whereas serum Ca level was decreased. At the same time, the protective role of waterborne zinc (Zn^{+2}, 1 mg l^{-1}) on the same parameters was also investigated. Results showing that daily treatment of fish with Zn^{+2}, increased the concentrations of Ca and ALP in serum by 2.07 and 1.86 fold and decreased serum Pi level by 57.7% in comparison with Cd^{+2} treatment. The combination of Cd^{+2} and Zn^{+2} on the same parameters was studied next. There was a significant ($P<0.05$) elevation in serum Ca and ALP levels in comparison with Cd^{+2} treatment. Decreasing in serum Pi level was not significant in comparison with Cd^{+2} treatments. Data from present study indicate that Zn^{+2} can likely inhibit the devastator effect of Cd^{+2} on bone metabolism in fish. The protective effect of Zn^{+2} on Cd^{+2} disturbances in serum parameters related to bone metabolism should be more addressed in the future studies to elucidate its exact mechanism.



COMPARISON BETWEEN SERUM DKK1 (DICKOPFF-1) AND BONE MINERAL DENSITY IN PATIENTS RECEIVING BISPHOSPHONATE TREATMENT AND PATIENTS WITHOUT TREATMENT

A. Memon[1], J.Harty[1]

[1]*Orthopaedics, Cork University Hospital, Cork, Republic of Ireland*

Complex pathways affect bone metabolism at the cellular level and a balance between osteoblast and osteoclast activity is critical to bone remodeling. One of the major pathways affecting bone metabolism is Wnt/β-catenin signaling and its disturbances leads to a wide range of bone abnormalities. An important antagonist of this pathway is Dickkopf-1 (Dkk1). Higher Dkk1 levels have been associated with increased bone loss due to inhibition of Wnt pathway. Currently, bisphosphonates are the most commonly used agents to treat primary osteoporotic patients. This study demonstrates the effect of bisphosphonates on Dkk1 levels and its correlation with bone mineral density. Eighty patients with low bone mineral density (BMD) were recruited and divided into two groups of 40 each (Bisposphonate treatment group and Control group). The mean Dkk1 level in the

treatment group was significantly reduced to 2358.18 pg/ml versus 3749.80 pg/ml in the control group (p<0.001). Pearson's correlation coefficient showed negative correlation between Dkk1 and BMD at lumbar spine (r= -0.55) and femoral neck in the control group, however no such correlation was found in the treatment group (r= -0.05). Hence bisphosphonate therapy leads to reduction in Dkk1 levels but it does not correlate with BMD in such patients.

SUSCEPTIBILITY TO OSTEOPENIA IN OBESE SUBJECTS MAY MODIFY BY ALTERATION OF SOME IMPORTANT GENE EXPRESSION AT INVOLVED PATHWAY IN OSTEOCLASTIC DIFFERENTIATION

K. Mirzaei[1], A. Hossein-Nezhad[1], H. Ansar[1], Z. Maghbooli[1], M. Khosrofar[1]

[1]Endocrinology and Metabolism Research Institute, Tehran University of Medical Sciences, Tehran, Islamic Republic of Iran

It has been reported that enhancing MAPK/AKT pathways cause inhibition of osteoclastic differentiation. Osteoclasts primarily involved in bone resorption derived from hematopoietic precursors of monocyte/macrophage series. One of the biological markers for osteoclastic function is Crosslaps. Expression of MAPK/AKT may affect in obesity and effect on osteogenic process in throughout of life. In the present study, we tested the hypothesis that the potential correlation between expression of MAPK and AKT in peripheral blood mononuclear cell and bone mineral density (BMD) in Lumbar spine (L2-L4) and Total hip BMD that measured by dual energy X-ray absorptiometry (DEXA) in obese subjects. Moreover, we analyzed the relationship between relative MAPK and AKT gene expression with crosslaps. Overall 251 obese subjects participated in this cross-sectional study. The PBMCs were separated from whole blood by Ficoll-hypaque technique. Total cellular RNA was extracted and the cDNA was synthesized. Real-time PCR using specific primer pairs for determine the *AKT, MAPK* and *beta actin* gene expression. Serum ANGPTL6 levels were quantified by ELISA method. The mean of age and BMI were 33.74±8.96 years and 33.24±3.24kg/m^2 respectively. Based on the BMD score, the prevalence of osteopenia in lumbar spine and hip were 35.1% and 9.2 % respectively. The relative expression of *AKT* and *MAPK* were significantly higher in obese osteopenic subjects. We found significant higher crosslaps concentration in osteopenic obese subjects also. However, Lumbar spine BMD was negatively correlated with relative *MAPK* gene expression, but there was no significant in total hip BMD. We have presented results demonstrating that impaired bone metabolism and increased bone resorption at various sites may be affected by this mechanism and the activation of MAPK/AKT pathway may be were a compensate mechanism to prevention of bone loss in obesity.

FEATURE OF THE ASSESSMENT OF BONE MINERAL DENSITY IN POSTMENOPAUSAL WOMEN

V. Novikova[1], G. Penzhoyan[1], F. Autleva[1], S. Autleva[1]

[1]Obstetrics, Gynecology and Perinatology Faculty of Postgraduate Education, Kuban State Medical University, Krasnodar, Russian Federation

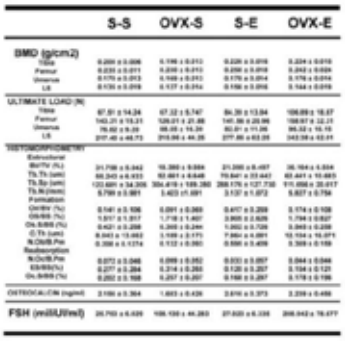
We surveyed 160 women, age 53,9 ± 1,49 years, duration of menopause 3,38 ± 0,5 years, weight 75,88 ± 3,43 kg, weight 161,94 ± 1,62 cm defining BMD produced by densitometer HOLOGIC (Delphia (S / N 71 476). Results and discussion: In the study of the femoral neck BMD: in the Neck 0,74 ± 0,03 g/cm2 (86,63 ± 3,4%; T-score -1,025 ± 0,26); Trochanter 0,68 ± 0 , 03 g/cm2 (96,13 ± 4,7%; T-score -0,27 ± 0,33); Inter 1,10 ± 0,06 g/cm2 (100,19 ± 5,2% T-score 0,0 ± 0,37); Femoral Total 0,91 ± 0,04 g/cm2 (96,38 ± 4,7%; T-score -0,26 ± 0,38). Consequently, the BMD of the femoral neck in 120 (75%) of women identified norm, in 30 (19%) osteopenia, and in 10 (6%) women osteoporosis. In L1-L4: BMD LI - 0,75 ± 0,02 g/cm2 (81 ± 2,68%; T-score -1,58 ± 0,22); LII - 0 , 87 ± 0,03 g/cm2 (84,8 ± 3,13%; T-score -1,41 ± 0,29); LIII - 0,9 ± 0,04 g/cm2 (83,2 ± 3, 3% T-score -1,66 ± 0,33); LIV - 0,9 ± 0,04 g/cm2 (81,7 ± 3,19%; T-score -1,87 ± 0 , 32). Thus BMD LI-LIV (Total) was 0,87 ± 0,03 g/cm2 (82,69 ± 2,9%; T-score -1,63 ± 0,27). Therefore, in 40 (25%) of women diagnosed osteoporosis, 50 women (31%) osteopenia and 70 (44%) women norm. In this study, it was decided to densitometry of the lumbar spine (L1-L4) in the lateral projection. BMD LII - 0,58 ± 0,03 g/cm2 (67,2 ± 3,81%; T-score -2,76 ± 0,32); BMD LIII - 0,55 ± 0,02 g/cm2 (64,69 ± 2,46%; T-score -3,43 ± 0,23); BMD LIV - 0,57 ± 0,02 g/cm2 (66,9 ± 2,78%; T-score -2 , 86 ± 0,24); BMD LI-LIV (Total) was 0,57 ± 0,02 g/cm2 (69,31 ± 2,4%; T-score -2,99 ± 0,24). So, in 110 (69%) was identified osteoporosis, 40 women (250%) osteopenia, and only 10 (6%) norm. It should be noted that the duration of menopause 3,38 ± 0,5 years in the state of women surveyed in the lumbar spine BMD was significantly different from the expected results, required for medical - preventive measures. Conclusions: Postmenopausal women should be encouraged to study bone mineral density in the lumbar spine. In the presence of osteoporosis supplement study to clarify the availability of X-ray Morphometrics deformation vertebral fractures. Obvious need to prevent abnormal reduction in bone mineral density before menopause.

INFLUENCE OF HIGH-IMPACT EXERCISE ON BONE IN OSTEOPENIC OVARIECTOMIZED RATS

R. Okubo[1], A. Zamarioli[1], V.A. Castania[1], F.J. Albuquerque de Paula[2], M.J. Quirino Louzada[3], J. Volpon[1], A. Shimano[1]

[1]Biomechanics, Orthopaedics and Rehabilitation; [2]Department of Internal Medicine, Universidade de São Paulo, Ribeirão Preto; [3]Department of Animal Support, Production and Health, Sao Paulo State University, Brazil

Purpose: We investigated the effects of jump training on osteopenic bones post-ovariectomy. Methods: This research was characterized as a single-blind study. Forty 10-wk-old Wistar rats were divided into the following four groups (n=10): sham sedentary (S-S), ovariectomized sedentary (OVX-S), sham exercised (S-E), and ovariectomized exercised (OVX-E). A 12-wk exercise period was introduced in which the rats from the exercised groups (S-E and OVX-E) jumped 20 times/day, 5 days/wk, with height of 40 cm. This was followed by 2-mo after surgery. At the end of the exercise period, bone formation marker (serum osteocalcin), follicular stimulating hormone (FSH) dosage, dual-energy X-ray absorptiometry (DXA), bone histomorphometry and biomechanical tests were statistically analyzed (p-Value<0.05). Results: OVX groups showed higher values of FSH (p<0.001) and body mass (p<0.05). The jump training significantly increased the bone mineral density of tibia, femur and L5 vertebra (p<0.05). Ultimate load (p< 0.05) of tibia, femur and L5 vertebra in the exercised groups were greater than in the sedentary groups. Osteocalcin dosage also showed higher values in the trained groups. (p<0.001). BV/TV, Tb.Th, Tb.N, OV.BV, OS.BS, Ob.S/BS, O.Th, N.Ob/B.Pm parameters (p<0.05) also showed higher values in the trained groups. Furthermore, Tb.Sp, N.Oc/B.Pm, ES/BS, Oc.S/BS parameters were lower in these exercised groups. *Conclusions:* These findings suggest that jump exercise increased bone strength. It also increased bone formation and decreased bone resorption, which were detected by both morphological and biochemical analyses, even under ovarian hormonal deficiency.



THE CROSS-TALK BETWEEN OSTEOCLASTS AND OSTEOBLASTS IN RESPONSE TO STRONTIUM TREATMENT: INVOLVEMENT OF OSTEOPROTEGERIN

S. Peng[1,2]
[1]*Department of Spine Surgery, Shenzhen People's Hospital, Jinan University School of Medicine, Shenzhen, China;* [2]*Bone Bioengineering Laboratory, Department of Biomedical Engineering Columbia University, New York, NY, USA*

Background: The mechanism for the uncoupling effects of Sr on bone remains to be evaluated. Osteoblasts play important roles in osteoclastogenesis through regulating receptor activated nuclear factor kappa B (RANK) ligand (RANKL) and osteoprotegerin (OPG) expression. We hypothesize that OPG plays an important role in the cross-talk between osteoclasts and osteoblasts in response to Sr treatment. Materials and methods: MC3T3E1 cells were treated with Sr chloride (0–3 mM) and conditioned media were collected at 24 h after the treatment. The effect of conditioned media on osteoclastogenesis was evaluated by tartrate-resistant acid phosphatase (TRAP) staining and bone resorption pits analysis. OPG and RANKL mRNA expressions in osteoblastic cells and protein secretion in the conditioned media were analyzed with real-time PCR and ELISA assay, respectively. The role of OPG in Sr-mediated inhibition of osteoclastogenesis was further evaluated with anti-OPG antibody in pre-osteoclastic cells. The role of OPG in Sr-mediated uncoupling effects on osteoporotic bone was evaluated by an animal study. Ovariectomized rats were oral administrated with vehicle or Sr chloride for two months supplemented with anti-IgG antibody (control) or anti-OPG antibody. The effects of OPG neutralization after Sr treatment on bone metabolism were analyzed by micro CT, bone histomorphometry and biochemical analysis. Results: The conditioned media derived from Sr-treated osteoblastic cells exerted a dose-dependent inhibitory effect on osteoclastic differentiation and resorptive activity in pre-osteoclastic cells. OPG mRNA expression and protein secretion in osteoblastic cells were significantly increased after Sr treatment. Neutralization with anti-OPG antibody abolished the inhibitory effect of conditioned media on RANKL-induced osteoclastogenesis. The uncoupling effects of Sr treatment on trabecular bone were evidenced by greater bone volume and trabecular number, greater osteoid surface and bone formation rate, while less osteoclast surface. These effects were attenuated by the OPG neutralization by anti-OPG antibody injection. Conclusion: The evidences from the in vitro and in vivo studies suggested that OPG played an important role in the uncoupling effect of Sr on bone metabolism, possibly by acting as a cross-talk molecule between osteoclasts and osteoblasts in response to Sr treatment.

DOES LEAD EXPOSURE IMPACT ON BONE CALCIUM CONCENTRATION?

J. Pereira[1], T. Fernandes[2], J. Brito[1]
[1]*Biophysics Dept.;* [2]*Pharmacy Dept., Instituto Superior Ciências da Saúde Egas Moniz, Monte de Caparica, Portugal*

Nutritional and toxicological studies carried out with single elements might project an inconclusive picture unless the levels of interacting elements in biological tissues are known. Therefore, in our approach to the association between lead exposure and bone turnover rates we have used the Wavelength Dispersive X-Ray Fluorescence (WDXRF) system available in our laboratory to perform multi-element determinations on samples of liver and bones collected from animals subject to increasing Pb exposure. Here we report on the analytical performance of the WDXRF method which offers several methodological advantages: 1) low minimum detectable limits for lead and a wide range of other elements is more than adequate to address the relationship between lead exposure and the biomarkers of bone turnover in cases of low bone lead concentrations; 2) feasibility for multi-element determinations on very small amount of samples as the ones collected from animals included in this study. Based on WDXRF determinations performed on the liver and lumbar spine of Pb exposed animals, increased Pb concentrations were observed in the liver and bone of animals exposed to higher levels of lead in water, who also showed decreased bone Ca and increased serum concentrations of C-terminal peptide-bound crosslinks of Type I collagen. These results suggest that Ca is replaced by Pb in the bone of animals; whether these results in weaker or stronger bones are being investigated and are open to debate.

CHANGES IN MARKERS OF BONE RESORPTION AND IMPACT ON BONE MINERAL DENSITY OVER THE FIRST 6 MONTHS AFTER PEDIATRIC HEMATOPOIETIC CELL TRANSPLANTATION

A. Petryk
Pediatrics Dept., University of Minnesota, Minneapolis, MN, USA

Objective: Low bone mineral density (BMD) is common within the first six months after hematopoietic cell transplantation (HCT). In adults, this is related to an increase in bone resorption and a reduction in bone formation. While there is some evidence that bone formation may also be reduced in children after HCT, it is currently unknown if bone resorption is increased. The objectives of this study were to evaluate changes in bone resorption over the first six months after pediatric HCT and determine if changes in bone resorption are associated with changes in BMD. Design: 6 month prospective observational study. Patients: Twenty-six participants (8 females) age 10.9±3.4 years entered the study prior to HCT and fourteen completed the final day +180 visits. Measurements: Bone resorption was measured by urine deoxypyridinoline (DPD), urine pyridinoline (PYD) and serum N-telopeptide (NTX). BMD was measured by dual energy x-ray absorptiometry (DXA). Results: DPD and PYD increased significantly between days +30 and +100. For every 10 nmol/L increase in DPD between days +30 and +180 total body BMD Z-score decreased by 0.48 (95%CI: -0.84 to -0.12). For every 20 nmol/L increase in PYD between days +30 and +180 total body BMD Z-score decreased by -0.13 (95% CI: -0.20 to -0.05). Finally, for every 10 nmBCE/L increase in NTX area under the curve from baseline to day +100 BMD Z-score decreased by 0.31 (95% CI: -0.52 to -0.11). Conclusions: This is the first pediatric study that examined changes in the markers of bone resorption after HCT. These pilot data suggest that bone resorption contributes to the pathophysiology of bone loss after pediatric HCT.

RELATIONSHIP BETWEEN EARLY MENOPAUSE, OESTROGENS RECEPTOR POLYMORPHISM AND OSTEOPOROSIS IN A MEDITERRANEAN POPULATION

D. Ronca[1], T. Esposito[2], M. Chierchia[1], G.F. Di Martino[1], B. Varriale[2]
[1]*Department of Orthopaedics & Traumatology;* [2]*Department of Experimental Medicine, Second University of Naples, Naples, Italy*

The multiple factors contributing to the pathogenesis of osteoporosis include genetic and environmental factors. Decrease in bone mineral density (BMD), microarchitectural deterioration of bone tissue lead to an increased risk of fracture. Although BMD is the major predictor of osteoporotic fracture risk, quantitative ultrasound (QUS) properties of bone have recently been found to predict osteoporotic fractures independent of BMD. The gene responsible for regulating these phenotypes are incompletely defined, but genetic linkage studies have identified several quantitative trait loci for the regulation of BMD and QUS. Moreover, polymorphisms in many candidate genes have been identified as determinants of BMD such as vitamin D receptor, estrogen receptor a (ESR1), COLIA1, TNFRSF1B, and many others. One of the most important and widely studied candidate genes for osteoporosis is ESR1. In order to clarify the role of ESR1 as a candidate gene for the osteoporosis related phenotypes, we have investigated among polymorphisms QUS in a population of women inhabiting the south of Italy that underwent to early (38-45 years old) menopauses. All the women studied underwent to vertebral body fracture, while only some of them had femoral neck fracture. All women showed an average DEXA value less of -2.5. We have identified polymorphisms in the coding region of ESR1 gene that well correlate with the bone status of the affected subjects. Vitamin D

receptor also present polymorphisms are evident only in the affected subjects. Normal bone subject do not show such polymorphisms.

ANTI-OSTEOPOROTIC DRUGS USE IN PATIENTS WITH RA UNDER BIOLOGICAL AGENTS

R. Roque[1], S. Ramiro[1], F. Vinagre[1], A. Cordeiro[1], P. Gonçalves[1], V. Tavares[1], J. Canas da Silva[1], M.J. Santos[1]
[1]*Rheumatology Dept., Hospital Garcia de Orta, Almada, Portugal*

Rheumatoid arthritis (RA) is a systemic rheumatic disease associated with an increased risk of bone loss that may be manifested as osteopenia or osteoporosis (OP). We aimed at evaluating the intake of anti-osteoporotic drugs among patients with RA on biologics and also at identifying its associated factors. Patients with RA on biologic therapy, followed at Hospital Garcia de Orta and included in the Portuguese Register of Rheumatic Diseases (Reuma.Pt) were studied. The frequency of anti-osteoporotic drugs use (antiresorptive drugs and/or calcium and/or vitamin D) at last visit was calculated and the factors associated with it were studied by logistic regression. Hundred-and-twenty-three patients were included (mean age 56.9 ± 13.2 years, mean disease duration 11.6 ± 7.9 years). A previous diagnosis of OP had been established in 13% of the patients. At last visit, 53% of the patients were under corticosteroids, of which 92% (a total of 49% of the population) were on corticosteroids for more ≥3months at a mean dosage of 5.2 ± 1.9 mg/day. Sixty-three patients (51%) were treated with anti-resorptive drugs and/or supplemental calcium and/or vitamin D (33 with bisphosphonates, 2 strontium ranelate, 1 raloxifene and 60 calcium +/- vitamin D). Age, previous diagnosis of OP and therapy with steroids were the factors identified as being associated with the use of anti-osteoporotic drugs (Table). More than half of the patients under biological treatment were under anti-osteoporotic drug therapy. Despite the lack of specific recommendations for this group of patients, we identified that, in clinical practice, older age, systemic corticosteroids and a previous diagnosis of OP were the determinants for the prescription of antiresorptive drugs and/or calcium and/or vitamin D.

Table

	Univariable Analysis OR (IC 95%)	Multivariable Analysis adjusted for age and gender OR (IC 95%)
Current Age (years)	1.05 (1.02-1.08)	1.05(1.01-1.09)
Osteoporosis (Yes vs No)	8.29(1.79 – 38.25)	5.83 (1.10 - 30.75)
Current Systemic Corticotherapy (Yes vs No)	3.71 (1.76 – 7.83)	4.38 (1.89 – 10.15)

RELATIONSHIP BETWEEN NEONATE AND MATERNAL BONE METABOLISM AND ANTHROPOMETRIC MARKERS

R. Tenta[1], I. Bourgiezi[1], E. Aliferis[1], A. Gounaris[2], M. Skouroliakou[1]
[1]*Department of Nutrition Science and Dietetics, Harokopio University, Athens;* [2]*General Public Hospital of Nikaia, Greece*

The objective was to investigate the possible relationship between neonatal anthropometric characteristics and bone turnover and growth markers in newborn neonates and their mothers, taking into account the size for the gestational age (GA). Therefore, elisa method was used to measure OPG (Osteoprotegerin), RANKL (Receptor activator of nuclear factor-kappaB Ligand), IGF-1 (Insulin-like growth factor 1) and IGFBP3 (Insulin-like Growth Factor Binding Protein 3) levels in a random sample which consisted of 20 new born neonates and their mothers. The results showed that birth weight and height were positively correlated with RANKL (p=0,004), (p=0,010), IGF-1 (p=0,008), (p=0,019), IGFBP3 (p=0,030), (p=0,072), and negatively with the ratio OPG/RANKL (p=0,010), (p=0,018). Maternal levels of RANKL were positively correlated with RANKL (p=0,003) and negatively with OPG/RANKL (p=0,014) of SGA (small for the gestational age) neonates. RANKL of SGA neonates was negatively correlated with maternal ratio OPG/RANKL (p=0,042), whereas positive correlation was observed between IGFBP3 of SGA neonates and maternal IGF-1 (p=0,036). According to linear regression, SGA newborns showed lower levels of IGFBP3 (p=0,037) and RANKL (p=0,036) and higher levels of OPG/RANKL (p=0,014) than AGA (appropriate for the gestational age) neonates. LGA (large for the gestational age) newborns had higher IGFBP3 (p=0,018) than AGA. These results reveal a strong relationship between neonatal bone metabolism and their anthropometric characteristics as well as bone metabolism of their mothers. The size for the gestational age was proved to be an important factor, as more apparent correlations were found in small for gestational age neonates.

ASSOCIATION OF SINGLE NUCLEOTIDE POLYMORPHISMS IN 4 GENES (VDR, COL1A1, CALCR AND BGLAP) WITH SUSCEPTIBILITY TO STEROID OSTEOPOROSIS IN PATIENTS WITH IDIOPATHIC PULMONARY FIBROSIS (IPF)

A. Ulitina[1], D. Dzadzua[2], L. Novikova[2], I. Pavlenko[2], J. Ilkovich[2], D. Ghorab[3], M. Dubina[3,1]
[1]*Department of Molecular and Genetic Technologies;* [2]*Research Institute of Pulmonology Pavlov State Medical University, St. Petersburg;* [3]*Nanotechnology Centre, Academic University - Nanotechnology Research and Education Centre RAS, Russian Federation*

Background: The most effective treatment of IPF is Corticosteroids (CS). Steroid osteoporosis is a serious medical and economic problem. At the same time, many genes have influence on bone metabolism, so osteoporosis is a polygenic disorder. Aim: To assess effectiveness of steroid osteoporosis prevention by antiresorptive agents (ARA – Bisphosphonates, Calcitonin) in patients with IPF with different genetic predisposition to osteoporosis. Subjects: 114 patients with IPF, 19 males, 95 females, age 56.7±10.6 years, treated with CS and ARA. Methods: Bone mineral density (BMD) measuring by DEXA, patients' questionnaires and genotyping were used. Genomic DNA was isolated from peripheral leukocytes. We investigated 5 SNPs by PCR-RFLP analysis of 4 genes (*see table*): vitamin D receptor *VDR*, collagen type1 alpha1 *COL1A1*, calcitonin receptor *CALCR* and osteocalcin *BGLAP*. Results: We revealed significant influence of only *VDR-FokI* on BMD (p=0.009), and *BGLAP* was about significant (p=0.081). Environmental factors, firstly ARA intake, seem to have stronger influence on BMD than genes (adjusted R^2=0.065). Conclusions: 1. ARA administration is necessary for all patients taking CS, irrespectively of genotype. 2. *VDR-FokI* analysis is useful to reveal subjects with increased risk of osteoporosis in order to more active BMD loss prevention. 3. Further efforts are required to clarify weight of *BGLAP*.

Gene Acronym	Gene OMIM	dbSNP	Restriction Enzyme	Minor Allele Frequency
VDR	601769	rs1544410	BsmI	0.382
VDR	601769	rs2228570	FokI	0.408
COL1A1	120150	rs1800012	Van91I	0.175
CALCR	114131	rs1801197	AluI	0.276
BGLAP	112260	rs1800247	HindIII	0.180

RISK FACTORS IN AN ORIGIN OF FRACTURES OF VERTEBRAL

Y. Varavko
Family Medicine, IIPT, Russian Federation

The osteoporosis is one of social significant pathologies in communication not only with wide prevalence in population is more 50 years, but also with high frequency of its heavy complications. Among

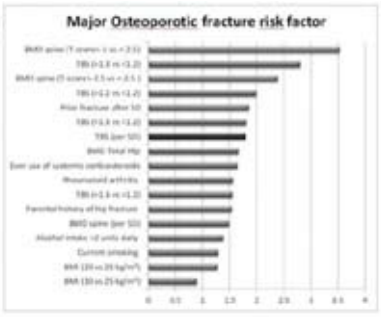
them the most adverse in the prognostic plan are osteoporotic fractures. However, despite all evidence of a problem, the majority of researchers mark extremely low interest of patients by which preventive maintenance and-or treatment of an osteoporosis and its complications is appointed. Donaldson et al. (2009) consider that 72 % of women are more senior 65 years and 93 % is more senior 75 should to receive антирезорбтивную therapy. However in traditional clinical practice in Russia these figures are almost unattainable. It is caused first of all by the limited possibilities of universal use of a x-ray density sensitometry and absence of motivation of earlier revealing of an osteoporosis both at doctors of a primary link, and at patients. The purpose of the present research – studying of risk factors of occurrence osteoporotic fractures of vertebral at the minimum physical trauma at women is more senior 50 years. We survey 300 women with osteoporotic a fracture of vertebral at a low-energy trauma (from height of own growth and more low). Also the control group of 105 persons, without fracture has been typed. Both groups have been stratified on age. At group with fractures of vertebral middle age has made 62 years (p=0,001), in control group – 60 years (p=0,003). Under the questionnaire developed by us following risk factors have been estimated: weight less than 60 kg, growth more than 160 sm, index weight of body less than 25 kg/m^2, a weight-age index (0ST <-1), a surgical menopause till 50 years, heavy and moderate severity level physical work after 50 years, loneliness, mineral density in a vertebral <0,900 g/sm^2, mineral density in proximal department of a hip (total hip) <0,850 g/sm^2, mineral density in a neck <0,800 g/sm^2, T-criterion in a hip from-1 to-2,4SD, T-criterion in a neck from-1 to-2,4SD, T-criterion in a vertebral <-2,5SD, T-criterion in proximal department of a hip <-2,5SD, T-criterion in a neck <-2,5 SD. The condition of mineral density of a bone fabric was estimated by a method of two-power radiological absorption (DXA). For acknowledgement остеопоротическоrо damages it was used T – the criterion showing a deviation from values of density of a bone fabric of persons of young age. It has been studied 30 major factors of risk leading to an osteoporosis. By means of logistical regression the analysis the factors promoting occurrence of crises are defined. Considering that authentically significant risk factors were anthropometrical indicators (weight, growth, an index of weight of a body), we estimate influence weight - growth an indicator (OST), calculated under the formula (weight - age) x 0,2 and being the indicator osteoporosis as for persons Asian races (Koh L.K.H. et al., 2001; Geusens P. et al, 2002; Reginster J.Y et al., 2002). An estimation of this indicator at the Russian women living in Irkutsk and Yaroslavl, with statistical data processing in Ekaterinburg (Lesnjak J.F., Ershov of the Island B., Menshikova L.V., Lesnjak O. M, the Organization of gathering of women is more senior 50 years for densitometrical research on the basis of definition weight-age an index//the Osteoporosis and an osteopathy, 2004, №2., with. 6-10), has allowed among 300 women is more senior 50 years with fractures of vertebral in Irkutsk to calculate standard values weight - growth an index for the Russian population: OST> 4 - low degree of risk of development of an osteoporosis, OST from - 1,0 to 4 - average degree of risk and OST <-1 assumes high risk. As has shown our research at weight-age an index (OST) less-1,0 risk of a fracture of vertebral increased in 3,4 times. It has not been revealed influences of insufficient reception of salts of calcium with food. In both groups low relative density of the persons regularly accepting dairy products is fixed. Low impellent activity, as well as high (walking on foot more than 2 hours a day), didn't raise the risk of fractures, unlike the expressed physical activity is elderly till 25 years and after 50 years (the risk of fractures increased in 3,6 and 2,8 times). Smoking, abusing alcohol took place at individual women in connection with unpopularity of these bad habits at women of the senior age groups. From the gynecologic status significant there was a surgical menopause till 50 years, leading to sharp decrease in level of sexual hormones and acceleration of rate of a decrease of bone weight. Age, duration of the reproductive period, quantity sorts, and duration of lactation didn't influence risk of fractures. From an accompanying pathology, most often met in both groups - hypertensive illness, according to prevalence of this pathology in population. It has not been revealed influence and such accompanying diseases, as: encephalopathy, decrease in sight, etc., reception of the medical products breaking coordination of movements and promoting falling and fractures. Considering that system decrease in mineral density of a bone fabric in a skeleton (indicators mineral density in g/sm^2 and T-criterion in lumbar department of a vertebral and a neck) was independent risk factor of fractures of vertebral, increasing risk in 4,5 times. Conclusion: 1. Significant risk factors of fractures of vertebral at women are: weight less than 60 kg, growth more 160см, an index of weight of a body less than 25 kg/m^2, weight-age an index less-1,0; and also a surgical menopause till 50 years, heavy and moderate severity level physical work till 25 years and after 50 years, loneliness. 2. At women with fractures of vertebral the mineral density of a bone fabric in all areas of measurement was statistically significantly more low, and frequency of an osteoporosis and osteosinging above, in comparison with population indicators of persons of corresponding age. So, frequency of an osteoporosis in one of the basic localizations (a vertebral and-or a neck) has made 90,0 % (in control of 24,4 %), osteopenic a syndrome - 10,6 % (in control of 51,2 %). Decrease mineral density took place in all age groups with faster rate of a decrease in the areas presented cortical by a fabric. 3. At osteosinging (T-criterion from-1 to - 2,4SD) in proximal department of a hip (total hip) and in a neck, but not in a vertebral, the risk of fractures raised in 2 times (OR=2,3 and 1,8), and at an osteoporosis (T-criterion less - 2,5SD) increased in all areas of measurements to 10 times. The normal mineral density of a bone fabric possesses protective action concerning fractures of vertebral.

CAN THE TRABECULAR BONE SCORE (TBS) BE CONSIDERED AS A MAJOR CLINICAL RISK FACTOR (CRF) OF OSTEOPOROTIC FRACTURES? A META-LIKE ANALYSIS

D. Hans[1], **R. Winzenrieth[1]**, B. Aubry-Rozier[1], D. Stoll[1], O. Lamy[1], M-A. Krieg[1]

[1]*Bone and Joint Department, Center of Bone Diseases, Lausanne, Switzerland*

To have an added value over BMD, a CRF of osteoporotic fracture must be predictable of the fracture, independent of BMD, reversible and quantifiable. There are many recognized major CRF such as previous fracture, family history of hip fracture, corticosteroids, smoking, and rheumatoid arthritis. Out of these factors many of them are indirect factor of bone quality. TBS predicts fracture independently of BMD as demonstrated from previous studies. The aim of the study is to verify if TBS can be considered as a major CRF of osteoporotic fracture. Existing validated datasets of Caucasian women were analyzed. These datasets stem from different studies performed by the authors of this report or provided to our group. However, the level of evidence of these studies will vary. Thus, the different datasets were weighted differently according to their design. This meta-like analysis involves more than 32000 women (≥50years) with 2000 osteoporotic fractures from two prospective studies (OFELY&MANITOBA) and 7 cross-sectional studies. Weighted relative risk (RR) for TBS was expressed for each decrease of one standard deviation as well as per tertile difference (TBS=1.300 and 1.200) and compared with those obtained for the major CRF included in FRAX® (FRAX® WHO report p121). Overall TBS RR obtained (adjusted for age) was 1.79 [95%CI-1.37–2.37]. For all women combined, RR for fracture for the lowest compared with the middle TBS tertile was 1.55[1.46-1.68] and for the lowest compared with the highest TBS tertile was 2.8[2.70-3.00]. TBS is comparable to most of the major CRF (Fig 1) and thus could be used as one of them. Further studies have to be conducted to confirm these first findings.



THE EFFECT OF LOW-FREQUENCY PULSED ELECTROMAGNETIC FIELDS ON OSTEOPOROSIS: A ESYSTEMATIC REVIEW

L. Xia

Rehabilitation Medicine Dept., Huaxi Hospital, Sichuan University, Chengdu, China

Objective: To assess the efficacy and safety of low-frequency pulsed electromagnetic fields (PEMFs) on osteoporosis. Methods According to the inclusion criteria, All randomized controlled trials of PEMFs on osteoporosis were performed. All of the clinical trials were searched from the Cochrane Controlled Trials Registered Medline, Embase, Medline, Chinese National Knowledge Infrastructure Database: The selection of studies, assessment of methodological quality and data extraction were performed by two reviewers independently according to predefined inclusion and exclusion criteria. Results Ten randomized controlled trials including 814 patients of osteoporosis met the inclusion criteria, which has 426 treated patients and 388 controlled patients. But most included trials were of low quality and small sample. A “Funnel plot” showed asymmetry, which indicated possible publication bias and low quality in methodology. And publication bias showed that the trials with negative results might not be published. The results of meta-analysis indicated that, the treatment of PEMFs on osteoporosis can increase BMD; the treatment of PEMFs combined with drug therapy can increase more BMD than patients treated drug therapy alone; the treatment of PEMFs and drug therapy has the similar efficacy on increasing BMD; the treatment of PEMFs can effectively relieve pain caused by osteoporosis. No significant adverse effects were reported. Conclusion PEMFs shows some effects and relatively safe on osteoporosis according to the resent researches. However, the evidence is not strong enough because of the low-quality trials and publications bias. Large sample, rigorous designs, randomized controlled trials of PEMFs for osteoporosis are needed to further assess the effect.

PASSIVE STANDING AND FUNCTIONAL ELECTRICAL STIMULATION PRESERVES BONE STRENGTH IN PARAPLEGIC RATS FOLLOWING ACUTE SPINAL CORD INJURY

A. Zamarioli[1,2], R. Battaglino[2,3], L. Morse[4,2,5], S. Sudhakar[5], D. Maranho[1], R. Okubo[1], J. Volpon[1], A. Shimano[1]

[1]Biomechanics, Orthopaedics and Rehabilitation, Universidade de São Paulo, Ribeirão Preto, Brazil; [2]Department of Cytokine Biology, The Forsyth Institute; [3]Department of Oral Medicine, Infection, and Immunity, Harvard School of Dental Medicine, Boston; [4]Department of Physical Medicine and Rehabilitation, Harvard Medical School, Cambridge; [5]Spaulding Rehabilitation Hospital, Boston, MA, USA

Purpose: To compare the effect of functional electrical stimulation (FES), passive standing (PS) and vibration therapy (VT) on bone mineral density (BMD) and bone strength in a rodent model of spinal cord injury (SCI). Methods: Seven-week-old male Wistar rats were divided into five groups: sham operation (Sham, n=10); SCI (n=7); SCI+PS (n=7); SCI+FES (n=7); SCI+VT (n=7). Complete SCI was generated by surgical transection of the cord at T10 level. Treatments were initiated three days after the surgery and continued for 30 days, 3 days/week, 20 minutes/day. SCI+PS rats were placed in a standing position held by a custom built static standing frame. Electrodes were placed over the motor points of the quadriceps and triceps surae muscles of SCI+FES rats (300-μsec pulses, 50 Hz, 5-sec on/15-sec off cycle and, adjusted amplitude, 20 to 150mA, to produce contraction). SCI+VT rats were placed in the custom built static standing frames with the hind legs resting on a vibration platform (60 Hz, vertical amplitude of 1 mm). Animals were euthanized on day 33 post-injury and bones were submitted to densitometry and biomechanical analyses. Results: SCI caused a significant decrease in BMD and bone strength (maximal load and stiffness). Passive standing prevented SCI-induced loss of stiffness at both femur and tibia. FES prevented SCI-induced loss of stiffness at the tibia only. A similar trend was noted with vibration therapy. Conclusions: Our findings showed that SCI caused a significant bone loss at femur and tibia in rats. Passive standing and electrical stimulation therapies protected bone strength in rodents with SCI.

Table1: Bone mineral density and biomechanical data

Bone Mineral Density (g/cm²) mean ± SD					
	Sham (n=10)	SCI (n=7)	SCI+FES (n=7)	SCI+PS (n=7)	SCI+VT (n=8)
Distal femur	0.29±0.07	0.07±0.01*	0.09±0.02*	0.11±0.03*†	0.12±0.02*†
Proximal tibia	0.25±0.06	0.07±0.01*	0.09±0.02*	0.1±0.02*	0.1±0.01*

Maximal Load (N) or Stiffness (N/mm) mean ± SD					
	Control (n=10)	SCI (n=7)	SCI+FES (n=7)	SCI+WB (n=7)	SCI+VP (n=8)
Distal femur					
Maximal load	96.44±9.86	31.56±9.97*	36.03±10.86*	42.23±14.77*	35.18±9.01*
Stiffness	153.66±32.84	99.98±21.35*	116.16±22.09*	140.92±29.59†	111.77±18.53*
Proximal tibia					
Maximal load	67.34±6.21	39.87±4.78*	42.24±2.80*	45.99±5.29*	39.38±2.45*
Stiffness	145.00±12.18	64.32±11.22*	86.96±3.73*†	94.78±8.96*†	79.67±7.29*†

*p<0.0001 vs sham
†p<0.03 vs SCI
‡p<0.07 vs SCI

Rheumatoid Arthritis

INVERSE RELATIONSHIP BETWEEN 25-HYDROXYVITAMIN D AND PARATHYROID HORMONE OBSERVED IN THE GENERAL POPULATION BUT NOT AMONG RHEUMATOID ARTHRITIS PATIENTS

A. Broder[3,5], A. Skversky[3,4], M. Melamed[2], J.N. Tobin[2,6], C. Putterman[1]

[1]Medicine/Rheumatology; [2]Epidemiology and Biostatistics; [3]Albert Einstein College of Medicine; [4]Nephrology Dept.; [5]Montefiore Medical Center, Bronx; [6]Cinical Directors Network, New York, NY, USA

Background/Purpose: Vitamin D deficiency and insufficiency are defined as 25-hydroxyvitamin D (25OHD) levels below 20 ng/ml and 30 ng/ml, respectively, based on data from the general population demonstrating that parathyroid hormone (PTH) levels normalize (below 65 pg/ml) at 25OHD concentrations above 30 ng/ml. Our hypothesis is that the relationship between 25OHD and PTH is altered in rheumatoid arthritis (RA) due to chronic inflammation and corticosteroid use. We studied the relationship between 25OHD and PTH using both the National Health and Nutrition Examination Surveys (NHANES) 2003-2006 and RA patients from a large tertiary care center. Method: For the NHANES cohort and for the tertiary care center cohort we included all adult participants with recorded values for 25OHD and PTH. Participants from both cohorts were excluded if their estimated glomerular filtration rate was < 50 ml/min/1.73 m2, because of the known altered relationship between 25OHD and PTH in chronic kidney disease. In the NHANES we compared participants with RA and participants without arthritis, based on self-report. Linear regression adjusted for age, gender, race/ethnicity and body mass index (BMI) was used for the NHANES cohort within each 25OHD interval (< 10, 10 to 20, 20 to 30, and >30 ng/ml). We constructed Kernel-weighted local polynomial smoothing curves for the RA cohort from our center. Results: In the NHANES cohort, there were 363 participants with RA, and 5995 without arthritis. In the no-arthritis group the relationship between PTH and 25OHD within each stratum of 25OHD was similar to what was previously described in the general population. However, there was no statistically significant relationship between PTH and 25OHD in any of the strata among RA participants. Similarly, among 47 RA patients from the tertiary care center who satisfied the inclusion criteria, PTH levels normalized at 25OHD levels slightly above 10

ng/ml and remained fairly constant at all 25OHD levels (Figure 1). Conclusion: The relationship between PTH and 25OHD is altered in RA compared with the general population. This finding has important implications for future clinical trials and for optimizing vitamin D replacement in RA.

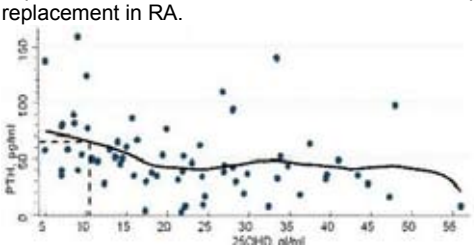


Figure 1: Polynomial curve for RA from a large tertiary care center (n=47)

SAFETY AND EFFICACY OF TOCILIZUMAB TREATMENT IN CHILDREN WITH SYSTEMIC ONSET OF JUVENILE IDIOPATHIC ARTHRITIS

E. Alexeeva[1], **R. Denisova[1]**, S. Valieva[1], T. Bzarova[1], T. Sleptsova[1], E. Mitenko[1], K. Isaeva[1]
[1]*Rheumatology Dept., Scientific Center of Children's Health of Russian Academy of Medical Sciences, Moscow, Russian Federation*

Objectives: To evaluate safety and efficacy of tocilizumab treatment in children with systemic onset of juvenile idiopathic arthritis (JIA). Methods: A retrospective observational study on JIA patients taking tocilizumab (n=39). Tocilizumab was administered intravenously at a dose of 8 mg/kg every 2 weeks during 2 months then every 4 weeks. All patients received DMARDs. Efficacy end points included the American College of Rheumatology (ACR) Pediatric 30 (Pedi 30), Pedi 50, Pedi 70, and Pedi 90 criteria for improvement. Results: A total of 39 patients (21 boys and 18 girls) were included in this Median age was 7.5 years (range; 3 to 15 years) and median disease duration was 4,2 years (range; 0.5 to 8,3 years). A total of 16 of the 39 patients (25%) entered 52 weeks of continuous tocilizumab treatment. The frequently observed non-severe adverse events were nasopharyngitis, upper respiratory tract infection and gastroenteritis. No cases of opportunistic infections, malignancies, autoimmune diseases, or death were reported. One case of pneumonia. 21 patients had incidences of neutropenia. The ACR Pedi 30, 50, 70 and 90 were achieved by 82%, 50%, 27% and 12% of patients at Week 4 (N=36), and by 100%, 81%, 69%, and 50% of patients at Week 24 (N=18), and by 100%, 85%, 78%, and 57% of patients at Week 52 (N=16), respectively. Conclusion: Clinical improvements in the signs and symptoms of systemic JIA were also achieved in favorable levels in tocilizumab in the treatment of children with JIA.

IL-17/RANKL INTERPLAY PROVIDED BY NEUTROPHILS

V. Milanova[1], N. Ivanovska[1], P. Dimitrova[1]
[1]*Department of Immunology, Institute of Microbiology - BAS, Sofia, Bulgaria*

Recently, much attention on the role of neutrophils in the pathology of rheumatoid arthritis (RA) has been paid. However, the capability of RA neutrophils from periphery and bone marrow (BM) to produce inflammatory cytokines like IL-17 and IFN-γ was not encompassed, therefore our aim was to recognize the cause of neutrophil distribution in BM, blood and synovium and to estimate IL-17 and IFN-γ production and surface expression of RANKL on neutrophils during the progression of zymosan-induced arthritis (ZIA) in SCID and BALB/c mice. We observed that IL-17 was able to induce its own production and to increase the incidence of IFN-γ producing peripheral neutrophils. This effect of IL-17 was supported by enhanced STAT3 phosphorylation and elevated RANKL expression. We found significantly higher number of activated $CD69^+/Ly6G^+$ neutrophils in the arthritic synovium and periphery with increased RANKL, IL-17 and IFN-γ expression (Figure 1) corresponding to considerably enhanced synovial and serum levels of IL-17 in SCID mice with ZIA compared to healthy group. Therefore, we suggest that attracting more neutrophils able to produce IL-17 and to express membrane-bound RANKL in synovium can contribute to the early destruction events in ZIA. Our study displays new aspect of the role of neutrophils in the pathology of RA and provides diverse ground for the development of novel therapeutic strategies.

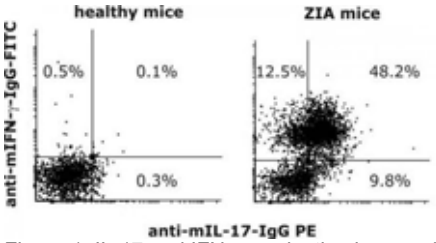


Figure 1. IL-17 and IFN-γ production in synovial neutrophils from healthy and ZIA mice. One representative experiment.

EFFICACY AND SAFETY OF ADALIMUMAB TREATMENT IN JUVENILE IDIOPATHIC ARTHRITIS

E. Mitenko[1], E. Alexeeva[1], R. Denisova[1], S. Valieva[1], T. Bzarova[1], T. Sleptsova[1], K. Isaeva[1]
[1]*Rheumatology Dept., Scientific Center of Children's Health of Russian Academy of Medical Sciences, Moscow, Russian Federation*

Relevance: The treatment of juvenile idiopathic arthritis (JIA) is the serious problem for the health care, therefore development and implementation of new high-tech methods of treatment is relevant. Humanized anti-TNFα monoclonal antibody (adalimumab) is promising drug for the treatment of JIA refractory to immunosuppressive drugs. Purpose of the study: To evaluate clinical efficacy and safety of treatments in patients with juvenile idiopathic arthritis (JIA). Patients and methods: 67 patients were enrolled in the study, 23 boys and 44 girls, 33 with poly-, 23 with oligoarthritis, 11 with enthesitis related arthritis. Mean age of patients was 10 years; mean duration of disease was 6,7 years. Adalimumab was administrated to all patients by subcutaneous injection at dose 40 mg every 2 weeks during 6 months. Results: After 4 weeks (N = 67) the following response rates were observed in patients with JIA, respectively: ACR-Pedi 30, 100% of patients; ACR-Pedi 50, 75% of patients; ACR-Pedi 70, 56% of patients. After 12 weeks of therapy(N=64) JIA patients achieved ACR-Pedi 30, 50 and 70 improvements rates were 100%, 88% and 72% respectively. After 24 weeks of therapy (N = 60) ACR-Pedi 30, 50, 70 and 90 improvements rates were 100 %, 91 %, 74 % and 52 % of patients was registered inactive disease. For the period supervision has developed one serious undesirable phenomenon – tuberculosis of lungs. Conclusion: Thus, our results indicate that adalimumab may be a useful therapy for children with JIA refractory to methotrexate, cyclosporine.

A PROPOSED APPROACH TO TREAT ACTIVE RHEUMATOID ARTHRITIS (RA) WITH CONCOMITANT HEPATITIC VIREMIA

O. Noguchi
Department of Rheumatology, Gennoki Clinic, Ina-Shi, Japan

Background: Patients with active RA accompanied by viral hepatitis tend to remain undertreated for not only active arthritic state but also viral hepatitis against their wishes. Objectives: To suggest how to treat such patients from the standpoint that every patient has a right to receive the best available treatment armamentarium. Methods: We tried to evaluate our experience with successful treatment of a HCV career patient with RA in light of relevant clinical reports and reviews. Results: The therapeutic algorithm we took in the case of HCV career with RA was initial IFN therapy by a hepatologist in cooperation with a rheumatologist followed by treatment with remission-inducing adalimumab after sustained viral extermination achieved in close contact with the hepatologist. It has been reported that HBV reactivation could occur under the immunosuppressive state even in HBsAg-negative but HBsAb-positive cases. Conclusions: RA patients

with hepatitic viremia should be treated initially with IFN from a safety viewpoint to achieve viral extermination, and then with a combination therapy of remission-inducing biologics and immunosuppressive methotrexate, although careful follow-up including blood tests for viremia is needed to defend patients from developing de novo hepatitis which can be easily progressed to fulminant hepatitis. The important challenge would be to determine any predictive risk factors in host as well as virus to develop fulminant hepatitis.

CO-MEDICATION WITH STEROIDS IN PATIENTS WITH RHEUMATOID ARTHRITIS UNDER BIOLOGIC AGENTS

S. Ramiro[1,2], R. Roque[1], F. Vinagre[1], P. Gonçalves[1], A. Cordeiro[1], V. Tavares[1], J. Canas da Silva[1], M.J.Santos[1]

[1]Rheumatology Dept., Hospital Garcia de Orta, Almada, Portugal; [2]Clinical Immunology & Rheumatology Dept., Academic Medical Center, Amsterdam, Netherlands

The timely prescription of an efficacious treatment enables an effective disease control of many patients with RA. Consequently, systemic corticotherapy is expected to be reduced or stopped in patients under biologics. We aimed at evaluating the intake of steroids among patients with RA on biologics and also at identifying its associated factors. Patients with RA on biologic therapy, followed at Hospital Garcia de Orta and included in the Portuguese Register of Rheumatic Diseases (Reuma.Pt) were studied. The frequency of steroids intake and their dosages in prednisolone equivalents at the onset of biologics and at last visit were calculated. The factors associated with the current intake of steroids were studied by logistic regression. The factors associated with the steroids dosage were studied by linear regression. A total of 123 patients were included (mean disease duration 11.6 ± 7.9 years, mean exposure to biologics 5.2 ± 9.9 years), 76% were on steroids at the onset of biologic (mean dosage 6.4 ± 4.4mg/day), whereas 54% were on steroids at the last visit (mean dosage 5.2 ± 2.0mg/day). Factors associated with steroids intake at last visit, adjusted for age and gender, were the patient's global evaluation of disease activity and the dosage of concomitant methotrexate (Table 1).

	Univariable Analysis OR (IC 95%)	Multivariable Analysis adjusted for age and gender OR (IC 95%)
Patient's global evaluation (0-100)	1.03 (1.01 ; 1.05)	1.04 (1.02 – 1.07)
Concomitant methotrexate dosage (mg/week)	1.11 (0.99 – 1.24)	1.14 (1.00 - 1.30)
Gender (female vs male)	0.78 (0.28 – 2.21)	0.76 (0.18 – 3.12)
Current age (years)	1.00 (0.98 – 1.03)	0.99 (0.97 – 1.03)
Painfult joints (0-28)	1.11 (1.00 ; 1.23)	¥
Current biologic duration (days)	0.99 (0.99 – 0.99)	¥
DAS28	1.61 (1.14; 2.27)	**
Pain visual analogue scale (0-100)	1.03 (1.00-1.05)	¥
HAQ (0-3)	2.04 (0.98 – 4.25)	¥
ESR (mm/h)	1.02 (1.00 – 1.03)	¥
Total biologic exposure (years)	0.92 (0.81 – 1.04)	¥
Nº DMARDs	1.69 (0.87 – 3.31)	¥
Swollen joints (0-28)	1.14 (0.96 – 1.36)	¥

Factors associated with the steroids dosage were disease duration, body mass index and duration of current biologic (the latter with an inverse association). With the introduction of biologic agents, 20% of the patients stopped steroids and the others had its dosage reduced. Still, half of the patients were maintained on steroids. A stricter inflammatory control is warranted in order to enable the reduction of chronic and prolonged corticotherapy.

** variable not included in the multivariable analysis, due to the inclusion of its individual components

¥ variables not selected during the multivariable regression (p≥0.05)

ASSESSMENT OF BLOOD TYROSINE LEVEL AS AN APPROACH TO INDIVIDUALIZED RATIONAL PRESCRIBING AND MONITORING GLUCOCORTICOID THERAPY IN RHEUMATOID ARTHRITIS

I. Rass

Center of Theoretical Pharmacology, Russian Academy of Sciences, Moscow, Russian Federation

Glucocorticoid (GC) preparations for more than 60 years are used in the treatment of rheumatoid arthritis (RA). But it is difficult to predict the effect of GGs in individual cases, GC therapy is associated with serious side effects, there are difficulties in abolishing these preparations, and, moreover, GCs are ineffective in about 30% of patients with RA. The problems associated with using GCs are essentially caused by absence of a specific parameter similar to blood glucose for insulin which could characterize the organism's provision with GCs, natural hormones or preparations, and a real need in them. But GC preparations along with their therapeutic properties retain the hormonal features, in particular, the ability to regulate physiological processes and metabolic reactions. Induction of synthesis of a hepatic enzyme tyrosine aminotransferase (TAT) is a well-known example of the regulatory action of GCs. However, TAT cannot be determined in blood, but the blood level of free tyrosine depends on the TAT activity and, consequently, on GC entrance into the liver (the functional validity of the liver must be taken into account!). Based on: 1) specific features of tyrosine catabolism, 2) correlation of GC effects in systemic lupus erythematosus with blood tyrosine levels, 3) observations at the substituting GC therapy in children with adrenogenital syndrome, 4) experimental data on injection–withdrawal of GCs in adrenalectomized rats blood tyrosine is proposed as a promising laboratory parameter for rational prescribing and monitoring GC therapy in patients with RA.

EFFICACY OF INFLIXIMAB TREATMENT IN PATIENTS WITH EARLY AND LONG-STANDING JUVENILE IDIOPATHIC ARTHRITIS

T. Sleptsova

Department of Rheumatology, Scientific Center of Children's Health of Russian Academy of Medical Sciences, Moscow, Russian Federation

BACKGROUND: Treatment of patients with JIA with DMARDs is started immediately after diagnosis, resulting in more effective suppression of disease activity. TNF blockers are recommended in cases of active JIA after the unsuccessful use of DMARDs. The exact role of these agents in the treatment of early-stage JIA is unknown. OBJECTIVE: To evaluate the efficacy of infliximab in patients (n=100) with early and long-standing JIA. METHODS: 100 (60 with early and 40 with long-standing JIA) patients who didn't respond to DMARDs received infliximab 6-7 mg/kg q8wks. Evaluation of efficacy included 30%, 50% and 70% improvement by the ACR-pedi criteria and remission. RESULTS: At 54 week 100% and 87.5% patients with early and long-standing JIA respectively achieved at least 50% response. After 2 years ACR-Pedi 70/90 response to infliximab was recorded in all patients with early JIA and 100%/88.9% of patients with long-standing JIA respectively. At weeks 54 following infliximab treatment, 89% and 60% of patients with early and long-standing JIA achieved remission. At the end of the second year, remission was reported in 97% of children with early JIA and 72% of patients in the second group. 34% of the patients discontinued due to an adverse event, mainly lack of efficacy (23 patients) and hypersensitivity

reactions (11 patients). CONCLUSIONS: this 2-years study suggest using IFX as initial treatment for patients with recent onset JIA is more effective than reserving it for patients with long-standing JIA. No difference between groups in adverse events and secondary inefficacy were observed.

Translational Science

DEMINERALIZED CALF FOETAL GROWTH PLATE EFFECTS ON EXPERIMENTAL BONE HEALING

A. Bighamsadegh[1], Z. Shafiei-Sarvestani[1]
[1]*Department of veterinary Surgery and Radiology, Shahrekord University, Faculty of Veterinary Medicine, Shahrekord, Islamic Republic of Iran*

To stimulate the process of bone healing, several methods have been used previously. These methods include use of ultrasound, electrical stimulation, exposure to electromagnetic field, bone grafts, interporous hydroxyapatite (as a bone graft substitute) and bone growth factors. The following study was designed to evaluate demineralized calf fetal growth plate (DCFGP) effects on bone healing process. Twenty adolescent, 2-kg- weighing, white New Zealand male rabbits were used in this study. In experimental group (n==10) mid radii bone defect created and filled with DCFGP. In control group (n=10) mid radii bone defect created and left without transplantation. Radiological and histopathological evaluations were performed blindly and results scored and analyzed statistically. Statistical tests did not support significant differences between two groups in radiographically union (P> 0.05). There was a significant difference for bone formation and remodeling at the 56th post-operative day (P<0.05). Group with demineralized growth plate was superior to control group at the 56th postoperative day. Histopathological evaluation revealed significant differences between two groups. Group with demineralized growth plate was superior to control group in bone marrow formation and union. In conclusion the results of this study indicate those experimental groups were superior to control group in radiological and histological evaluation.

EFFECTS OF CINNAMON EXTRACT ON BLOOD GLUCOSE LEVEL IN MICE

N. Djaya[1], J. Hidayat[1], J. Hueichi[1], Y. Gerald[1]
[1]*Department of Nutrition and Department of Biochemistry, School of Medicine, Atma Jaya Catholic University of Indonesia, Indonesia*

Background: Cinnamon is dried bark of trees from the genus *Cinnamomum*.[1] From recent studies, it is found that cinnamon can be used to control blood glucose level. Several contents of cinnamon have insulin-like characteristic that has been studied could lower the blood glucose level. These contents are also fathomed to have insulin-like characteristic which allows them to act like insulin in the body.[7] Another theory stated that cinnamon contents could affect insulin receptor on the tissues which decreased the insulin resistance.[8] The mechanism of action of cinnamon is by increasing the sensitivity of insulin receptors, which is: activation of PI 3-kinase receptor and inhibition of tyrosine phosphatase, increasing the concentration of phosphorylated IRS-1 and its binding on PI 3-kinase, activation of glycogen synthesis, stimulation of glucose uptake, and activation of insulin receptor kinase. Objective: The goal of this study is to find out the effect of cinnamon extract on blood glucose level in mice. Method: This intervention study is conducted on 40 white mice with average weight of 217.5 grams, which were divided into 4 groups A, B, C and D. Each group consisted of 10 mice. Group A was given 40 mg cinnamon extract in 50 ml water, group B was given 50 ml glucose 75%, group C was given 50 ml glucose 75% and 40 mg cinnamon, and group D was only given 50 ml of water. Results: There are no significant differences in blood glucose level between the mice in group B (was given glucose 75%) and group C (was given glucose 75% and 40 mg cinnamon extract). Conclusion: In this study, there seems to be no decrease in blood glucose level after the administration of cinnamon extract for 4 days in non-diabetic mice. This shows that cinnamon doesn't give hypoglycemic effect in non-insulin resistant mice (non-diabetic).

DEVELOPMENT OF THE "WHICH HEALTH APPROACHES AND TREATMENTS ARE YOU USING?" (WHAT) QUESTIONNAIRES: A MULTIDIMENSIONAL ASSESSMENT OF COMPLEMENTARY AND ALTERNATIVE MEDICINE USE IN CHILDREN WITH JUVENILE ARTHRITIS

K. Toupin April[1], D. Moher[2], J. Stinson[3], B. Heather[4], D. Ciaran[5], P. Tugwell[6]
[1]*Department of Epidemiology and Community Medicine, Institute of population health, University of Ottawa;* [2]*Department of Epidemiology and Community Medicine, Ottawa Hospital Research Institute and University of Ottawa, Ottawa;* [3]*The Hospital for Sick Children and University of Toronto;* [4]*University of Toronto, Toronto;* [5]*Children's Hospital of Eastern Ontario and University of Ottawa;* [6]*Ottawa Hospital Research Institute and University of Ottawa, Ottawa, Canada*

The aim of this study was to develop child self- and parent proxy-report questionnaires to provide a multidimensional assessment of complementary and alternative medicine (CAM) use in pediatric rheumatology. An interdisciplinary consensus conference, using nominal group technique, was held to develop consensus among stakeholders on the domains and items of the questionnaires. Panel members were presented with information on the content of existing pediatric CAM questionnaires gathered from a systematic review as well as domains and items found to be relevant according to a Delphi survey of experts in CAM and rheumatology. During the conference, discussions among fourteen stakeholders were used to resolve disagreements concerning the content of the questionnaires. Four CAM domains were found to be relevant: child's CAM use, factors associated with CAM use, perceived impact of CAM use and communication about CAM use with medical providers. A total of fourteen items were agreed upon, including types of CAM used by the child, health conditions treated by CAM, modes of payment for CAM, reasons of use, source of information about CAM, difficulty to access CAM as well as benefits and harms of CAM. The research team agreed upon suggested items and developed child and parent report questionnaires. The "WHAT" questionnaires are currently undergoing rigorous validity and reliability testing across two clinical pediatric rheumatology settings in Ontario, Canada. A reliable, valid and feasible CAM questionnaire will ultimately improve the quality of CAM research as well as knowledge translation about the use, benefits and harms of CAM in clinical practice.

AN INTERVENTION TO REDUCE PSYCHOSOCIAL AND BIOLOGICAL INDICATORS OF STRESS IN AFRICAN AMERICAN LUPUS PATIENTS: THE BALANCING LUPUS EXPERIENCES WITH STRESS STRATEGIES (BLESS) STUDY

E. Williams
Epidemiology and Biostatistics, University of South Carolina, Columbia, SC, USA

Psychosocial stress is believed to be positively associated with lupus disease activity due to its ability to compromise immune function. Very little is known about the impact of psychosocial stress on underlying biological mechanisms, although data indicate that lupus patients differ from healthy controls in stress-induced immune responses. Even less is known about this phenomenon in African American lupus patients, although African American women display the highest rates of lupus. Due to the exposure of African Americans to a unique trajectory of stressors throughout the life course, it may be critical to understand the relationship between psychosocial stress and underlying biological mechanisms that influence disease activity and pathology in this high risk group. Linking a psychosocial stress intervention with clinical measures of stress in African American lupus patients will assess the utility of this method in reducing perceived stress, and provide the necessary preliminary steps toward future investigations of potential mechanisms. To begin to fill this research void, a stress intervention was piloted and both biological specimens

and questionnaire responses collected to assess changes in stress state following the intervention in patients who participated in the intervention compared to those who did not participate in the intervention. Research activities were conducted among a cohort of African American lupus patients at the Medical University of South Carolina. Preliminary findings will be shared.

POTENTIATING THE OSTEOGENIC CAPACITY OF BONE MARROW STEM CELLS USING NELL-1 IN AN OSTEOPOROTIC RAT MODEL

J. Zara[1], J. Kwak[1], R. Ngo[1], M. Chiang[1], J. Shen[1], A. James[1], X. Zhang[1], K. Ting[1], C. Soo[1]
[1]*University of California, Los Angeles, Los Angeles, CA, USA*

INTRODUCTION: With less than optimal bone regenerative response due to decline in the number of inherent bone marrow stem cells (BMSCs), osteoporosis complicates the treatment of fractures. Consequently, an osteogenic adjunct to prevent and treat fractures in osteoporotic patients would be of clinical advantage. Nell-1 (Nel-like molecule-1), a novel osteoinductive growth factor, has previously been shown to be effective in bone regeneration. In this study, we aim to demonstrate the osteogenic capacity of Nell-1 in an osteoporotic rat model. MATERIALS AND METHODS: 24 10-month old female rats underwent either sham surgery or bilateral ovariectomy (OVX). Subsequently, 50 uL of 600 ug/ml Nell-1 lyophilized onto 0-50 um tricalcium phosphate (TCP) carrier was injected into the femur bone marrow cavity while phosphate buffered saline (PBS) control was injected into the contralateral femur. Femurs were harvested at 2, 4, and 8 weeks post-operation. Analysis was by microCT, histology, histomorphometry, and immunohistochemistry for osteoblast (RUNX2, Osteocalcin) and osteoclast specific markers (CTR1). RESULTS: MicroCT analysis showed that control treated femurs had continuous decrease in bone volume (BV) and bone mineral density (BMD) from 2 to 8 weeks, and reached near non-treated OVX levels by 8 weeks. In contrast, the Nell-1 treated femurs showed resistance to osteolysis, showing BV and BMD recovery through 4 and 8 weeks, reaching near Sham levels by 8 weeks. Histology showed decreased adiposity in the bone marrow of Nell-1 treated femurs compared to control. Nell-1 treated femurs also showed increased staining for RUNX2, osteocalcin, and CTR1. CONCLUSIONS: Nell-1 effectively increases bone volume in an OVX rat model. This data highlights Nell-1's role in enhancing *in situ* osteogenesis in the bone marrow. Given Nell-1's known promotion of RUNX2 and the Wnt signaling pathway, Nell-1 has potential to be useful in the prevention and treatment of osteoporotic fractures.

POSTER ABSTRACT

Joint Biology

P1

ASPIRIN: IMPACT ON BONE CELLS BEHAVIOUR

E. De Luna-Bertos[1], J. Ramos-Torrecillas[1], O. García-Matínez[1], L. Díaz-Rodríguez[1], C. Ruiz[1,2]
[1]*Department of Nursing, Biomedical Group, Faculty of Health Sciences;* [2]*Institute of Neuroscience, University of Granada, Granada, Spain*

Background: Non-steroidal anti-inflammatories (NSAIDs) as aspirin are usually used after bone surgery because they exhibit favorable anti-inflammatory, analgesic and antipyretic properties. There is increasing evidence that NSAIDs can adversely affect bone repair. Studies in vitro have shown that NSAIDs inhibit osteoblast proliferation and stimulate protein synthesis, but either animal tissues or cell lines. Objective: to study the effect of aspirin on human osteoblast-like cells proliferation, antigenic phenotype profile and phagocytic capacity. The human osteosarcoma line MG-63 was regarded as a study model. Methods: Human osteoblast-like lines were cultured with two different concentrations of aspirin (1µM and 10µM). Osteoblasts proliferation was examined by MTT assay after 24h of culture. Flow cytometer was used to analyze the following molecules: CD54, CD80 and CD86. The analysis of the phagocytic capacity was carried out by a cytometric technique. The target particles were little fluorescent latex bears. Results: After 24 hours of treatment with aspirin at 1, 10 µM, there was no change in cell proliferation. Therefore, our results showed an increase of the expression of CD80 and CD86. We also detected a significant decrease of CD54 expression in both cases. Our results show that the aspirin at 1 and 10 µM reduces in a significant way the percentage of cells having a phagocytic capacity (p=0.004, p=0.034 respectively). Conclusions: These findings suggest that aspirin activates the osteoblast, inducing its immunogenic action and its phagocytic capacity, without any effect on bone formation capacity at therapeutic doses.

P2

THREE-PHASE BONE SCINTIGRAPHY WITH SPECT – DIAGNOSTIC TOOL FOR AVASCULAR NECROSIS OF THE HIP

S. Dugonjic[1], D. Stefanović[1], M. Ćirković[1], B. Ajdinović[1]
[1]*Clinic of Rheumatology, Institute of Nuclear Medicine, Medical Military Academy, Belgrade, Serbia*

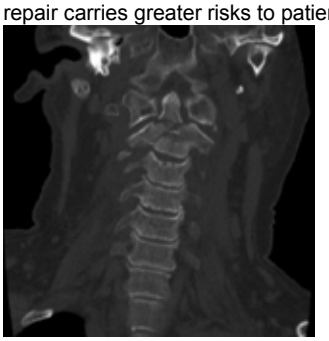
Three-phase bone scintigraphy (3FBS) and MRI are the diagnostic tools to detect early stage of avascular necrosis (AVN) when x-ray findings are normal in patients with bone-type pain. AVN is most common in the hip joint. In patients with AVN of the hip 3FBS with SPECT is significant in early detection and separation of patients with spontaneous healing from those who need surgery. The aim of study was detection and staging of AVN of hip using 3FBS with SPECT in patients with suspected AVN. METHODS: 3FBS with SPECT of hips were done in 32 patients with suspected AVN. AVN was due to: high doses of corticosteroid therapy in 16 pts, hip trauma in 8 pts, SLE in 4 pts. In 6 pts AVN was idiopathic. In 19 pts AVN was diagnosed by BS, in 13 pts AVN was diagnosed by MRI and confirmed by BS. Scintigraphic results were classified in three scintigraphic stages: 1-early, 2-intermediate and 3-late stage of AVN. RESULTS: 3FBS with SPECT was positive in all patients (100%). In 8 pts (25%), AVN was in early stage. Sixteen pts (50%) had intermediate stage, and 8 pts (25%) had late scintigraphic stage of AVN. Twenty seven pts had unilateral and 5 pts had bilateral AVN of the hip. CONCLUSION: 3FBS with SPECT is very sensitive method for AVN detection. 3FBS with SPECT can establish stage and prognosis of AVN and influenc its further therapy.

P3

CASE REPORT OUTLINING THE MANAGEMENT OF A VERTEBRAL ARTERY PSEUDOANEURYSM FOLLOWING A MALUNION OF A TRAUMATIC ODOINTOID PEG FRACTURE

A. Ghatahora[1], S. Ahuja[1], P. Rao[1], V. Paringe[1]
[1]*Orthopaedic Surgery Dept., NHS - Cardiff and Vale Health Board, Cardiff, UK*

Vertebral artery pseudoaneurysms with arteriovenous fistula (VAPAF) are rare occurrences usually reported following blunt c penetrating cervical trauma. The management of these rare cases as described in literature, depends on location, size, and symptom and can be either surgical, conservative or endovascular. They ar generally clinically occult but cases have been described wit numerous presenting symptoms including altered neurology, tinnitus sub arachnoid haemorrhage. We report a case presentation c vertebral pseudoaneurysm and AV fistula following a mal-united C fracture with right sided C5 and C6 myotonic and sensory weaknes Purpose of case report: To highlight a rare occurrence of vertebr artery pseudoaneurysms and arteriovenous fistula secondary to a unusual mechanism. Methods: Review of current scientific literatur followed by extensive investigation of patients' case notes an imaging. Results: A 73 year old female presented with right sided C and C6 myotonic and sensory weakness 4 months following a ma united C2 fracture sustained from falling backwards down a sma flight of stairs. Her original fracture was managed in a Halo. Cerebr angiography demonstrated a right sided direct arteriovenous fistula a the level of C2. Her VAPAF was managed endovascularly wit embolization coils (gel covered and bare platinum coils) followin which, her neurological symptoms improved. Conclusion: To dat there is no current literature describing formation of pseudoaneurysi secondary to microtrauma due to a mal-united C2 fracture. Curren literature review in VAPAF indicates an endovascular techniqu seems to be the treatment of choice as a gold standard open surgic repair carries greater risks to patients.



P4

CALCIUM TRANSPORTERS OF INTRACELLULAR AND CELLULAR MEMBRANE IN INDUCED OXIDATIVE STRESSED RATS DURING PREGNANCY

E-B. Jeung[1], H. Yang[1]
[1]*Chungbuk National Univ, College of Vet Medicine, Cheongju, Republic of Korea*

Preeclampsia is a pregnancy-specific disease characterized by de novo development of concurrent hypertension, proteinuria an oxidative stress in placenta. Hypoxia occurs during the developmer of placenta in the first trimester and is implicated in trophobla

differentiation. The oxidative stress, resulting from deficient remodelling of spiral arteries, is an importance of preeclampsia. Last trimester of human placenta, the calcium (Ca^{2+}) transport from mother to fetus dramatically increase in response to the accelerated demand for Ca^{2+} caused by bone mineralization in the fetus. The plasma membrane and cytosolic calcium processing genes, TRPV5/6, NCXs, Calbindin-$D_{9/28k}$ and PMCA1, plays a critical role in the transport of intracellular calcium across the cell membrane and intracellular calcium homeostasis. In this study, the roles of cell membrane and cytosolic calcium processing genes were examined in the intestine, kidney and placenta of hypoxic rats at gestation 19.5 days (GD 19.5). From normoxic or hypoxic pregnant rats, fetal weight were not difference, however, from hypoxic placental weight were heavier than placenta of normoxic pregnant. In GD 19.5, renal NCKX3, NCX1, TRPV5/6, PMCA1 and Calbindin-$D_{9/28k}$ expression were increased in hypoxic rat compared with normoxic pregnant rat. Also, the levels of NCKX3, NCX1, TRPV5/6, PMCA1 and Calbindin-$D_{9/28k}$ were induced in the duodenum of hypoxic rat. The expression of NCKX3, NCX1, TRPV5/6, PMCA1 and Calbindin-$D_{9/28k}$ were highly expressed in the placenta of hypoxic rat. Taken together, these results indicate that renal, duodenal and placental calcium exchangers are potential roles in oxidative stress between normoxic and hypoxic rats, suggesting that induced calcium exchangers and placental weight of hypoxic rats may be involved in preeclamptic oxdative stress in the intestine, kidney and placenta, is a determinant factor affecting calcium transport in hypoxic intestine, kidney and placenta.

P5

THE BIOTECHNOLOGY RESEARCH AND DEVELOPMENT SUPPORTED BY THE KOREA SCIENCE AND ENGINEERING FOUNDATION

T. Min

Department of Natural Sciences, National Research Foundation, Daejon, Republic of Korea

This research was conducted to make suggestions for the promotion of research activities in the Biotechnology field, and we evaluated the research funding trend and the present status of research funding offered by KOSEF in this field. Researchers in this field have received more research funding from the group-based programme than from the individual-based programme. Also, they have received less money (per project) than did researchers in other Science and Technology fields. The portion of research funds given to the Medical Sciences fields has markedly increased year by year, whereas the portion of funding given to the Agricultural Sciences and Biological Sciences fields has decreased annually. Researchers who have been selected by the Mission-oriented Basic Grants programme have been given the lion's share in submitting their thesis most, whereas researchers who have been selected by the Program for the Leading Scientists have loaded their thesis to the SCI journals most. To encourage research activities in the Biotechnology field in Korea, the following actions and systems are required: 1) formulation of a mid- and a long-term research master plan, 2) development of a database on man power in related fields, 3) activation of top-down research topics, and associated increase of individual research grants, 4) development of special national programs for basic researches in Life Sciences, 5) organization of a committee for policy and planning within related societies, and 6) system development for fair evaluation of the results of research activities.

P6

THERAPEUTIC REHABILITATION OF PATIENTS WITH HAEMOPHILIC ARTHROPATHY

B. Daniszewska[1], **J. Raczkowski**[2]

[1]Rehabilitaion Clinic; [2]1st Dept. of Orthopaedics, Traumatology and Rehabilitation Medical University of Lodz, Lodz, Poland

Introduction: The publication presents a suggestion of therapeutic rehabilitation after haemarthrosis in the course of haemophilia. Aim: Presentation of the selected procedures of physiotherapeutic rehabilitation] after blood extravasation to soft tissues and joints. Presentation of the set of physical exercises in the prophylaxis of idiopathic intratissue extravasation. Assessment of the return of functional efficiency after applied physiotherapeutic procedures. Assessment of the decrease of pain factor after haemarthrosis after applied physiotherapeutic procedures. The applied research methods: Analysis of medical documentation; Functional examinations; Observation Medical history. Conclusions: Haemarthrosis are most frequent in the area of knee and elbow joints. The applied medical procedures after extravasation include: cooling of haemarthrosis area and administration of a coagulant, then decompressing exercises, massage, hydrogymnastics, decompressing exercises with gradual resistance, positioning therapy, functional exercises. Magnetic field (individually selected parameters) and underwater vibratory massage are in the range of physiotherapeutic procedures adjunctive to the process of blood absorption after extravasation. Prophylactic exercises protecting against injuries and thus against haemarthrosis include: flexibility, strengthening, agility, dexterity exercises. Exercises contraindicated in the diagnosed haemorrhagic diathesis include: jumping up and down, traumatic sports, strength-requiring exercises with high isometric tone and strength-endurance exercises.

P7

STUDY OF THE EFFECT OF DIFFERENT DOSES OF METAMIZOL ON HUMAN MG-63 OSTEOSARCOMA CELL LINE

J. Ramos-Torrecillas[1], E. De Luna-Bertos[1], L. Díaz-Rodríguez[1], O. García-Matínez[1], C. Ruiz[1,2]

[1]Department of Nursing, Biomedical Group, Faculty of Health Sciences; [2]Institute of Neuroscience, University of Granada, Granada, Spain

Nonsteroidal anti-inflammatory drugs (NSAIDs) are commonly prescribed for acute post-surgical and post-traumatic pain. Several studies have demonstrated that bone growth, remodeling, and repair are suppressed by NSAIDs although the mechanisms underlying these effects have not been fully elucidated. The objective of the study has been to set, in vitro, the effect of different doses of Metamizol on growth, cell cycle, apoptosis induction and cellular adhesion in Human MG-63 osteosarcoma the cell line. MG63 line was cultured during 24 hours, at 37ºC in an atmosphere of CO_2 at 5% with two doses of Metamizol (1µM and 10µM). The effect of this drug on growth and cellular adhesion was determined through a spectrophotometric technique (MTT). The effect on cell cycle and apoptosis induction was studied by flow cytometry. All experiments included an internal control i.e., incubated without NSAID under the same conditions. The outcomes showed a significant decrease in the MG63 cell line growth after 24 hours of incubation with 1 and 10µM of Metamizol assayed (p=0.001). In this sense, the cell cycle study showed a slight not significant increase the cell distribution in its different phases with both doses. In addition, we detected a significant increase in the number of apoptotic cells with two doses (p=0.000). In relation to adhesion, the data showed a significant increase on adherence MG63 within the first hours with 1 and 10µM (p=0.01). In conclusion our results suggest that Metamizol should be used with precaution in the process of bone regeneration.

P8

THE EFFECTS OF LOW-LEVEL LASER THERAPY (685 NM) ON EXPERIMENTAL MODEL OF OSTEOARTRITHIS

A.C. Renno[1], P. Oliveira[2], A. Santos[3], L. Rohn[3], K. Pinto[3]

[1]Federal University of São Paulo, Santos, Brazil; [2]Univ Caen, Caen, France; [3]Departament of Biosciences, Federal University of São Carlos, São Carlos, Brazil

Osteoarthritis (OA) is a chronic degenerative disease characterized by gradual loss of articular cartilage, which culminate in loss of joint function, pain and sensory motor loss. In this context, biophysics devices have been developed in an attempt of improving the process of tissue repair. The aim of this study is investigate the effect of low level laser therapy on arthritic cartilage of knees of rats. We used 40

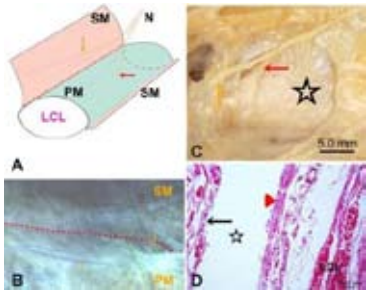
male rats distributed in 2 groups: injured control group and injured treated group. Both groups were divided in 2 sub-groups, sacrificed in 2 different periods post-surgery (sub-group A: 5 weeks post-surgery and sub-group B: 8 weeks post-surgery). Animals were submitted to the total section of the cruciate ligament in the knee. After 2 weeks, the laser treatment started and it was performed at one point, above the knee joint. A 685nm laser, at 10 J/cm2 was applied during 15 (sub-group A) and 30 sessions (sub-group B). To evaluate the effects of the laser therapy on arthritic cartilage, histological sections were made and stained with Safranin (to analyze the amount of proteoglycans) and Hematoxylin and Eosin (to analyze the cellularity). Results: histology revealed that, at the first period evaluated, no difference in the amount of proteoglycans and number of cartilage cells was found between the control and treated group. Interestingly, 5 weeks of treatment, the amount of proteoglycans found in the laser group was significantly higher compared to control. Also, the number of chondrocyte cells was higher in the treated group. Conclusion: In this study laser therapy was able of improving cartilage metabolism in a model of experimental OA in knees of rats.

P9

OBSERVATIONS OF THE LATERAL COLLATERAL LIGAMENT IN THE HUMAN KNEE JOINT

J. Yan[1], W. Sasaki[1]
[1]*Anatomy Dept., Iwate Medical University, Yahaba, Japan*

Thirty-six cadavers (55 sides) were used to observe the innervation of the lateral collateral ligament (LCL) and its circumference structures with the gross anatomical and histological methods to clarify the cause of indistinct pain in the lateral part of the knee joint. The innervating branches of the LCL could be divided into three types: 1) from the muscular branch of the biceps femoris muscle at lower 1/3 level of the thigh; 2) from the common fibular nerve (CFN) at the higher level of the fossa popliteal; 3) from the CFN at the level of the caput fibular. Furthermore, the three branches could singly or plurally distribute to the LCL (six types). Two of the connecting tissue membranes surrounding the surface of LCL formed an incomplete sheath structure, and a shutting “gap” was observed between the two of membranes. Fine peripheral nervous branches were also observed in the two of the membranes. On the other hand, three types of nerve endings in the LCL (Type I/Ruffini mechanoreceptor; Type III/Golgi mechanoreceptor; Type IV/Free nerve ending) were observed, and their presence was consistent with the ankle joint of humans. Therefore, the innervation of two of membranes (to form the shutting gap) in the surface of LCL may be associated with an indistinct pain when the knee joint is damaged.



Muscles

P10

ACHILLES TENDON RECONSTRUCTION SECONDARY TO FOREIGN BODY GIANT CELL REACTION - CASE REPORT AND REPAIR TECHNIQUE

L. Ciliberti[1], J. Miller[1]
[1]*Orthopaedics & Podiatry Dept., PA Orthopaedic Center, Malvern, PA, USA*

Purpose: Partial and total Achilles tendon ruptures are commonly seen in the Orthopaedic setting. Primary open debridement and repair is considered the standard of care in the United States. The post-operative course is typically uneventful with good outcomes reported. We report on one case of a foreign body reaction following open repair approximately five years earlier. Materials & Methods: A retrospective chart and imaging review of a 37 year old male was performed. He reported a previous Achilles tendon rupture in 2006 which was repaired via the standard open technique. He presented with pain to the distal Achilles tendon after attempting to board a train. Multiple tender nodules were noted along the distal Achilles tendon upon exam. MR imaging was obtained and severe fusiform thickening with a superimposed interstitial tear was noted. Intra-operatively, the previously repaired Achilles tendon was found to be nodular with irregular margins. Caseous material was noted throughout the tendon and just below the dermal layer. The previously used suture was found to communicate with the caseous material. Sharp excisional debridement and debulking was performed. The repaired tendon was reinforced with a permeable synthetic porous graft (Artelon Ò Tissue Reinforcement, Artimplant, Sweden). Results: The patient was placed in a posterior splint and transitioned to a fracture boot at postoperative week three. Specimens sent to Surgical Pathology were found to be consistent with fibrosis and foreign body giant cell reaction. Good wound healing was noted with no dehiscence or postsurgical complications. Conclusions: Achilles tendon ruptures are often repaired via the standard technique with no evidence of foreign body reaction when repaired without graft augmentation. Our findings suggest an alternative technique for tendon reconstruction following foreign body reaction with a permeable synthetic porous graft.

P11

THE CLINICAL PROFILE OF CASES OF INFLAMMATORY MUSCLE DISEASE IN UNIVERSITY OF MALAYA MEDICAL CENTRE (UMMC)

R. Jasmin[1], T.E. Cheah[1], K-J. Goh[2], A. Azlan Zain[1], S. Sockalingam[1]
[1]*Division of Rheumatology;* [2]*Neurology;* [3]*Department of Medicine, University of Malaya, Kuala Lumpur, Malaysia*

Introduction: Inflammatory muscle diseases commonly present with proximal myopathy. However, important differential diagnoses include muscular dystrophy and metabolic myopathy. Objectives: To study the clinical profile of inflammatory muscle disease in our patients and to compare the clinical and histopathological diagnosis in these patients. Methods: A retrospective study of 25 patients who presented to Rheumatology unit, UMMC from January 2007 to

September 2011 with the clinical diagnosis of possible inflammatory myopathy was done. All had muscle biopsy done. Results: Mean age was 53.3 years. Of the 25 patients, 17(68%) had diagnosis based on clinical presentation. 16(64%) had diagnosis based on muscle biopsy in which 9(36%) had the histopathological diagnosis of dermatomyositis, 3(12%) polymyositis, 2(8%)muscular dystrophy, 1(4%)inclusion body myositis (IBM) and 1(4%) metabolic myopathy. The remainder 9(36%) had inconclusive histopathological diagnosis. Significant correlation (p=0.01) was seen between clinical diagnosis and the histopathological diagnosis. Final diagnosis of dermatomyositis was made in 11(44%) patients, amyopathic dermatomyositis 2(8%), polymyositis 5(20%), Becker's muscular dystrophy 2(8%), MCTD 2(8%) and 1(4%) each for IBM, fibromyalgia, and metabolic myopathy. 19 patients had inflammatory myositis conclusively. The most common clinical presentation was proximal myopathy (23, 92%), followed by muscle pain (13, 52%). Raised serum creatinine kinase was seen in all patients and 21(84%) had transaminitis. 18(72%) had positive ANA titre. ENA was positive in 7(28%) out of which 4 were anti-Jo-1 positive. 88% received corticosteroids and 72% received immunosuppressive agents. 9(36%) attained clinical remission.
Conclusion: Diagnosis of muscular pathologies through muscle biopsies significantly correlated with our clinical diagnosis. Dermatomyositis is the prominent inflammatory muscle disease.

P12

FAMILIAL VITAMIN D DEFICIENT OSTEOMALACIA AND RENAL OSTEODYSTROPHY: SHAPING UP THE DEBATE

W. Jebur
Nephrology Dept. NMC Specialty Hospital, Dubai, United Arab Emirates

Osteomalacia is a common occurrence the world over due to the deficiency in vitamin D and calcium intake. We present here two sisters with features of sever osteomalacia, myopathy and hypophosphatemia hyperparathyroidism and 25(OH)D2, 25(OH)D3 and 1,25(OH)D3 levels were very low. It is rarely reported nowadays the severe skeletal manifestations of osteomalacia secondary to vitamin D deficiency, especially among young females of Arabic descent who are working outdoors and residing in the Persian gulf region where a hot sunny climate prevails around the year. The main risk factors are usually dark skin and intake of vegetarian diet. Similarly the renal osteodystrophy related to vitamin D deficiency is often encountered and has still debatable etiology. By reporting these patients we are trying to discover the probable etiology and the pathological mechanisms underlying osteomalacia and renal osteodystrophy.

P13

MOLECULAR GENETICS IN THE DIAGNOSIS OF CALPAINOPATHY

J. Poste[1], M. Khan[1], S. Holstein[1], P. Basak[1], S. Jesmajian[1]
[1]*Sound Shore Medical Center of Westchester, New Rochelle, NY, USA*

The incidence of Limb Girdle Muscular Dystrophy (LGMD) syndromes is estimated to be 5-70 per 1 million. LGMD can be autosomal dominant (LGMD1) or autosomal recessive (LGMD2). Calpainopathy or LGMD2A is the result of a mutation in the gene encoding calpain 3 protease on chromosome 15. It is the most common subtype, accounting for 8-26% of all LGMDs. A 20 year old male was seen in the clinic. He was adopted from Romania shortly after birth. He had delayed milestones, and at the age of 6 years, was noted to walk on his toes with a spread out gait. On physical exam, his calves were not enlarged and girdle muscle strength was grade 2-3/ 5. He walked with a waddling gait. Creatine kinase was 7600U/dl, and MRI of the spine and hip were normal. Multiplex Ligation-dependent Probe Amplification analysis showed a homozygous deletion of exons 2-8 of CAPN3, thus confirming the diagnosis of calpainopathy. Patients with calpainopathy present between 2 to 40 years, with difficulty in running, climbing stairs or frequent falls. It is predominantly symmetrical and atrophic, with Achilles tendon contractures as an early sign. Pelvic girdle weakness is present with sparing of the hip abductors. Confinement to a wheelchair occurs typically 11–28 years after the onset of symptoms. Diagnostic whole blood DNA allows screening of multiple proteins that are responsible for different forms of LGMD. Advancement in molecular genetics has made it possible to pinpoint specific mutation sequences in LGMD, leading to carrier detection and prenatal diagnosis.

P14

TREATMENT OF FIBRODYSPLASIA OSSIFICANS PROGRESSIVA WITH HIGH DOSE OF NICOTINAMIDE IN TWO CHILEAN CHILDREN: 5 YEARS FOLLOW UP

I. Quevedo
Department of Endocrinology, Osteology Institute, Concepcion, Chile

Fibrodysplasia ossificans progressiva (FOP) is a rare disease causing progressive ossification of soft tissues. The first manifestations begin in childhood when the recurrent soft tissue swelling (flare-ups) appear and the body starts to generate new heterotopic bone. There is no widely known effective therapy for FOP. Nicotinamide in high doses, in vitro, prevents mineralization and bone differentiation. We describe two children (nine-year-old boy and one fifteen-year-old girl) who were treated for 5 years with high-dose nicotinamide (150 mg/kg/day). Before nicotinamide the flare-up were observed every 3 weeks in mean. During the follow up only four flare-ups in each child were observed. Three of these four flare-ups occurred after a major trauma. The first clinical benefits from the treatment became clear after two months. After the first year the girl discontinued the treatment for three months recommenced the flare-ups attacks. At the beginning of the study both children suffered from neck stiffness. After five years, neck rotation increased to 45 degrees in the girl, and 35 degrees in the boy. When the study began, the right upper extremity of the boy was together with the thorax, causing axillary fungus. After five years of treatment, he can now move his extremity in 40 degrees. Before treatment, the boy could not sit of his incapability to bend the spinal column. Nowadays he can sit and also run. Treatment did not affect their growth. Control radiograph no showed neither improvements nor worsening in the size of heterotopic ossifications. Data suggest that nicotinamide therapy may inhibit the flare-ups attacks and show a major clinical improvement in patients with FOP.

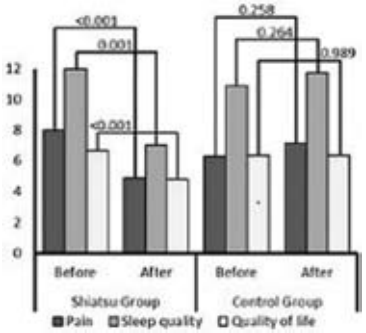
P15

THE EFFECTIVENESS OF SHIATSU ON PAIN, QUALITY OF SLEEP AND QUALITY OF LIFE OF INDIVIDUALS WITH FIBROMYALGIA: PRELIMINARY STUDY

S. Yuan[1], A. Berssaneti[1], A. Marques[1], **F.J.R. Franca**[1]
[1]*Departamento de Fisioterapia, Fonoaudiologia e Terapia Ocupacional Universidade de São Paulo, São Paulo, Brazil*

Introduction: Fibromyalgia is a painful musculoskeletal disorder that compromises function and quality of life. Studies show that conventional treatment is unsatisfactory and patients often seek complementary and alternative medicine. However its evidence is still insufficient. This clinical trial aimed to verify the effectiveness of Shiatsu (Japanese massage technique) in the improvement of pain, sleep quality and quality of life of patients with fibromyalgia. Method: This study involved 29 women aged 33 to 62 years, divided into two groups: Shiatsu Group (n=17), which received 16 sessions of Shiatsu lasting 50 minutes, twice a week, and Control Group (n=12), who received educational guidance through a booklet. Both groups were evaluated before and after 8 weeks. The following instruments were used: Visual Analog Pain Scale, Pittsburgh Sleep Quality Index and Fibromyalgia Impact Questionnaire. Intragroup statistical analysis was performed using the one-way RM ANOVA for data sets with normal distribution and the same variance and Friedman RM ANOVA for data sets without normal distribution. The Holm-Sidak method and Tukey test respectively were used for multiple comparisons procedure. The

significance level was α=0.05. Results: Shiatsu Group showed statistically significant improvement in pain, quality of sleep and quality of life at the end of treatment. The Control Group showed no statistically significant improvement in any variable. Conclusion: The results indicate that the technique of Shiatsu is effective in improving pain, sleep quality and quality of life of individuals with fibromyalgia.



P16

EFFECT OF LOW LEVEL LASER THERAPY ON TIBIAL MUSCLE REPAIR IN RATS

N. Rodrigues[1], R. Brunelli[2], N. Parizotto[1], D. Ribeiro[3], D. Abreu[4], K. Fernandes[3], A.C. Rennó[5]
[1]Physiotherapy Dept., Universidade Federal de São Carlos, Sao Carlos, [2]Surgery Dept., Universidade de Campinas, [3]Physiotherapy Dept., Universidade Federal de São Paulo; [4]Physiotherapy Dept., Universidade de São Paulo; [5]Universidade Federal de São Paulo, São Paulo, Brazil

The purpose of this study was to investigate the effects of low-level laser therapy (LLLT) used in two different fluencies, on injured skeletal muscle by means of histopathological analysis, collagen evaluation and Immunohistochemistry. Twenty eight rats were distributed into 2 groups: control group and laser group irradiated with 50 J/cm². Each group was divided into 2 different subgroups (n=7) and on days 7 and 14 post surgery were sacrificed. Histopathological findings revealed mild degenerative modifications in the muscle tissue in laser exposed group used when compared to the control group after 7 days. On day 14th, the animals irradiated also showed minor histopathological changes in the muscular tissue. Regarding collagen deposition, no difference was found between control group and irradiated group on days 7 and 14 post surgery. Decreased expression of COX-2 protein was noticed in the groups exposed to LLLT for all periods evaluated. VEGF showed expression in the control on days 7 and 14 post surgery. Taken together, our results demonstrate that LLLT has positive effects on muscle repair as a result of increasing collagen synthesis and reducing COX-2 expression.

P17

IS THE RELATIONSHIP BETWEEN WHOLE BODY BONE AND SOFT TISSUE SEEN IN CHILDHOOD MAINTAINED IN ADULTHOOD?

T. Sanchez[1], J. Wang[2], F. Rajan[3], K. Dudzek[4]
[1]Norland--a CooperSurgical Company, Socorro; [2]Research and Development, CooperSurgical Company; [3]Siemens Healthcare; [4]Research and Development, Norland Corporation, USA

Reports indicate a strong relationship between total body bone and lean mass in children and a moderate relationship between total body bone and fat mass in girls but not in boys. The current study explores if those relationships are continued in adult men and women. A population of 150 subjects (75 males between 20 and 51 years old and 75 females between 20 and 67 years) underwent whole body studies to assess total body bone, lean and fat using the same DXA system (Norland XR-46 fitted with Illuminatus software) used earlier to assess total body bone, lean and fat mass in a population of children. Analysis of the relationship between bone and lean or fat in male and female subjects was by regression with covariance analysis. Analysis shows strong significant relationships between bone and lean mass in adult males (BMC = 0.0387X + 1124; r = 0.6853; P<0.0001; RMSE = 303) and females (BMC = 0.03078X + 1577; r = 0.5456 P<0.0001; RMSE = 289). Examining the relationship between bone and fat mass reveals a relatively strong relationship in adult females (BMC = 0.0175X + 2336; r = 0.4742; P<0.0001; RMSE = 304) and a more moderate relationship in adult males (BMC = 0.0146X + 3207; r = 0.3603; P<0.001; RMSE = 388). The data indicate that--as observed in children--bone mass is significantly related to lean mass in men and women and that a significant relationship also exists between bone and fat in the women.

P18

ACKNOWLEDGING DIFFERENT CAUSES OF CPK ELEVATIONS

J. Scali[1], S. Visentini[1], G. Pacheco[1], J. Salomón[1], R. Berruezo[1]
Rheumatology/ Osteology Unit, Hospital Carlos G. Durand, Ciudad de Buenos Aires, Argentina

INTRODUCTION: CPK raising (Creatine-Phosphokinase enzyme) is normally observed in the course of inflammatory myopathies and other autoimmune diseases. Clinical manifestations of muscle pathology, and marked enzyme elevations (CPK), are prevalent in polymyositis /dermatomyositis (PM/DM), (weakness and pain over scapular/ pelvic areas during resting and physical exercise), leading to difficulties in normal life activities. On certain occasions, CPK elevations are not completely understood out of context, especially in asymptomatic patients. OBJETIVES: To determine different clinical associations in the presence of CPK elevations in a rheumatologic patient population and Identify asymptomatic cases for further study. PATIENTS AND METHODS: Population: We include Patients over 18 years old who regularly attended our Rheumatology Unit, or derived from other centers, between the years 2005 and 2010. Cases: We studied all patients in whom we found elevations of CPK, regardless of their levels: (RA, SLE, SSc, PM / DM, Sjogren' s syndrome, systemic vasculitis, Sarcoidosis, etc.). with repeated laboratory determinations, with or without symptomatic expression. Isolated elevations of the enzyme, required more intensive investigations as to verify laboratory data, history of major physical effort / unusual, falls, EMG, intramuscular injections and / or any situation likely to generate elevations of CPK. RESULTS: Of a total of 128 patients of both genders, with elevated CPK, we find the following distribution: PM / DM / MCI (78%), others such as RA, SLE, SSc, vasculitis, sarcoidosis (8.6%), Toxic / drugs (statin / zidovudine) (4.7%);Endocrine hypo / hyperthyroidism / hypoparathyroidism (3.9%), intense physical exercise (0.78%), SRCD (Sudek's) (0.78%), idiopathic (0.78%), muscular dystrophies (Steinert, Nieman Pick,etc) (1.56%), ALS (0.78%). Of all patients without PM / DM, 60% were symptomatic and 40% represented unclear symptoms. CONCLUSIONS: Regardless of the largest group of our patients, represented by PM / DM are different diseases / conditions with isolated elevation of CPK, either associated with other autoimmune diseases or not. Further evaluation and thorough evaluation of asymptomatic patients with hiper -CK-emia (muscle biopsy: routine histological, histochemical, immunohistochemical, western blot and genetic study of Duchenne, DNA analysis) allowed us to arrive at a diagnosis. It should emphasize the clinical relevance of these findings, mainly in asymptomatic cases for a possible therapeutic approach required.

P19

COMFREY ROOT EXTRACT CREAM IN CLINICAL RESEARCH OF PAINFUL MUSCLE AND JOINT COMPLAINTS: WHERE DO WE STAND TODAY?

C. Staiger
Global Medical Affairs Dept., Merck Selbstmedikation GmbH, Darmstadt, Germany

Topical treatment options for muscle and joint complaints include phytotherapeutic preparations. In particular comfrey root extract cream has proven efficacy in several randomised clinical trials (RCT). In blunt injuries, a double-blind, placebo-controlled, multicentre RCT involved 142 patients with unilateral ankle sprains. During treatment, pressure pain, ankle oedema, and ankle mobility regressed significantly more in the verum group [1]. The same cream was compared with a prominent diclofenac gel in a single-blind multicentre RCT with 164 patients. The results of various variables (pain on pressure, the circumference of the joint, pain at rest and during movement) showed that the Comfrey cream was not inferior to the diclofenac gel; it had equivalent or even better activity [2,3]. A double-blind, placebo-controlled RCT investigated the effect over 3 weeks on 220 patients with painful osteoarthritis of the knee. As a result, the VAS total score decreased by 54.7% for verum and 10.7% for placebo. The WOMAC score showed also a significant reduction ($p<0.001$). In respect of the SF-36, angle measurement and clinical global impression, the superiority of the verum over the placebo was also confirmed [4]. The most recent double-blind, multicentre RCT included 120 patients with acute upper and lower back pain. The results were clear-cut and consistent across all primary and secondary efficacy variables. Comfrey root extract reduced not only acute back pain, for the first time a fast-acting effect within 1 hour was also witnessed [5].The ESCOP and the Hager-ROM monograph acknowledge the recent clinical findings [6,7]. References: 1. Koll R, et al. Phytomedicine 2004; 11: 470-477; 2. Predel H-G, et al. Phytomedicine 2005; 12: 707-714; 3. D'Anchise R, et al. Arzneim Forsch/Drug Research 2007; 57: 712-716; 4. Grube B, et al. Phytomedicine 2007; 14: 2-10; 5. Giannetti BM, et al. Br J Sports Med 2010; 44: 637-641; 6. ESCOP Monographs. 2nd ed., Supplement 2009; 249-254; 7. Staiger C. DrugBase, Hagers Enzyklopädie. HagerROM 2009.

P20

ASYMMETRIC DIMETHYLARGININE (ADMA) LEVELS ARE INCREASED IN PATIENTS WITH FIBROMYALGIA: CORRELATION WITH TUMOR NECROSIS FACTOR-ALPHA (TNF-ALPHA) AND 8-ISO-PROSTAGLANDIN F2ALFA (8-ISO-PGF2ALFA)

G. Topal[1], A. Donmez[2], B.S. Uydes Dogan[1], M. Kucur[3], D. Taspınar Cengiz[5], F. Begum Berkoz[4], N. Erdogan[4]
[1]Department of Pharmacology, Faculty of Pharmacy; [2]Department of Medical Ecology and Hydroclimatology, Istanbul Medical Faculty; [3]Fikret Biyal Central Biochemistry Laboratory, Cerrahpasa Medical Faculty; [4]Department of Medical Ecology and Hydroclimatology, Istanbul Medical Faculty, Istanbul University; [5]Department of Statistics, Istanbul Commerce University, Faculty of Arts and Sciences; Istanbul, Turkey

The aim of the study was to investigate serum levels of asymmetric dimethylarginine (ADMA), tumor necrosis factor-α (TNF-α), interleukin-6 (IL-6) and plasma levels of 8-iso-prostaglandin $F_{2\alpha}$ (8-iso-$PGF_{2\alpha}$) in patients with fibromyalgia. 27 patients with fibromyalgia and 20 healthy controls were enrolled in this study. ADMA, TNF-α, IL-6 and 8-iso-$PGF_{2\alpha}$, levels were measured by enzyme-linked immunosorbent assay (ELISA). Serum levels of ADMA and TNF-α and plasma levels 8-iso-$PGF_{2\alpha}$ were significantly increased in patients with fibromyalgia compared to controls. However, no significant difference was observed in IL-6 levels between the two groups. ADMA concentrations were positively correlated with TNF-α and 8-iso-$PGF_{2\alpha}$ levels in patients with fibromyalgia. This is the first study reporting that ADMA levels are significantly elevated in patients with fibromyalgia in association with increased 8-iso-$PGF_{2\alpha}$ and TNF-α concentrations. Thereby, ADMA could be suggested as a reliable marker of endothelial dysfunction in patients with fibromyalgia.

Osteoarthritis

P21

ASSOCIATION OF SYNOVIAL NERVE REGENERATION AND PAIN IN THE KNEE JOINT OSTEOARTHRITIS

A. Ahmed
Department of Clinical Neuroscience, Karolinska Institute, Stockholm, Sweden

Introduction: Knee osteoarthritis (OA) is most prevalent chronic painful joint disease. The contribution of synovial inflammation to the development of OA joint pain and cartilage degradation has been implicated. However, the role of various pro-inflammatory sensory (substance P (SP), calcitonin gene-related peptide (CGRP)) and autonomic (neuropeptide Y (NPY), vasoactive intestinal polypeptide (VIP), tyrosine hydroxylase (TH)) neuropeptides in OA pain is poorly studied. Objective: Observe correlation between neuropeptidergic nerve density with clinical signs of OA. Material and Methods: Synovial biopsies were harvested from medial, lateral and suprapatellar compartments from 13 patients undergoing knee joint replacement surgery. Clinical outcome of pain and function was evaluated by knee society score and synovial inflammation was evaluated by histology. Single and double immunohistochemistry staining was used for semi-quantitative analysis of synovial nerve fiber density containing sensory and autonomic neuropeptides and growth associated protein 43 (GAP 43), in three compartments of OA knee. Result: Clinical evaluations indicated pain predominantly in the medial compartment of knee in all patients. Histological analysis revealed severe inflammatory changes in the medial and suprapatellar compartments compared to lateral and immunohistochemistry analysis indicated a 70% increase in GAP 43, 80% increase in SP and CGRP and 50% increase in TH-positive nerve fibers in the medial compared to lateral compartment. Double staining analysis showed a co-expression of SP and CGRP with GAP43 in the medial compartment. Conclusion: There is an association of sensory and autonomic nerve fibers with OA pain and inflammation. Pharmacological tools targeting neuropeptides may ameliorate pain in OA.

P22

COMPARISON OF THE USE OF PHYTOTHERAPY ASSOCIATED WITH GEOTHERAPY AND KINESIOTHERAPY VERSUS GEOTHERAPY ASSOCIATED KINESIOTHERAPY IN PATIENTS WITH OSTEOARTHRITIS: A DOUBLE-BLIND CLINICAL TRIAL

F. Alfieri[1], K. Arthur[1], L. Nascimento[1], D. Figueiredo[1], L. Souza[1]
[1]Faculdade de Fisioterapia UNASP, São Paulo, Brazil

Osteoarthritis of the knee is a high prevalence of rheumatic disease needing rehabilitation. Objective: To compare the efficacy of phytotherapy associated with geotherapy and kinesiotherapy versus geotherapy associated kinesiotherapy in patients with osteoarthritis of the knee. The study was approved by the ethics committee of the institution. The assessment of pain intensity was made with the Visual Analogue Scale (VAS). To evaluate the weight-bearing foot was used the Nintendo Wii Fit R. The 25 volunteers were randomized by lot to the intervention groups: TNP-therapy with a poultice of argil (25 m) followed by kinesiotherapy and proprioceptive training. TWP performed the same treatment, except for phytotherapy (Uncaria guianensis) in a poultice of clay. Both groups performed 10 sessions. Results: TWP was 63.92 ± 6.7 years and 28.8 ± 7.9 kg and the TNP, 58.58 ± 95 years and 24.7 ± 5.7 kg, is similar. The intensity of pain increased from TWP 7.6 ± 1.6 cm before to 3.4 ± 2.6 cm after the intervention ($p = 0.0001$) and TTNP, 7.7 ± 1.9 cm before to 4.3 ± 2.2 cm after the intervention ($p = 0.003$), but no difference between groups. There were no differences within and between groups in

distribution of body mass. Individuals undergoing therapy geotherapy associated kinesiotherapy can benefit in reducing pain, but not in weight-bearing among members. Also show that the phytotherapy associated with geotherapy produced no additional benefit.

P23

THE INFLUENCE OF SOCIODEMOGRAPHICS, CLINICAL AND FUNCTIONAL VARIABLES IN QUALITY OF LIFE OF ELDERLY WITH KNEE OSTEOARTHRITIS: A SYSTEMATIC REVIEW

R. Alves[1], M. Rampazo[2], M.J. D'Elboux[2]
[1]Gerontology Department, [2]Nursing Department, University of Campinas, Campinas, Brazil

Knee osteoarthritis (OA) is the most common of joint disease, the chronic disease among the elderly, characterized by progressive degenerative changes of cartilage, with pain and functional limitation. Objective: This systematic review aimed to identify the sociodemographics, clinical and functional variables that influences the quality of life of older people with knee osteoarthritis. Methods: Articles were selected following a comprehensive search of Medline, CINAHL, SciELO, and Lilacs of the last five years. Inclusion criteria involved 1) cross-sectional and longitudinal designs, 2) sample of subjects with knee osteoarthritis and when individuals have osteoarthritis knee and hip. we selected studies that reported separate results of each joint, 3) use of questionnaires for assessing health-related quality of life (HRQL) generic or specific, 4) estimates of association clinical or functional variables with quality of life, 5) access of the full published text. Two independent reviewers assessed the methodologic quality of each study and the association between variables and knee OA. Results: 32 abstracts were selected, after the consensus of the reviewers, and six studies were included. The variables evaluated in the studies selected were: age, gender, level of education, wage, pain, comorbidities, gait, radiography, BMI and function. These variables showed association with the HRQL measured by generic and especific instruments. Conclusion: The variables that most influence the compromised quality of life of the elderly with knee OA are the clinical, functional or physical limitation and its associated with worse performance in aspects physical and emotional of the quality of life.

P24

THE INFLUENCE OF SOCIODEMOGRAFIC, CLINICAL AND FUNCTIONAL VARIABLES IN HEALTH-RELATED QUALITY OF LIFE IN THE ELDERLY PEOPLE WITH KNEE OSTEOARTHRITIS

R. Alves[1], M.J. D'Elboux[2]
[1]Reference Center for the Elderly; [2]Gerontology Dept., State University of Campinas, Campinas, Brazil

Objective: To evaluate the health-related quality of life (HRQoL) of elderly patients with knee osteoarthritis (OA) and the influence of the variables: age, gender, BMI, pain, comorbidities, x-ray (Kellgren & Lawrence) and functionality in the knee HRQoL. Methods: The descriptive, correlational and cross study with 133 elderly people with knee OA a rehabilitation center. The HRQoL was assessed using the Brazilian versions of the generic instrument. The Short Form Health Survey (SF-36) and specific Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC). The knee function was assessed by the Index Lequesne. Analysis of variance (ANOVA) and multivariate (MANOVA) to investigate the influence of variables on the dimensions of the SF-36 and WOMAC and the Mann-Whitney and Kruskal-Wallis test for comparisons of scores between the instruments the variables. Results: The mean age at follow up was 69 years. For the WOMAC and SF-36, the dimensions involving the physical aspects were the most affected. The knee function according to the Lequesne was the variable that showed statistically significant influence on the HRQoL of elderly patients with knee OA ($p<0,001$). The number of comorbidities ($p=0,001$), and knee function were the variables that showed significant differences in the dimensions of the SF-36 and WOMAC ($p<0,001$). Conclusion: The physical dimensions had greater impairment on HRQoL. The function of the knee was the variable that significantly influenced the HRQoL.

P25

HYALURONIC ACID FOR THE TREATMENT OF OSTEOARTHRITIS IN ALL JOINTS EXCEPT THE KNEE: WHAT IS THE CURRENT EVIDENCE?

S. Colen[1], D. Haverkamp[2], M. Mulier[1], M. Van den Bekerom[3]
[1]Orthopaedic Surgery, University Hospital Leuven, Leuven, Belgium; [2]Orthopedic Surgery, Slotervaart Hospital, [3]Orthopaedic Surgery, Spaarne Hospital, Hoofddorp, Netherlands

The use of intra-articular hyaluronic acid (HA) is a well-known treatment in patients with knee osteoarthritis (OA). In other joints less evidence is available about the efficacy of the treatment with intra-articular HA. HA is also used intra-articularly in the metatarsophalangeal-1 joint, the ankle, the hip, the sacroiliac joint, the facet joints, the carpometacarpal-1 joint, the shoulder and the mandibular joint. In this systematic review we include all prospective studies about the effects of intra-articular HA in the above mentioned joints. Its use in the knee joint however will be discussed in a separate article in this same journal. When performing a solid systematic review using a rigid methodology and trying to pool the outcomes of different studies we came to the conclusion that, compared to baseline, there is statistical evidence for a positive effect of intra-articular HA. On the other hand, however, there is limited evidence that HA is superior to placebo and no evidence that intra-articular HA is better than CS or other conservative therapies. Our recommendation for future research is that one should focus on adequately powered randomized trials comparing HA treatment with other types of intra-articulator conservative treatment. We think it is useless to further perform and publish (large) non-comparative prospective studies about the use of HA in the treatment of problems caused by OA. It is well perceived that HA exerts positive effects in the treatment of OA, but up to now there is no (strong) evidence available that HA is superior other treatments of OA like corticosteroids, physiotherapy or other conservative measures.

P26

ELASTIC LIPOSOMES MEDIATED TRANSDERMAL DELIVERY OF ACECLOFENAC

K.R. Gajbhiye
Pharmacy Dept., Dr. H. S. Gour University, Sagar, India

In the present study, transdermal delivery of novel anti-inflammatory drug aceclofenac has been probed by means of elastic liposomes, which are adequately flexible to cross the intact skin barrier. These ultradeformable vesicles were formed using Soya phosphatidylcholine (SPC) with sodium cholate used as surfactant. The lipid/surfactant ratio (*w/w*) was 84:16. The size and shape of elastic liposomes were evaluated by transmission electron microscopy. The amount of aceclofenac permeated through rat skin was found to be about 3 and 10 times higher in case of elastic liposomes as compared to conventional liposomes and free drug, respectively. These ultradeformable vesicles revealed a transdermal flux of 44.1±1.6 $\mu g/h/cm^2$ which was significantly higher than conventional liposomal formulation (14.81±1.21) and free drug solution (4.0±1.3). The results suggested that elastic liposomes can be used for sustained transdermal administration of aceclofenac.

P27

IDENTIFICATION OF WORKERS VULNERABLE TO KNEE OSTEOARTHRITIS THROUGH PROBABILISTIC ANALYSIS OF KNEE KINEMATIC DATA

N. Gaudreault[1], N. Mezghani[2], L. Ayoubian[2]
[1]Rehabilitation Science, University of Sherbrooke, Sherbrooke; [2]Centre de Recherche du Centre Hospitalier Universitaire de Montréal Laboratoire de Recherche en Imagerie et Orthopédie, Canada

Background: The knee osteoarthritis (OA) management paradigm needs to shift towards prevention by identifying persons at risk for knee OA and those with early asymptomatic knee OA. Scientific evidence demonstrates that gait analysis provides measurements of biomechanical factors that may help identify an individual's knee as being vulnerable to OA. Moreover, studies have shown that some of these factors can be modified with physiotherapy. This study explores a probabilistic approach for analyzing gait kinematic data to investigate the vulnerability of persons exposed to mechanical knee overloading to develop knee OA. Methods: A kinematic database of three groups of participants (knee-overloaded (KO) workers, knee OA patients and asymptomatic (AS) persons) was used. Based on subject kinematic features, we used the Bayesian decision theory to assess the probability of each worker having kinematic features that belong to either the OA or AS group. Results: The Bayesian classifier could split the kinematic feature space into two groups (i.e., OA or AS). In the sagittal plane, 9 out of 24 workers had their kinematic features classified in the OA group; whereas in the frontal plane, 20 of them had their curve profiles classified in the OA group. The transverse plane data was the least discriminant. Conclusion: The findings show that workers' knee gait kinematics in the frontal plane correlate well with knee OA group. This analysis can potentially be used as a preventive means of identifying persons vulnerable to knee OA. Preventive actions can be suggested to these persons to prevent development or progression of the disease.

P28

BARRIERS AND FACILITATORS TO USING GAIT ANALYSIS FINDINGS IN THE MANAGEMENT OF PATIENTS WITH KNEE OSTEOARTHRITIS

N. Gaudreault[1,2], M. Bernier[2], M-J. Durand[1,2], A-M. Côté[1], N. Roy[1]
[1]Rehabilitation Science, University of Sherbrooke, Sherbrooke; [2]Centre d'Action en Prévention et Réadaptation de L'incapacité au Travail, Centre de Recherche de l'Hôpital Charles-Lemoyne, Canada

Background: Gait analysis can be used by physiotherapists to better understand the causes and consequences of knee disorders such as knee osteoarthritis (OA). However, its use is not widespread among clinicians working with this clientele. Objective: To identify the barriers and facilitators to using gait analysis in the management of patients with knee OA. Methods: A qualitative descriptive study design was used. Eleven physiotherapists received training on the principles of knee gait analysis assessment and data interpretation. Each physiotherapist was instructed to send two knee patients for a gait analysis assessment and then incorporate these new data into their practice with these patients. A semi-structured interview was conducted to ascertain the physiotherapist's perception of the barriers and facilitators to using gait analysis. The verbatim transcripts were analyzed using content analysis software (NVivo 9). Results: The main barriers were as follows: 1) difficulty reading and interpreting the gait analysis data report; 2) gait analysis testing procedures appear lengthy and complex; and 3) cost involved. The facilitators were: 1) data report should offer some strategies for guiding therapeutic action; 2) favorable perception of kinematic analysis by work colleagues; and 3) assessment of costs partly reimbursed by the client's insurers and lower cost for repeated measurements. Conclusion: We were able to pinpoint the barriers and facilitators likely to promote the use of gait analysis in physiotherapy practice among knee OA patients. Gait analysis can help identify biomechanical factors associated to knee OA that can be modifiable with physiotherapy.

P29

TREATING TIBIAL STEM TIP PAIN IN REVISION KNEE REPLACEMENT WITH THE USE OF LOCKED BRIDGING PLATE

A. Ghatahora[1], A. Sanjeev[1]
[1]Orthopaedic Surgery Dept., NHS - Cardiff and Vale Health Board, Cardiff, UK

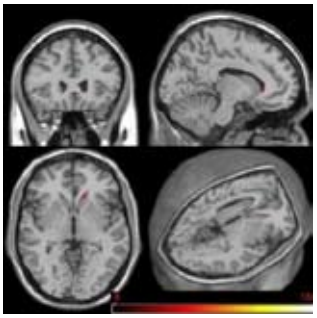
Purpose of the study: Pain at the tip of the stem can be present in 10 to 20% patients following revision knee arthroplasty using stemmed tibial components, especially where the stem is well fitting in the canal. This is believed to be due to the narrow transition zone between the rigid stem and relatively elastic cortical bone. We propose a novel method to deal with this using a bridging plate and without revision of the tibial component. Methods: A 56 year old woman presented two years following a right total knee revision with stem tip pain on the tibial side. The knee joint itself was asymptomatic with 0 to 100 degrees of movement and no instability. Tenderness was specifically localized to the tibial shaft in the region of the stem tip. Radiographs showed no evidence of loosening of the implant, but the stem tip was tightly fixed in the canal. Tc-99 bone scan showed increased activity at the tip of the tibial stem. The patient was managed with a six hole locking plate to bridge the stress at the tip of the stem, and the knee prosthesis was not revised. Results: Following the procedure the patient reported complete resolution of pain at the tip of the stem. A postoperative bone scan showed resolution of the increased uptake at the stem tip. Conclusions: Pain at the tip of well fixed stems can be a problem in many patients. Usual management strategy involves revision to a narrower stem with or without cementing. Our method to bypass the stress riser with a locking plate appears to be a simple intervention to deal with the problem.

P30

A PRELIMINARY DTI STUDY PAIN OF KNEE OSTEOARTHRITIS

H. Guo[1], C. He[1]
[1]Rehabilitation Key Laboratory of Sichuan Province, Department of Rehabilitation Medicine, West China Hospital, Sichuan University, Chengdu, China

Background: Osteoarthritis (OA) is the most common degenerative disease in elder humans, which is dominated by pain during joint use [1]. Neuropathic pain syndromes are clinically characterized by spontaneous and evoked types of pain, which are based on various distinct pathophysiological mechanisms in the peripheral and central nervous systems [2]. Many methods to relieve pain are not effective, and can not to improve the existing pathology. Method: In this study, we used Diffusion tensor imaging (DTI) to study the process of OA pain, the brain mechanisms of pain. Result: We find significantly increased values of factional anisotropy (FA) in genu of corpus callosum close to anterior cingulate cortex (ACC) in OA, comparing with that in normal. Conclusion: The genu of corpus callosum play a role in anatomical connection and information transmission of ACC between two hemispheres. Some previous researches confirm that ACC involves in both sustained attention and pain perception [2, 3]. Our results reveal that the pain of knee OA is associated mainly with the abnormal anatomical connection of ACC between two hemispheres. This result suggests that there may be some functional interactions of ACC between two hemispheres, implying some mechanisms of OA pain.



P31

THE LOWER EXTREMITY FUNCTIONAL SCALE SHOULD BE THE SELF-REPORT MEASURE FOR THE ASSESSMENT OF PHYSICAL FUNCTIONING IN HIP OR KNEE OSTEOARTHRITIS

T. Hoogeboom[1,2], R. de Bie[2], A. den Broeder[1], C. van den Ende[1]
[1]Department of Rheumatology, Sint Maartenskliniek, Nijmegen; [2]Department of Epidemiology, Maastricht UMC, Maastricht, Netherlands

Background: Although the WOMAC is the most widely used self-report measure to evaluate physical functioning in hip or knee osteoarthritis (OA), its ability to discriminate pain and physical functioning (i.e. discriminate validity) has repeatedly been questioned. Little to no data is available on the discriminant validity of alternative questionnaires that measure the same construct, for instance the Hip and Knee Osteoarthritis Outcome Score (HOOS and KOOS, respectively) and the Lower Extremity Function Scale (LEFS). Objective: We first translated the LEFS to Dutch and studied its psychometric properties. Consequently, we assessed the discriminate validity of the LEFS, HOOS and KOOS. Study design and setting. Internal consistency and construct validity were evaluated in 401 individuals with hip or knee OA. Reliability and responsiveness were assessed in a sample of 106 and 108 individuals, respectively. Discriminant validity was examined by contrasting the scales' correlations with the physical functioning subscale of the SF-36 with the scales' correlations with the bodily pain subscale of the SF-36. Results: The LEFS had good internal consistency (0.96), good reliability (ICC=0.86) and good construct validity. The minimal detectable change was 10 points and its responsiveness was good. Discriminant validity for pain was apparent for the LEFS (p<0.01), but not for the HOOS and KOOS (p=0.21 and p=0.20, respectively). Conclusion: Considering the LEFS' good psychometric qualities and ability to discriminate between pain and functioning, we recommend the LEFS as the outcome measure of first choice to assess physical functioning in individuals with hip or knee OA.

P32

AUTOLOGOUS BONE MARROW MONONUCLEATED CELL IMPLANTATION FOR OSTEONECROSIS OF THE FEMORAL HEAD

J.S. Kang
Department of Orthopaedics, Inha University Hospital, Incheon, Republic of Korea

Purpose: We prospectively analyzed the clinical results of autologous bone marrow mononucleated cell implantation for osteonecrosis of the femoral head. Materials and Methods: In a prospective evaluation, 61hips in 52patients with osteonecrosis of the hip were treated with core decompression combined with implantation of autologous bone marrow cells. The average density of the autologous marrow monocytes was ranged from 16 to 52 million/mL, with a mean of 38±6 million/mL. After concentration, an average of 2.7 x10^7 progenitor cells was obtained. The average duration of clinical follow-up of the patients was 5 years. (ranging 4 to 7 years). This research was approved by Inha University Hospital institutional review board. Results: In total of 61 hips, 20 hips (33%) were initially present with large necrotic lesion while 26 hips (43%) and 15 hips (24%) showed medium and small sized necrotic lesion respectively, based on Steinberg classification. At the final follow up, 20 cases with severe necrotic lesion included 14 cases (72%) of poor and failed clinical results while 6 cases (28%) claimed excellent and good results. Among 26 cases of medium sized necrotic lesion, 9 cases (35%) were present with poor and failed clinical results and the other 17 cases (65%) showed excellent and good results. Among 15 hips with mild necrotic lesion, 6 cases (40%) showed poor and failed clinical results while 9 cases (60%) claimed excellent and good results. Among 20 cases with severe necrotic lesion, 9 cases (45%) were laterally located and this group showed the worst outcome with 83% of poor and failed clinical result. Conclusion: The surgical results were worse when the lesion was larger and laterally located. Implantation of autologous bone marrow cells after core decompression showed a competent clinical result compared to other head preserving procedure. Significance: With successful implantation of the bone marrow cells, the outcome will be promising by opening up the new treatments to the patients.

P33

OUTCOME OF TOTAL HIP REPLACEMENT FOR SUB CAPITAL NECK OF FEMUR FRACTURE IN YOUNGER ACTIVE PATIENTS – OUR EXPERIENCE IN A NON-SPECIALISED CENTRE

C. Lamb[1], N. Unnikrishnan[2], N. Emms[1]
[1]Orthopaedics Dept., [2]Orthopaedic Surgery Dept., Whiston Hospital, Liverpool, UK

There is an increasing number of Total Hip Replacements (THR) being carried out primarily on patients with a sub capital fracture reflecting the change of opinion nationally towards a more positive view on replacement as the initial choice of treatment for these fractures.[(1)] A number of randomized trials have shown that THR results in better function and improvement in health-related quality of life (HRQoL) and has a lower failure rate than internal fixation.[(2,3)] To compare the early results of THR in our younger, active patients after fracture neck of femur (NOF) with large series from specialized centers. Between June 2008 and June 2011, there were 18 patients who underwent THR for a fracture NOF. All were fit active prior to fracture. There were 11 female and 7 male, average ages 69.5 (46-83). Fourteen were performed via the posterior approach, two via the hardinge approach, two anterior lateral approaches. Surgery was performed by one of five general consultant orthopaedic surgeons. Nine implants were uncemented with 36mm heads; nine were cemented with 28 mm heads. There have been no dislocations, no post-operative complications or revision procedures. The mean follow up is 22 months (6 – 41 months). Average length of hospital stay was 8 days. At the last review, all patients had returned to the same level of mobility as pre operatively including manual work and regular everyday activity. The average Harris Hip Score was 88.84 (51-100). All patients are satisfied with their outcomes. Our results compare favorably with larger published series from specialized centers. We share the positive view on replacement as the initial choice of treatment for these fractures in more active patients. However, we believe that patient selection is an important factor. Longer term follow up is required in our cohort of patients. References: 1. Leonardsson O, Rogmark C, Kärrholm J et al. Outcome after primary and secondary replacement for sub capital fracture of the hip in 10 264 patients; J *Bone Joint Surg (Br*) 2009;91-B:595-600;2. Johansson T, Jacobsson SA, Ivarsson I, Knutsson A, Wahlstrom O. Internal fixation versus total hip arthroplasty in the treatment of displaced femoral neck fractures: a prospective randomized study of 100 hips. *Acta Orthop Scand* 2000;71:597-602;3. Keating JF, Grant A, Masson M, Scott NW, Forbes JF. Randomized comparison of reduction and fixation, bipolar hemiarthroplasty, and total hip arthroplasty: treatment of displaced intracapsular hip fractures in healthy older patients. *J Bone Joint Surg (Am)* 2006;88-A:249-60

P34

LINKING AN ADAMTS5 SPECIFIC MONOCLONAL ANTIBODY THERAPEUTIC TO A SENSITIVE BIOCHEMICAL MARKER OF TARGET ENGAGEMENT AND ACTIVITY WITH POTENTIAL APPLICATION AS A COMPANION DIAGNOSTIC

J. Larkin[1], T. Lohr[1], F. Germaschewski[2], L. Cooper[2], C. Genell[3], R. Polsky[3], L. Abberley[4], F. Liu[5], C. Maier3, C. Matheny[1]

[1]Biopharm R&D, GlaxoSmithKline, King of Prussia, PA, USA; [2]Biopharm R&D, GlaxoSmithKline, Stevenage, UK; [3]Platform Technology & Science - Immunological Toxicology; [4]Platform Technology & Science - Drug Metabolism and Pharmacokinetics; [5]Medicines Discovery and Development - Quantitative Sciences, GlaxoSmithKline, King of Prussia, PA, USA

The goal of co-developing a companion diagnostic alongside a therapeutic has distinct advantages for drug development and has recently been suggested by some regulatory agencies to be the preferred scenario for future approvals. The ability to utilize research tools to identify patient subsets most likely to respond to and benefit from a treatment not only allows for focused stratification and reduced development costs, but also has the potential to reduce healthcare expenditures through defined treat/non-treat guidelines. A critical early developmental objective is to identify meaningful preclinical endpoints and establish their relationship to the specific therapeutic being developed. With this in mind we have characterized an assay that quantifies levels of the aggrecan ARGS neoepitope, an immediate downstream marker of ADAMTS5 activity in cartilage, with the intent of drawing a distinct link to response to treatment with an ADAMTS5 neutralizing monoclonal antibody currently in development. Using the human cartilage explant system (knee cartilage donated from osteoarthritis patients undergoing joint replacement), varying levels of ARGS neoepitope were observed, allowing categorization of patients with 'low' and 'high' aggrecanase activity. Importantly, 'high' activity was associated with response to ADAMTS5 antibody treatment in this model, whereas 'low' activity was associated with a reduced response. The duration of treatment response following a single pulse chase administration was greater following treatment with ADAMTS5 antibody compared to a small molecule inhibitor, potentially suggesting that increased binding affinity and/or slower off rate of the therapeutic to the target is advantageous. The ARGS neoepitope assay was also used to demonstrate dose responsive changes in circulating levels of the marker and duration of effect following ADAMTS5 monoclonal antibody treatment of cynomolgus monkeys, which may translate into better clinical dose prediction.

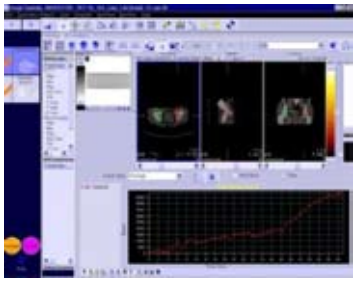
P35

BLOOD PERFUSION AND BONE FORMATION BEFORE AND AFTER MINIMALLY INVASIVE PERIACETABULAR OSTEOTOMY ANALYSED PET COMBINED WITH CT

I. Mechlenburg[1], T. Thillemann[3], F. Hermansen[2], K. Soballe[1]

[1]Orthopaedic Research Unit; [2]PET Center; [3]Aarhus University Hospital, Aarhus, Denmark

Purpose: A new minimally invasive technique for periacetabular osteotomy (PAO) has been developed in our institution. The osteotomized acetabular fragment is reoriented three dimensionally in order to achieve a better acetabular coverage. Bone healing is believed to be completed eight weeks after surgery and from that time, the patients are allowed to fully weight-bear on the operated leg. Sufficient blood perfusion is held to be essential to successful bone healing after PAO. It is never examined in vivo how blood perfusion to the acetabular fragment is affected by PAO and whether perfusion contributes to new bone formation in the acetabular fragment. The purpose of this study was to quantify blood perfusion and bone formation before and after PAO analyzed by Positron Emission Tomography (PET) combined with Computed Tomography (CT). Methods: Twelve dysplastic patients (nine women) were included consecutively in the study all operated by the senior author (KS). Median age was 33 (23-55) years. Initially, two patients were PET scanned in a pilot study to test our models for calculation of the physiological parameters. The following ten patients had their hip joints PET/CT scanned immediately before PAO and 3-4 weeks after. Due to patients moving on the scanner bed while scanning, data of sufficiently high quality was only available for six out of ten. [O-15]-water was used to quantify blood perfusion and [F-18]-fluoride was used to produce quantitative images interpreted as new bone formation in/around the acetabular fragment. The perfusion [ml blood/min/ml bone] was determined from a one-compartment model, with the parameters: K1, k2 and the delay. The fluoride-clearance per volume bone (Ki) [ml blood/min/ml bone] was determined by applying Patlak graphical analysis to the fluoride scan, fitting the data from 45 to 90 min. Results: The blood perfusion on the operated acetabulum before surgery was 0.07+0.02 ml/min/ml, and after surgery 0.19+0.03 ml/min/ml ($p<0.00$). Blood perfusion on the non-operated acetabulum was 0.07+0.02 ml/min/ml before PAO and 0.07+0.02 ml/min/ml after surgery ($p=0.47$). The fluoride-clearance per volume bone on the operated acetabulum was 0.02+0.01 ml/min/ml preoperatively, and 0.06+0.01 ml/min/ml postoperatively ($p<0.00$). Fluoride-clearance on the non-operated acetabulum was 0.01+0.01 ml/min/ml before PAO and 0.02+0.01 ml/min/ml after PAO ($p=0.49$). Conclusion: Blood perfusion and new bone formation increased significantly in the acetabular fragment demonstrating that blood perfusion to the acetabular fragment is not critically compromised after minimally invasive PAO a.m. Soballe. Three to four weeks after PAO, bone formation in the acetabular fragment on the operated side had increased significantly. This is the first paper applying PET/CT to quantify blood perfusion and bone formation before and after PAO. (Patlak et al., 1983). Reference List: 1. Patlak CS, Blasberg RG, Fenstermacher JD. Graphical evaluation of blood-to-brain transfer constants from multiple-time uptake data. J Cereb Blood Flow Metab. 1983;3:1-7.



P36

WHAT ARE YOUNG PATIENTS DOING AFTER HIP RECONSTRUCTION?

L. Delasotta[1,2], A. Rangavajjula[3], F. Orozco[2], **A. Ong**[2]

[1]Surgery, Temple University; [2]Orthopaedic Surgery, Rothman Institute; [3]School of Medicine, Thomas Jefferson University, Philadelphia, PA, USA

Purpose: To assess patient activity levels by patient-reported function and activity participation in young primary THA patients. Our hypothesis is that young THA patients are more active postoperatively than previously reported. Methods: Sixty-one patients were contacted for the survey (~65%); they were 43.18yoa (±5.54). Patient inclusion criteria: DJD of hip, elective primary THA, and age range of 18 to 50 years. Patient exclusion criteria: trauma, past surgical history relating to hip; medical conditions affecting function (i.e. cancer, musculoskeletal disability, congenital disease). Hip society postoperative activities were utilized to create our survey. Physician activity recommendations (unlimited, occasional, and discouraged) were compared to patient-reported participation in activities (regularly, occasionally, and rarely). Patients were asked why activities were stopped. Patient-reported HAAS and UCLA scores were collected. Results: A 33% increase in recommended activities occurred. Occasional/Discouraged activities decreased. Obese individuals (BMI>30) had decreased HAAS compared to overweight

(25<BMI<29.9) individuals; Obese individuals trended towards significance relative to overweight and normal (18.5<BMI<25) individuals (UCLA). A higher BMI was associated with joint pain (trend). UCLA and HAAS patient-reported scores were 6.87 and 11.69, respectively. As BMI increased, the HAAS and UCLA scores decreased (positive correlation). Activities were stopped postoperatively due to fear of injury (29%), physician recommendation (26%), hip pain (14%), early fatigue (17%), and decreased interest (14%). Conclusions: Young patients reported great function and activity participation. BMI, non-THA joint pain, and job mobility may also be associated with postoperative function. Physician-induced patient postoperative activity may occur. Recommendations/guidelines should be a balance between joint prosthesis preservation and regular activity participation.

P37

SHOULD WE GIVE EPOETIN-α TO THE REVISION TOTAL KNEE ARTHROPLASTY PATIENT?

L. Delasotta[1,2], A. Rangavajjula[3], **F. Orozco**[2], A. Ong[2]
[1]Surgery, Temple University; [2]Orthopaedic Surgery, Rothman Institute; [3]School of Medicine, Thomas Jefferson University, Philadelphia, PA, USA

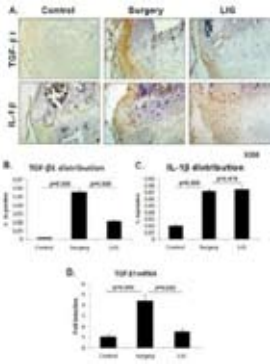
Introduction: To evaluate the efficacy of 2-3 epoetin-α injections prior to revision TKA. Our hypothesis is that epoetin-α injections will reduce peri- and postoperative transfusions. Methods: Fifty-six patients were compared in this retrospective review; twenty-eight patients received our dosing regimen. Patient matching occurred by attending physician, gender, bmi, complexity of surgery, and age. The need for transfusion was determined based on Hb level (<8 gr/dL) and/or presence of clinical symptoms. Blood salvage was not used. Results: Allogeneic transfusion, length of stay, and blood loss decreased significantly. None of the patients who received epoetin-α underwent a peri or postoperative transfusion. Hgb increased from 11.97 to 13.8, preoperatively. Hgb at day of surgery and discharge were significantly increased relative to controls despite control group transfusions. Length of stay and surgical duration were significantly decreased in the epoetin group. Gender, BMI, total blood loss, hidden blood loss, calculated blood loss, preop PLT, PT, PTT, and INR were similar between groups. One Epogen patient had an uncomplicated DVT (3.6%). Conclusions: Epoetin-α increased preoperative Hgb counts, reduced transfusions, and reduced hospital length of stay. The success of our institution's blood program may suggest its future standardization in the revision knee patient.

P38

LIGUSTRAZINE INHIBITS OSTEOPHYTE-LIKE FORMATION VIA SUPPRESSION OF TGF-β1 NOT IL-1β EXPRESSIONS IN OSTEOPHYTIC CELLS

Q. Bian[1], **L. Qian Qian**[1], W. Yong Jun[1]
[1]Department of Orthopaedics & Traumatology, Institute of Spine

Osteophyte is one of the characteristics of osteoarthritis (OA). Nowadays, few drugs have been reported to have direct effect on osteophyte formation. Ligustrazine (LIG), extracted from ligusticum chuanxiong hort, has a therapeutic effect on OA. In the study, it is supposed to have inhibitory effect of osteophyte development. We investigated whether LIG could attenuate osteophyte-like formation in lumbar spine of bipedal rats. Safranin O and Fast green staining as well as morphometry were performed to observe the edge of end-plate and the sizes of non-cartilaginous outgrowth. The mRNA expressions of three osteogenetic markers: type I collagen (Col1a), ALP, runt-related transcription factor 2 (Runx2) as well as TGF-β1 were detected by real time reverse transcription PCR (RT-PCR). TGF-β1 and interleukin-1 beta (IL-1β) protein distributions were observed using immunohistochemical method. Moreover, the osteophytic samples were obtained from ten patients during the surgery of vertebral fusion, and the cells were isolated and identified. To further determine the inhibitory effect of LIG *in vitro*, cellular proliferation, the mRNA and protein levels of Col1a, Runx2, TGF-β1 and IL-1β were assayed by MTT, real time RT-PCR, immunofluorescence and western blot. In results, LIG attenuated osteophyte-like formation on lumbar vertebrae of bipedal rats by reducing TGF-β1 distribution as well as ALP, Col1a, Runx2 and TGF-β1 mRNA expressions. Cells from the osteophytic samples showed osteogenetic and adipogenic capacities in enriched conditions with CD73 and CD90 positive expression. LIG down regulated Col1a and TGF-β1 gene expressions as well as TGF-β1 protein levels, but not IL-1β expression in osteophytic cells of patients *in vitro.* In conclusions, LIG exerted a preventive effect of osteophyte development via suppression of TGF-β1 levels, which could be used as an alternative therapeutic method for OA or spinal degeneration disease accompanied with osteophyte formation.



P39

QUALITY OF LIFE IN THE ELDERLY WITH TOTAL HIP ARTHROPLASTY: RELIABILITY OF TWO TOOLS

M. Rampazo[1], M.J. D'Elboux[1], A. Coimbra[2]
[1]Nursing Department; [2]University of Campinas, Campinas, Brazil

In assessing the health-related quality of life (HRQL) in patients with total hip arthroplasty (THA), several instruments have been used, although few are specific to the elderly population. Objective: The objective of this study was to compare the reliability of two assessment tools of HRQOL in elderly patients suffering from THA. Methods: The generic tool *The Medical Study 36-item Short-Form Health Survey (SF-36)* and the specific tool *Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC)* were applied to 88 elderly patients undergoing primary THA for hip osteoarthritis and hip fracture. Results: Scores on both assessment tools of HRQOL showed that the issues of physical nature affect the quality of life of these seniors more. The ceiling effect was shown in some areas of both the SF-36 and WOMAC revealed that these tools have some limitations in this evaluated group. The reliability of the tools was considered satisfactory, with Cronbach's alpha <0.70, only in the WOMAC stiffness scores. Conclusion: We conclude that the WOMAC and SF-36 tools are adequate to evaluate the HRQOL of this population, but some regards must be considered when used in elderly patients with THA.

P40

FASTING IN OSTEOARTHRITIS

S. Schmidt[1], K. Stoy[1], D. Loth[2], R. Stange[3], E. Lischka[4], O. Peter[5], A. Hochhaus[6], C. Uhlemann[7]
[1]Internal Medicine Dept.; [2]Epidemiology and Biostatistics Dept., Ambulanz für Naturheilkunde und Integrative Onkologie, Klinik für Innere Medizin II, Universitätsklinikum Jena, Jena; [3]Internal Medicine Dept., Abteilung für Naturheilkunde, Immanuel-Krankenhaus, Charité Campus Benjamin Franklin Berlin Wannsee, Berlin; [4]Internal Medicine Dept., Klinik Buchinger am Bodensee, Fachklinik für Heilfasten, Psychosomatik und Naturheilverfahren, Überlingen; [5]Rheumatology Dept., Abteilung für Rheumatologie, Klinik für Innere Medizin III; [6]Haematology and Oncology Dept., Abteilung Hämatologie und Internistische Onkologie, Klinik für Innere Medizin II; [7]Clinic of first Physical Medicine and Rehabilitation Ambulanz für Naturheilkunde und Integrative

Onkologie, Klinik für Innere Medizin II, Universitätsklinikum Jena, Jena, Germany

Background: The aim of this study was to evaluate the efficacy of fasting therapy according to Buchinger on pain, quality of life, and articular function in patients with osteoarthritis (OA) and to analyse the potential association of the disease duration (≤/> 5 y) with fasting-induced clinical outcome. Design: This was a prospective uncontrolled clinical study. Inclusion and exclusion criteria for fasting therapy were checked thoroughly and specific recommendations given. Outcomes were assessed on baseline (BL), 1st pre-fast day (1), 5th fast day (8), 4th re-feed day (15) and 1 (I) and 3 (III) months after the dietary intervention. Setting: The study took place in an academic outpatient specialized center of natural therapy. Subjects: Sixty patients (50 f, 10 m) with a median age of 60 years (range 37-72 years) with OA (Kellgren stages I-III) of the hand (N=22), hip (N=17) and knee (N=21) were investigated. Interventions: Patients underwent fasting therapy (intake of 300 kcal/day) for 8 days with 3 pre-fast days and 4 re-feed days simultaneously receiving nutritional/lifestyle education. Outcome measures: Global intensity of pain (visual analogue scale, VAS); joint pain with activity, with start of walking, at rest (VAS); pressure pain threshold (PPT); articular function (range of motion); health-related quality of life (SF-36); Western Ontario and McMasters Universities Arthritis Index (WOMAC); painDETECT©-questionnaire (Pfizer); analgesics; weight; body mass index (BMI); waist circumference; dietary history; hemodynamic and a variety of serological parameters. Results: Parameters of pain, quality of life, and articular function improved significantly ($p \leq 0.05$); significant reduction in weight, BMI, and waist circumference during fasting and over the complete course of the study ($p \leq 0.05$). There was a transient reduction in analgesics in fasting. There was evidence of changes in nutritional habits at follow up. Patients at early stages of OA were less affected by OA symptoms and showed larger improvements than those at advanced stage. Fasting was well tolerated and no serious fasting-related adverse effects, e.g. abnormalities in cardiovascular, metabolic, or blood parameters, were reported. Conclusions: Medically supervised fasting therapy according to Buchinger can ameliorate symptoms of patients with moderate OA, especially at early stage. These preliminary data should be consolidated in larger cohorts of patients treated in randomized controlled trials.

P41

THE UTILITY OF BLOOD CULTURES IN ASSESSMENT OF EARLY POSTOPERATIVE FEVER IN NECK OF FEMUR FRACTURE SURGERY

B.S. Sivakumar[1], P. Vijaysegaran[1], M. Ottley[1], C. Coulter[1], C. Crawford[1]
[1]*Queensland Health, Brisbane, Queensland, Australia*

Introduction: Postoperative fever is a common phenomenon in surgical patients of all disciplines, and although thought to be benign and multifactorial, it can pose a diagnostic dilemma for those unfamiliar with the normal thermoregulatory response. A number of studies have assessed the utility of blood cultures in the assessment of postoperative fever in elective orthopaedic patients, as well as patients from other surgical fields. None, however, have been performed looking at neck of femur fracture patients – a diverse group with larger proportions of institutionalized patients with poorly controlled co-morbidities at inherently greater risk of infection. Aims: 1) To assess the utility of blood cultures for assessment of fever alone in the early postoperative setting. 2) To allow comparison between culture-negative and culture-positive groups, and provide recommendations for institution of high-yield blood cultures. Methods: A retrospective cohort study was performed on patients who had blood cultures performed from the NOF unit at this institution. After application of inclusion/exclusion criteria, it was determined that 101 cultures from 61 patients were performed for investigation of postoperative fever alone during a 16 month period. Results: Only 2 sets returned positive results. Both were deemed skin contaminants, and did not requisite a change in patient management. Neither patient developed infectious sequlae. Clinical significance: Blood cultures are of little utility in assessing early postoperative fever post NOF surgery. Although statistically significant comparison was not possible due to minute numbers in the culture-positive group, a review of the literature suggests that culture in the setting of fever after postoperative day 4, recurrent febrile episodes, spikes of temperature greater than 39°C or in patients with more than 2 indwelling catheters is of higher yield.

P42

EVALUATION OF EFFICACY OF HYALORONIC ACID AND GLUCOSAMINE ON WOMAC INDEX IN OSTEOARTHRITIS PATIENTS

K. Esalatmanesh[1], **Z. Soleimani**[1], M. Sayayh[1]
[1]*Internal Medicine Dept., Kashan University of Medical Sciences, Kashan, Islamic Republic of Iran*

Introduction: Osteoarthritis is a common disease that has been seen in all geographic areas. Various treatments were suggested for it, all of them had their benefits and harms. One of the main indexes for evaluating the severity is WOMAC score was used through the current study to assess the effect of Hyaluronic acid and Glucosamine on the index in patients with osteoarthritis, in order to choose the best treatment. Methods & Materials: The current study was an experimental study in patients with osteoarthritis referred to rheumatology clinic in Kashan, 2011. At first WOMAC questionnaire was filled for all patients. Then in a group 2 CC intra articular injection of Hyaluronic acid (20 mg per ml) weekly for three weeks and another group 500mg Glucosamine tablet three times a day were administered. After 6 weeks treatment, WOMAC index was assessed again. In the questionnaire pain, symptoms, joint stiffness and activities in two joints of hip and knee were evaluated each of them with 32 questions. Finally gathered data entered SPSS#12 and been analyzed through paired T-test. Findings: Finally 80 patients with osteoarthritis in two Hyaluronic acid and Glucosamine groups had been assessed before and after treatment. Among patients mean age was 59.76±7.04 years old (min. 48 and max. 79 years). In the current study both groups had significant effect on all factors of symptoms, pain, activity and WOMAC after treatment compare with before that ($P<0.001$). But joint stiffness only were affected by Glucosamine significantly ($P<0.001$). Conclusion: In the current study effect of Hyaluronic acid and Glucosamine were assessed in patients with osteoarthritis and it seems that they can effectively decrease the disease severity. Therefore it can be suggested to use them for alleviating pain, joint stiffness, and activity limitations.

P43

EVALUATION OF FREQUENCY OF OSTEOARTICULAR COMPLICATIONS OF BRUCELLOSIS IN PATIENT ADMITTED TO BEHESHTI HOSPITAL, KASHAN

Z. Soleimani
Department of Adolescent Medicine, Kashan University of Medical Sciences, Kashan, Islamic Republic of Iran

Background and Aim: Regarding the high prevalence of brucellosis and frequency of osteoarticular complications of brucellosis and abnormal physical examination due to it, this study was conducted on hospitalized brucellosis patients in Kashan Beheshti Hospital. We conducted this study due to updating our formation and determination of frequency of osteoarticular complications in admitted brucellosis patients. Materials and Methods: This study was performed through existing data in 248 admitted brucellosis patients demographic, osteoarticular complications were extracted and collected data were analyzed. Results: The most common osteoarticular symptom was low back pain (38.3%), and after that respectively knee pain (14.1%), hip pain (9.3%), ankle pain (9.3%) and elbow pain (1.2%), were osteoarticular symptoms of patients. Low back pain got a growing path with increasing age and ankle pain had a decreasing process. Hip pain was more common in the less than 20 years old group.

Abnormal physical examination had been detected in sacroiliac (32.2% of patients), knee (14.1%), hip (9.3%), vertebra (6.0%), ankle (3.6%) and elbows (1.2%) and in sacroiliac and vertebra got a growing path with increasing age. Abnormal physical examination in hip and ankle, were more common in the less than 20 years old group. Abnormality of physical examination of knee was the only complication that had a noticeable difference in different sexes (28.1% in males in compare of 11.2% in females). The most common arthritis was in knee (7.7%), and then hip arthritis (3.6%) and ankle arthritis (1.2%). elbow arthritis had seen in only 1 patient (0.4%). Conclusion: Our research reviled that the most common osteoarticular symptom was low back pain, abnormal physical examination was regnant in sacroiliac and knee arthritis was the most common arthritis in brucellosis patients. Because of high frequency of low back pain and other joints pain, brucellosis must be considering in deferential diagnosis in any patients with back pain and arthralgia (especially with prolonged fever). Further because of the high frequency of abnormal physical examination especially in sacroiliac and knee, careful osteoarticular exam in all of the patients with general complaints and osteoarticular symptoms was suggested. Vice versa if abnormal physical examination in joints or arthritis was detected, brucellosis must be considering the head of deferential diagnosis.

P44

DEVELOPMENT OF A STEPPED DECISION AID FOR PATIENTS CONSIDERING OSTEOARTHRITIS MANAGEMENT OPTIONS

J. McGowan[1], G. Hawker[2], **K. Toupin April[1]**, V. Welch[1], T. Rader[1], C. Bennett[3], A. Saarimaki[3], G. Wells[5], A. O'Connor[4], D. Stacey[4], P. Tugwell[1]

[1]Institute of population health, University of Ottawa, Ottawa; [2]Women's College Research Institute and University of Toronto; [3]Ottawa Hospital Research Institute and University of Ottawa; [4]School of Nursing; [5]University of Ottawa, Canada

Our team wished to develop an osteoarthritis (OA) decision aid, using a stepped approach to incorporate a wide spectrum of evidence-based interventions, to help patients and health providers select the best treatment option. A systematic development process was used to create a tool to assist patients in discussing treatment options with their health provider. The research team included experts in rheumatology, clinical epidemiology, decision aid development, knowledge translation and graphic design. The development process, guided by the Ottawa patient decision aid development methods and the International Patient Decision Aid Standards, involved: a) conducting a needs assessment of OA patients and their practitioners; b) synthesizing the spectrum of evidence-based OA interventions (n=14) and the evidence supporting the use of each modality using the GRADE (Grading of Recommendations Assessment, Development and Evaluation); c) assessing and reporting on methodological quality of the data using the GRADE; and d) incorporating the assessment of patients' pain level. A decision aid was created to incorporate the following components: 1) assessment of OA pain and disability; 2) information on benefit and side effects of interventions, with interventions listed under one of five steps that increase according to their efficacy; 3) assessment of patients' values; 4) consideration of other information patients need for decision making; and 5) review of the steps patients wish to undertake. This stepped decision aid encompassing multiple interventions is a unique adaptation of conventional decision aids. Once validated, it will assist OA patients and their providers to make informed treatment decisions.

Osteoporosis

P45

EVALUATION OF RISK FACTORS FOR OSTEOPOROSIS

R. Alimanovic-Alagic

Clinic of Nuclear Medicine, Clinical Center University of Sarajevo, Sarajevo, Bosnia and Herzegovina

Introduction: Osteoporosis is a disorder characterized with decreased bone mineral density. After thirties year of life reduction of bone tissue is inevitable process, there is a change in bone remodeling cycle what can lead to fragility of bones and increase risk of fractures. Genetic and risk factors are numerous and there is no single cause of the disorder. Patients and methods: As a part of the investigational project 500 female patients were examined at the Clinic for Nuclear medicine of the University Clinical Center of Sarajevo, age 35 to 75 during 18 months. The study was designed as prospective. For each patient we did personal history, BMI, menarche, menopausal period and diagnostic procedure, ultrasound of calcaneus and DXA of femur and lumbar spine. We established presence of risk factors (smoking, alcohol, coffee), menstrual cycle, poor nutrition, chronic diseases, immobility, vitamin D deficiency, low estrogen levels and physical activity. Results: of investigation: In investigated group of 500 patients three factors leading for osteoporosis development are: smoking (43%), genetic factors (22%) and endocrine conditions (44,1%). Malignancies (35,5%), immobility (20,6%) and no physical activity (44%) are presence of osteoporosis very often. Menarche and menopausal period at early age (49%) are presence frequently. Conclusion: Genetic factors, smoking, endocrine conditions and no physical activity are demonstrated highest efficiency in osteoporosis. Menstrual cycle, poor nutrition, BMI, immobility, vitamin D deficiency, low estrogen levels are presence of osteoporosis very often. Early diagnosis osteoporosis is important for proper, adequate and rapid treatment.

P46

SAFETY AND TOLERABILITY OF DENOSUMAB IN HEMODIALYSIS PATIENTS: A CASE SERIES

G. Aperis[1], E. Tsampikaki[1], C. Paliouras[1], A. Kaikis[1], M. Mantzouranidou[1], P. Alivanis[1]

[1]Nephrology Department, General Hospital of Rhodes, Agioi Apostoloi, Rhodes, Greece

Background: Safety and tolerability of denosumab in the treatment of osteoporosis in patients undergoing hemodialysis. Patients and Methods: Four hemodialysis patients with a T-score of less than -2.5 were treated for osteoporosis. All had no previous exposure to bisphosphonates, corticosteroids or selective estrogen receptor modulators. We did not exclude individuals with osteoporosis due to secondary or tertiary hyperparathyroidism, chronic metabolic acidosis, malnutrition, hypogonadism, hyperprolactinemia, and long-term use of heparin. Denosumab was administered at 60 mg subcutaneously at the end of the haemodialysis session. Three out of four individuals were taking paricalcitol for secondary hyperparathyroidism. We measured Ca, P, and PTH pre- and at one, two and three months post-treatment. Results: In the routine biochemical examination a two- to seven-fold rise of PTH in all individuals was observed. Moreover, serum calcium levels were significantly decreased while phosphate levels were decreased in two patients and raised in the others. Although no symptoms of hypocalcemia were reported, oral calcium was prescribed for one month. Calcium levels were normalized at one month and thus, calcium replacement was discontinued. At 2 months, all patients displayed a substantial reduction of PTH levels, and at 3 months PTH returned to baseline. Conclusions: In hemodialysis patients denosumab can lead to remarkable increase in PTH triggered by the low Ca levels. Frequent monitoring of Ca and PTH levels and calcium replacement is recommended when necessary.

However, large studies are needed in order to draw firm conclusions on the role of denosumab in osteoporosis at this patient population.

P47

NADPH OXIDASE INHIBITORS AS DRUG CANDIDATES FOR OSTEOPOROSIS

Y.S. Bae
Department of Life Science, Ewha Womans University, Republic of Korea

Several lines of evidence indicate that activation of NADPH oxidase (Nox) is involved in osteoclast differentiation. Here, we show that Nox inhibitors have been developed and applied to drug candidate for osteoporosis. We screened chemical library (45,000 compounds) based on the inhibition of Nox activity. Prototype chemical compound was subjected into structure-activity-relationship (SAR) and drug candidate (EB18-278) was developed from 300 chemical derivatives of prototype. The drug candidate showed EC_{50} = 0.2μM for inhibition of Nox activity, whereas it did not inhibit xanthin oxidase and glucose oxidase. Pharmacokinetic profile indicated 78% of oral bioavailability for drug candidate (EB18-278) compared to intravenous injection. Toxicological analysis showed that drug candidate (EB18-278) has LD_{50}>2,000 mg/kg (single oral administration in rat), NOAEL>250 mg/kg (repeated oral administration for 7 days in rat), and no hERG inhibition. To evaluate the efficacy of drug candidate (EB18-278), we established ovariectomy (OVX)-induced bone resorption model. After the generation of OVX mice, EB18-278 (20mg/kg) was applied to the mice through oral administration (11 times, one time/2days) and the mice were subjected into microCT analysis. The analysis demonstrated that bone volume, bone mineral density, number and thickness of trabecular from mice administrated by EB18-278 were significantly increased compared to that from control OVX mice. The results indicate that EB18-278 as Nox inhibitor is first-in-class osteoporosis drug.

P48

EXPRESSION OF P16 IN OSTEOSARCOMA AS PREDICTIVE NEO-ADJUVANT THERAPY FACTOR

D. Borys[1], R. Canter[2], R. Tamurian[4], B. Hoch[5], B. Murphy[3], J. Bishop[1], A. Horvai[6]
[1]*Pathology Dept.;* [2]*Oncology Surgery Dept.;* [3]*Veterinary Pathology Dept.;* [4]*Orthopedic Surgery, University of California Davis, Sacramento, CA;* [5]*Pathology Dept., University Of Washington, Seattle, WA;* [6]*Pathology, UCSF, San Francisco, CA, USA*

Background: Osteosarcoma (OS) is a common malignant primary tumor of bone affecting adolescent and young adults. Osteosarcomas are high grade sarcomas with aggressive behavior. There are few if any molecular markers to predict behavior and prognosis of osteosarcoma. The objective of this study is to investigate expression of p16 in correlation with neo-adjuvant chemotherapy response in osteosarcoma. Design: A tissue micro array was created using paraffin embedded samples from 40 pretreatment osteosarcoma cases from two institutions UC Davis and UCSF. Immunohistochemistry was performed with commercially available p16 monoclonal mouse antibody (mtm laboratories AG, Germany). Expression for p16 was defined as nuclear staining in at least 10% of cells. Percent tumor necrosis was measured in post-chemotherapy resection specimens with good" response set at >90% necrosis. Result: Patients age ranged from 9 to 75 years (mean 20). Most common locations were tibia and femur. 21 patients were female and 19 male. The clinical and p16 results are summarized in table 1. P16 expression correlated positively with median percent necrosis and fraction of cases with "good" chemotherapy response (p=0.004 and 0.003, respectively). Conclusion: Immunohistochemical expression of p16 significantly correlates with good chemotherapy response in osteosarcomas. p16 immunohistochemistry may be useful adjunctive marker of prognosis in osteosarcoma.

TABLE 1. Comparison of Clinicopathologic Characteristics among p16 Over- and Under-Expressing Tumors

Characteristic	p16 Positive	p16 Negative	P
	(N=25)	(N=15)	Value
Median Age, IQR	15,12-21	17, 13-26	0.51
Sex: Male/Female	15 (60%)/10 (40%)	4 (27%)/11 (73%)	0.06
Median Percent Necrosis, IQR*	95/ 90-99	40/ 10-90	0.004
Pathologic "good" response (>90%)* : Yes/ No	18 (78%)/ 5 (22%)	4 (27%)/ 11 (73%)	0.003

*Indicates statistically significant difference

P49

EFFECTS OF PHYSICAL THERAPY INTERVENTION ON OSWESTRY SCORES FOLLOWING PERCUTANEOUS VERTEBRAL AUGMENTATION IN OLDER ADULTS WITH VERTEBRAL COMPRESSION FRACTURES

P. Cahoj[1], J. Cook[1], M. Halliday[1], C. Horton[1], C. Sterban[1]
[1]*Physical Therapy Dept., Missouri State University, Springfield, MO, USA*

Purpose: Osteoporosis affects over 200 million individuals and is the leading cause of vertebral compression fractures (VCF). Surgical intervention may be indicated when conservative treatment is not successful in controlling pain and mobility limitations related to VCF. Percutaneous vertebral augmentation (PVA) is a minimally invasive surgery where cement is injected into the vertebral body to stabilize the fracture site and decrease pain. The purpose of this study was to determine if postural education and cervicothoracic extension exercises would further reduce back pain related disability in older adults as measured by the Oswestry Disability Index (ODI) following PVA for VCF. Subjects: Six individuals with a mean age of 75.3 (58-85). Methods: A group pretest-posttest design compared ODI scores for back pain related disability over a six week period. Patients received education and performed cervicothoracic extension exercises weekly during the six weeks between measurements. Results: Although not statistically significant, the large effect size (d=0.976) suggests a trend of improvement in low back disability as indicated by ODI scores (lower scores reflect less disability). Average score reduction for the ODI was 8.73 (± 13.73) out of 45 possible points. Conclusions: Our trend suggests that postural education and cervicothoracic extension exercises may be an effective treatment reducing back pain related disability in older adults following PVA for VCF. In order to control for the confounding variable of the passage of time, a longitudinal study with adequate samples in control and experimental groups should be carried out.

P50

EFFECTS OF LOW-INTENSITY PULSED ULTRASOUND STIMULATION ON BONE HEALING IN A RAT CALVARIAL DEFECT MODEL

K. Chen[1], H. Jia[1], N. Kanako[1], W. Poh[1], Y. Yu[1], K. Shinji[1], K. Shohei[1]
[1]*Oral Implantology and Regenerative Dental Medicine, Tokyo Medical and Dental University, Tokyo, Japan*

Purpose: Biomechanical and biophysical stimuli have been focused as a promising invasive treatment in many clinical fields including bone healing. Low intensity pulsed ultrasound stimulation (LIPUS) has been used as a biomechanical treatment to promote the bone formation, although the mechanism of LIPUS therapy is still lacking conclusive evidence. The aim of this study was to evaluate the effect of low intensity pulsed ultrasound stimulation on bone healing by a rat calvarial defect model with a customized membrane. Materials and methods: In eighteen Wistar/ST rats (14 weeks old), we prepared a 5 mm defect on the each side of parietal bone in the skull, and a customized gelatin membrane containing the α-TCP particle was placed under the periosteum. Five treated groups based on the application period of LIPUS treatment and one untreated group were studied. LIPUS (160 mW/cm^2,15min/day) was applied to the defect area by an active transducer externally in the treated group according to the time table: Group 1 (day 6-12), Group 2 (day 13-19), Group 3(day 20-26), Group 4 (day 6-19) and Group 5 (day 6-26). All the

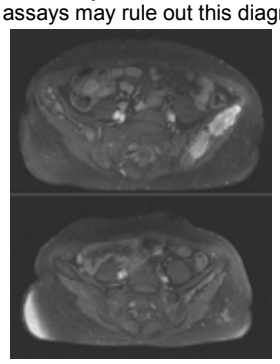
animals were sacrificed at 28 days. Radiological images were taken and histological analysis was done after the sacrifice. Results: Bone volume in the each defect was calculated. The bone healing in all the treated groups showed better results than the untreated group. Comparing to the untreated group, the groups in which LIPUS treatment was applied in the earlier healing period showed significantly more new bone formation almost fulfilling the whole defect area. Conclusion: The present study demonstrated that amount of new bone formation in the bone defect depended on the time and period of LIPUS application.

P51

PRIMARY HYPERPARATHYROIDISM PRESENTING WITH A BROWN TUMOUR AND OSTEOPOROSIS IN A YOUNG WOMAN

D. Cucchiari[1], M. Mirani[1], G. Graziani[1], C. Angelini[1], S. Badalamenti[1]
[1]*Department of Medicine, Istituto Clinico Humanitas IRCCS, Rozzano - Milano, Italy*

INTRODUCTION: Since calcium assays availability in clinical practice from 1970s, the awareness of hyperparathyroidism is grown and usually patients are diagnosed before they can develop late complications, such as overt skeletal disease. CASE REPORT: a 38-year-old woman presented to the ambulatory of rheumatology, complaining of low back pain radiating to the thighs. Clinical examination revealed dolorability of right sacro-iliac joint and limited flexion-extension of the lumbosacral spine. The NMR of the lumbosacral spine revealed the presence of two lesions, respectively on the left ilium and on the right supero-anterior margin of the iliac crest, suspected with malignancy. Laboratory analysis showed hypercalcemia (total calcium 3,79 mmol/L), elevated PTH levels (PTH 1719 ng/L) and renal failure (creatinine 1,72 mg/dL). Bone densitometry performed on the femur neck showed a T-score of -2,8 DS. Echography of the neck demonstrated the presence of an hypoechogenic nodule of 2 cm, posterior to the lower right pole of thyroid, consistent with adenoma, and a Tc-99 sestamibi scintigraphy confirmed this finding. A CT-guided biopsy of the left iliac mass showed a fibrous proliferation with osteoclastic giant cells, a picture compatible with brown tumour. The patient underwent lower right parathyroidectomy with intraoperative PTH assays. One year later she was asymptomatic, the pelvic lesions were decreasing and calcium and PTH values returned into the normal range. CONCLUSIONS: brown tumours, although rare, are disabling conditions which enter into differential diagnosis with other primary or secondary bone lesions. In these cases, a simple calcium and PTH assays may rule out this diagnosis.



P52

FREQUENCY OF SECONDARY HYPERPARATHYROIDISM IN LOW BONE MASS POST-MENOPAUSAL WOMEN

G. Dallanezi[1], **C.F. da Silva Mazeto**[1], E.A.P. Nahas[2], B.F. Freire[1], J. Nahas-Neto[2], C.R. Padovani[3], G.M.F. da Silva Mazeto[1]
[1]*Internal Medicine;* [2]*Department of Gynecology and Obstetrics, Botucatu Medical School;* [3]*Biostatistics, Botucatu Biosciences Institute, Botucatu, Brazil*

Introduction: Aging is associated with a decrease in the vitamin D serum levels, raising the probability of developing secondary hyperparathyroidism (SH), which increases the bone turnover and diminishes the bone mineral density (BMD). Low BMD is the main cause of osteoporosis, a serious problem of public health. Post-menopausal women are one of the main risk groups for osteoporosis. Objectives: To evaluate the frequency of SH in post-menopausal women with low bone mass. Material and Methods: The medical records of 55 post-menopausal female patients were reviewed: 35 with osteoporosis, 13 with osteopenia and seven with normal BMD. The three groups were compared as to the percentage of SH cases, demographic characteristics, femoral-neck (FN), Ward's triangle (WT) and lumbar spine (LS) BMD (g/cm^2), urinary levels of calcium (Ca) and serum levels of PTH, Ca, phosphorus, alkaline phosphatase and albumin. Results: SH occurred in 62.9%, 46.2% and 28.6% in the osteoporosis, osteopenia and normal BMD groups, respectively. The PTH serum levels presented a negative correlation with the FN BMD ($r=-0.434$, $p<0.01$) and with the WT BMD ($r=-0.473$, $p<0.01$). The osteoporosis group presented a greater age and lower weight, body mass index and BMD in all three evaluated sites, than the normal BMD group ($p<0.05$). The groups did not differ statistically as to biochemical and hormone levels. Conclusions: In the group studied, of post-menopausal women, a high frequency of SH was observed, particularly in those with lower bone mass. Moreover, the FN and WT BMD presented a negative correlation with the PTH serum levels.

P53

BONE TURNOVER MARKERS AND PHARMACOKINETICS OF A NEW SUSTAINED-RELEASE FORMULATION OF THE NOVEL CATHEPSIN K INHIBITOR, ONO-5334, IN HEALTHY POST-MENOPAUSAL WOMEN

S. Deacon[1], S. Nagase[1], Y. Hashimoto[2], M. Small[1], M. Ohyama[3], J. Manako[3], T. Kuwayama[1]
[1]*Ono Pharma UK LTD., London, UK;* [2]*Ono Pharmaceutical Co., Ltd., Tsukuba;* [3]*Ono Pharmaceutical Co., Ltd., Osaka, Japan*

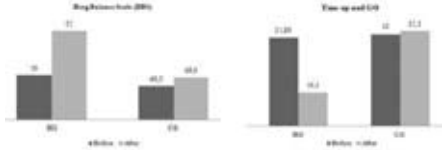
A sustained release tablet (SRT) was developed and compared to the immediate release tablet (IRT) dose that showed comparable effects on BMD to ALN [1]. The single dose phase was a randomized, partial single-blind, crossover study where 50, 100 and 300mg SRT and 300mg IRT was administered to 9 post-menopausal women (PMW). The multiple dose phase was a randomized, double-blind, placebo-controlled, parallel-group study where 100, 300mg SRT or placebo (PBO) was administered in repeated doses to 12 PMW (9 active, 3 PBO). After a single administration of 300mg SRT, mean Cmax was 3.3-fold lower, mean AUCinf 0.83 fold lower and mean C24h was 5.4 times higher vs. 300mg IRT. Repeated dosing of SRT was not considered to majorly affect PK. After a single ONO-5334 dose, serum CTX-I was suppressed by approx. 50% within 1h of administration reaching maximum suppression 6h post-dose. Greater suppression was maintained longer by 300mg SRT vs. 300mg IRT. Second morning void and cumulative 24h urine CTX-I showed clear dose response effects for SRT with maximum suppression at 24h for all treatments except 300mg SRT in 24h cumulative urine where maximum suppression occurred 24-48h. With repeated dosing there appeared to be greater suppression in the 24h cumulative urine CTX-I. Compared with the IRT, the SRT shows reduced Cmax, greater C24 but comparable overall AUCinf dose for dose. The SRT shows clear dose response suppression on bone resorption markers and greater efficacy dose for dose versus the IRT. [1] Eastell R et al, JBMR 1 Feb 2011 [Epub]

P54

EFFECTS OF A TREATMENT FOR 12 WEEKS AQUATIC PHYSICAL THERAPY ON POSTURAL CONTROL IN WOMEN WITH OSTEOPOROSIS: A RANDOMIZED CONTROLLED TRIAL

P. Driusso[1], M. Aveiro[2], J. Oishi[3]
[1]*Physiotherapy Dept., Federal University of São Carlos, São Carlos;* [2]*Physiotherapy Dept., University Federal of São Paulo;* [3]*Statistics Dept., Federal University of São Carlos, São Carlos, Brazil*

The aim of this study was to investigate the effect of hydrotherapy on postural control in women with osteoporosis. This is a randomized controlled trial. The study included 34 volunteers diagnosed with osteoporosis, 17 underwent hydrotherapy (GI) for 12 weeks (mean age 68.94 ± 2.79 years) and 17 constituted the control group (CG) (mean age 69 ± 2.50 years). All responded to the Berg Balance Scale (BBS) conducted the test "Timed Up and Go" (TUG) test and performed postural control of the force platform BERTEC. All subjects were evaluated after 12 weeks. The treatment was performed in a pool with 1 hour duration, twice a week. Data analysis between groups was used nonparametric Mann-Whitney, since the comparison before and after treatment was used nonparametric Wilcoxon test and the evaluation of the qualitative data was used Chi-square. The significance level was 5% ($p \leq 0.05$). The questionnaire of Berg and the TUG test, both showed improvement with a statistically significant difference for the intervention group ($p = 0.002$) and ($p = 0.015$) (Figure 1). With the evaluation of the force platform BERTEC in bipedal stance with eyes open and with eyes closed, not improvement was found with significant difference ($p > 0.05$) in tanden position with right foot forward and left foot forward, we can see improvement with only difference with the right foot forward ($p < 0.05$), whereas in single leg stance with right foot and one foot with his left foot, was seen improvement with a significant difference in the two positions. According to the results obtained in this study, we can conclude that the protocol of exercise water was effective for improving balance in elderly women with osteoporosis.



P55

BIOSILICATE® AND LOW LEVEL LASER THERAPY IMPROVE BONE REPAIR IN OSTEOPOROTIC RATS

P. Bossini[1], **R. Fangel[2]**, D. Ribeiro[1], O. Peitl-Filho[2], E. Zanotto[2], N. Parizotto[2], A.C. Rennó[1]

[1]Department of Biosciences, Federal University of São Paulo, Santos; [2]Department of Physiotherapy, Federal University of São Carlos, São Carlos, Brazil

The aim of this study was to investigate the effects of a novel bioactive material (Biosilicate®) and low level laser therapy (LLLT) on bone fracture consolidation in osteoporotic rats. Forty female Wistar rats were submitted to the ovariectomy (OVX), to induce osteopenia. Eight weeks after surgery, animals were randomly divided into four groups, with 10 animals each: bone defect control group (CG); bone defect filled with Biosilicate® group (BG); bone defect filled with Biosilicate® and irradiated with LLLT, at 60 J/cm^2 group (BG60); bone defect filled with Biosilicate® and irradiated with LLLT, at 120 J/cm^2 group (BG120). Bone defects were surgically performed on both tibias. The size of particle used for Biosilicate® was 180-212 micrometers. LLLT, either with 60 J/cm^2 or 120J/cm^2 was able to increase collagen, Cbfa-1, VGEF and COX-2 expression in the circumjacent cells of the biomaterial. A morphometric analysis revealed that the Biosilicate® plus laser groups showed a higher amount of newly formed bone ($p \leq 0,05$). Our results indicate that laser therapy improves bone repair process in contact with Biosilicate® as a result of increasing bone formation as well as COX-2 and Cbfa-1 immunoexpression, angiogenesis and collagen deposition in osteoporotic rats.

P56

ROLE OF P2X7 SPLICE VARIANTS IN BONE HOMEOSTASIS

A.L. Giuliani[1], E. Adinolfi[1], T. Ricco[1], F. Di Virgilio[1]

[1]Dept of Experimental and Diagnostic Medicine, University of Ferrara, Ferrara, Italy

P2X receptors are plasma membrane receptors for extracellular ATP; they are ion channels that allow the influx of Ca^{2+}/Na^{+} and the efflux of K^{+}. Among P2X receptors, the P2X7 subtype thanks to its long C-terminal cytoplasmic tail can also form a pore which allows the passage of molecules up to 900 Da. Among the nine different naturally occurring splice variants of the receptor, P2X7A is the well-characterized full-length isoform, whereas P2X7B is a shorter one which only maintains ability to form the plasma membrane channel in response to ATP. Recent reports (reviewed in Grol et al. 2009) have shown that: i) P2X7 receptor promotes osteogenesis affecting osteoblasts proliferation and differentiation, ii) P2X7 knock-out mice show decreased periosteal bone formation in long bones and reduced osteogenesis in response to mechanical loading; iii) two loss of function P2X7 polymorphisms are associated with fracture risk in postmenopausal women. Altogether these data suggest an interesting role for P2X7 in bone homeostasis. To assess the possible role of P2X7 splice variants in osteogenesis, a human osteosarcoma cell line TE85, which do not express P2X7, was transfected with either P2X7A, P2X7B or both (P2X7A+B). P2X7A expression in Te85 cells induced increased [Ca2+]i and pore formation besides to confer a proliferative advantage in absence of serum and increased NFATc1 (Nuclear factor of activated T lymphocytes) activity. P2X7B expression also increased [Ca2+]i whereas did not induce pore formation, unless co-transfected with P2X7A; furthermore it potentiated P2X7A responses. Preliminary data show that RANK-L expression was reduced in P2X7 transfected cells: this could result in a lower activation of osteoclast activity and increase of bone mass. In conclusion, P2X7 receptor and its splice variants, could be relevant in osteoblast functions and a potential target for osteoporosis treatment.

P57

INTRAUTERINE FRACTURES: OSTEOGENESES IMPERFECTA´S FIRST CLUE

A. Gonçalves[1], M.R. Mascarenhas[1], G. Lopes[2], A.P. Barbosa[1], J. Monteiro[2], V. Simões[1], M. Sarmento[2], I. Carmo[1]

[1]5. Department of Endocrinology and Diabetes; [2]1st Dept. of Orthopaedics, Traumatology and Rehabilitation, Santa Maria Hospital, Lisbon, Portugal

Introduction: Osteogenesis imperfecta is a secondary cause of osteoporosis, characterized by extremely fragile bones and one of the following: blue sclerae, dentinogenesis imperfecta, hearing loss, and scoliosis. It is a rare inherited disorder of connective tissue integrity that affects up to one in 10 000 people. Diagnosis of mild OI is challenging due to its variable phenotypic expression and inconstant course. In some cases it may be done prenatally, through sonography as early as 13 to 15 weeks of gestational age. Objectives: To present a case of OI and review related literature, highlighting the importance of prenatal screening and diagnosis. Case Report: A nine year-old Caucasian boy, was admitted to our department with history of multiple minor trauma fractures, including intrauterine fractures. There was no family history of congenital anomalies. Physical examination revealed blue sclera, conical-shaped skull, bowing deformities and scoliosis. His ambulation was limited by intense pain. Routine biochemical tests were normal. X-ray revealed generalized osteoporosis, multiple rib and limbs long bones fractures at different stages of healing with excessive callus formation. A clinical diagnosis of osteogenesis imperfecta was made, confirmed by direct collagen analysis from fibroblast culture through skin biopsy. Conclusion: Physicians must maintain a high index of suspicion, as diagnosis, along with proper follow up and counselling, can prevent many complications and morbidity of this disorder.

P58

THE EFFECT OF PHYSICAL ACTIVITY ON BONE MINERAL DENSITY OF LUMBAR SPINE IN POSTMENOPAUSAL WOMEN: META-ANALYSIS

A. Grgurevic[1], G. Trajkovic[2], Z. Gledovic[1]
[1]Epidemiology Dept.; [2]Statistics Dept., School of Medicine, University of Belgrade, Serbia

Conflicting evidence exists regarding the optimum level of physical activity for prevention of postmenopausal bone loss. The aim of this study was to assess the effect of different types of exercises on bone mineral density (BMD) of lumbar spine in postmenopausal women. A systematic review and meta-analysis were undertaken to evaluate the effects of physical activity analyzed in nonrandomized and randomized controlled trials on BMD of lumbar spine. Structured electronic searching of MEDLINE database and hand-searching of reference lists were undertaken to locate relevant studies published from January 1990 to July 2010. Study treatment effect was defined as the weighted mean difference between percentage change in bone loss in the training group and in the control group. Random or fixed effect models were applied according to study heterogeneity observed from the Q statistic. The findings of the study demonstrate that physical activity had an effect at lumbar spine BMD (1.148, $p<0.001$) according to the random effects. Resistance training and weight-bearing training showed positive effect on BMD of lumbar spine ($p=0.001$, $p=0.007$, respectively). The effect of exercise was higher in women with osteopenia or osteoporosis (2.855, $p<0.001$) than in healthy postmenopausal women (0.823, $p=0.001$). In conclusion, physical activity has a significant effect on preservation of BMD at lumbar spine. Furthermore, the effect of physical exercise is higher in women with osteopenia and osteoporosis suggesting nonpharmacological contribution to osteoporosis treatment, but more investigations are needed to confirm these findings.

P59

TAZ IS REQUIRED FOR THE OSTEOGENIC AND ANTI-ADIPOGENIC ACTIVITIES OF KAEMPFEROL

J-H. Hong[1], E.S. Hwang[2]
[1]Department of Life Science, Korea University, Seoul; [2]Department of Pharmacy, Ewha Womans University, Republic of Korea

Kaempferol (KMP) exerts protective effects against both osteoporosis and obesity by regulating cellular activities, but the underlying molecular mechanisms have not been fully elucidated. TAZ (transcriptional coactivator with PDZ-binding motif) modulates both osteoblast and adipocyte differentiation from mesenchymal stem cells by stimulating the activities of RUNX2 (runt-related transcription factor 2) and suppressing the activities of PPARγ (peroxisome proliferator-activated receptor γ). In this study, we investigated the effects of KMP on TAZ regulated osteoblast and adipocyte differentiation. KMP increased the osteoblast differentiation of mesenchymal cells by facilitating the physical interaction between TAZ and RUNX2, thus the increasing transcriptional activities of RUNX2. KMP also enhanced the association of TAZ with PPARγ, thereby suppressing the gene transcription of PPARγ targets and resulting in diminished adipocyte differentiation. Interestingly, the regulatory effects of kKaempferol on RUNX2 and PPARγ mediated transcriptional activity were impaired in TAZ-null mouse embryonic fibroblasts but recovered by restoration of TAZ expression. Our results demonstrate that KMP fortifies TAZ activity, which enhances RUNX2-mediated osteoblast differentiation and suppresses PPARγ-stimulated adipocyte differentiation, indicating the potential of KMP as an effective therapeutic reagent for controlling bone loss and adiposity through TAZ activation.

P60

DIETARY EFFECT OF CALCIUM AND VITAMIN D ON TIGHT JUNCTION GENES EXPRESSION IN DUODENUM AND KIDNEY OF CALBINDIN-D9K OR/AND D28K KNOCKOUT MICE

E-B. Jeung[1], I. Hwang[1]
[1]Chungbuk National Univ, College of Vet Medicine, Cheongju, Republic of Korea

Paracellular transport is responsible for calcium (re)absorption. This passive transport level is determined by the permeability of tight junction. Generally, the permeability of tight junction is inversely proportional with expression of tight junction genes. The paracellular transport is selective and regulative. Especially, among tight junction genes, claudin and occludin are concerned directly with permeability of the tight junction. We confirmed the effect of reduced dietary supply of calcium and vitamin D to paracellular gene expression in calbindin-D9k, -D28k, and –D9k/D28k knockout (KO) mice. Duodenum and kidney are main organs that calcium (re)absorbtion is occurred, so they were used as samples in this experiment. The tissue-specific mRNA and protein expression of tight junction genes in duodenum and kidney of mice was examined using Real-time PCR and WESTERN blot analysis. The tissue localization of tight junction gene was investigated by Immunohistochemistry. In this experiment, most tight junction genes mRNA and protein were less expressed in knockout mice than in duodenum of wild-type (WT) mice. But they are over expressed in Kidney of KO mice than that of WT mice. The expression level of tight junction genes mRNA and protein was similar between in each CaBp-D9k and –D28k single KO mice. That of CaBP-D9k/-28K double KO mice was sometimes similar with that of single KO mice or more/less expressed than in single KO mice in kidney/duodenum. Calcium deficiency diet and vitamin D deficiency diet more increased this difference and calcium/vitamin D deficiency diet was most effective. Localization of tight junction genes was well observed in apical site of paracellular region. Take together these results may imply that the reduced dietary calcium and/or vitamin D concentration and disability of transcellular calcium transport due to knockout of calcium binding protein lead to accelerate the paracellular transport by less expression of paracellular barriers, and over expression of calcium specific pores to keep essential calcium metabolism.

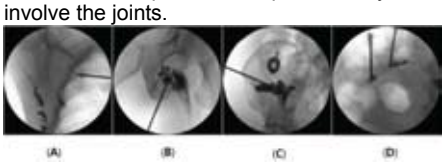
P61

PERCUTANEOUS OSTEOPLASTY IN THE TREATMENT OF PAINFUL BONY METASTASIS

K-H. Kim[1], L. Sung-Hwa[1]
[1]Anesthesia and Pain Medicine Dept., Pusan National University, Yangsan, Republic of Korea

Background: Percutaneous osteoplasty (POP), as a technical extension of percutaneous vertebroplasty, is a highly effective minimally invasive procedure that alleviates the painful effects of metastatic bone disease by injecting bone cement to support weakened bones, provides immediate and substantial pain relief even in patients with a poor general condition. Pain on extraspinal lesions may not be provoked by weight-bearing position but be provoked by specific motion. This study was performed to evaluate patient motion-related pain (MRP) and the resulting pain-related impairment (PRI) by specific motion according to the involved sites where extraspinal POP was performed. Methods: We performed a retrospective study that evaluated the MRP and resultant PRI by reviewing the charts of 66 patients treated with 70 extraspinal POPs. The numeric rating scale (NRS) scores in 5 different positions including while lying on the back, lying on the affected side, sitting, standing, and walking and the Karnofsky performance scale (KPS) scores before and after POP were used to evaluate MRP and PRI, respectively. Results: The postoperative mean NRS scores became significantly lower when patients were in specific 1 of the 5 positions: lying on their affected side following scapuloplasty; sitting following ischioplasty; lying on their affected side in ilioplasty; and lying on their affected side following costoplasty. The mean KPS scores in all patients became

higher after POP. Conclusion: The characteristic preoperative MRP and the resulting PRI according to the involved sites in cancer patients with extraspinal metastases developed by specific motion and alleviated pain and impairment by POP, if the cancer did not involve the joints.



P62

MAJOR AND MINOR DISCORDANCE IN THE DIAGNOSIS OF POST MENOPAUSAL OSTEOPOROSIS AMONG INDIAN WOMEN USING HIP AND SPINE DUAL-ENERGY X-RAY ABSORPTIOMETRY (DEXA)

M. Meeta[1], T. Kaur[2]
[1]*Obstetrics & Gynaecology, St. Theresa;* [2]*Obstetric & Gynaecology Tanvir Hospital, Hyderabad, India*

Objective: To determine discordance in the diagnosis of osteoporosis among post-menopausal Indian women using hip and spine Dual-energy X-ray Absorptiometry. Methods: The study included post-menopausal women who underwent bone mineral densitometry (BMD) for suspected osteoporosis at a referral hospital at Hyderabad, India. The BMD measures at the hip and spine were used to derive T-scores and to determine the prevalence of discordance. Factors potentially associated with discordance were explored in univariate and a multivariate regression model. Ethical Consideration: Approved by Independent Ethical Committee India. Results: The mean age of the 348 postmenopausal women in the study was 53.62±8.94years (median 53.00years, range 37.00 to 80.00years). Major discordance was seen in 16.67% (95%CI:29.46,39.50%) of the study population. Age>50years (adjusted OR:2.60,95%CI:1.24,5.46,p value=0.01), premature menopause (adjusted OR:2.94,95%CI:1.27,6.81, p value=0.03) and multiple pregnancies (adjusted OR:2.64,95%CI:1.28,5.41,p value+0.008) were found to be significantly associated with major discordance. Conclusions: The large prevalence of discordance may reflect the differences in risk factors associated with osteoporosis in different populations and suggests the need to redefine ranges used for the diagnosis of osteoporosis in India.

P63

IS THERE A CORRELATION BETWEEN BONE STATUS OF OBESE SUBJECTS AND FATTY ACID–BINDING PROTEIN 4 EXPRESSION?

A. Hossein-Nezhad[1], **K. Mirzaei**[1], H. Ansar[1], Z. Maghbooli[1], M. Khosrofar[1]
[1]*Endocrinology and Metabolism Research Institute, Tehran University of Medical Sciences, Tehran, Islamic Republic of Iran*

Common differentiation pathways that involved in adipocyte and osteoblast cells from stem cells previously discussed. The correlation and balance between expressions of the adipocyte and osteoblast specific gene markers has been proposed. The lipid chaperone proteins, also known as fatty acid–binding proteins (FABPs), are a group of molecules that coordinate inflammatory and metabolic responses in adipocytes and macrophages. Expression of FABP4 may affect in obesity and effect on osteogenic process in throughout of life. In the present study, we tested the hypothesis that the potential correlation between expression of FABP4 in peripheral blood mononuclear cell and bone mineral density (BMD) in Lumbar spine (L2-L4) and Total hip BMD that measured by dual energy X-ray absorptiometry (DEXA) in obese subjects. Ninety-six obese subjects participant in this cross-sectional study. The PBMCs were separated from whole blood by Ficoll-hypaque technique. Total cellular RNA was extracted and the cDNA was synthesized. Real-time PCR using specific primer pairs for determine the *FABP4* and *beta actin* gene expression. The mean of age and BMI were 36.74±10.96 years and 31.24±3.24kg/m^2 respectively. We showed Lumbar spine BMD was negatively correlated with relative FABP4 gene expression (r=-0.6, p=0. 03). Regression analysis confirmed these correlations after adjustment for age. We found significant higher FABP4 gene expression in osteopenic patients in Lumbar spine (L2-L4) compare to healthy subjects (2.20±0.56 vs. 1.04±0.44). These results demonstrated the similar pathway towards adipogenesis at the expense of osteogenesis in obesity.

P64

EFFICACY OF ONO-5334, A CATHEPSIN K INHIBITOR, ON VERTEBRAL AND NON-VERTEBRAL BONE MINERAL DENSITY AND GEOMETRY IN OVARIECTOMIZED CYNOMOLGUS MONKEYS

H. Mori[1], H. Yamada[2], Y. Nakanishi[1], S. Nishikawa[1], Y. Hashimoto[1], Y. Ochi[1], M. Sugitani[1], K. Kawabata[1]
[1]*Ono Pharmaceutical Co., Ltd., Osaka, Japan;* [2]*Ono Pharma UK LTD, London, UK*

We evaluated the efficacy of ONO-5334, an orally-active inhibitor of cathepsin K, on BMD and geometry in the lumbar vertebra and distal radius in ovariectomized (OVX) monkeys. Female cynomolgus monkeys were assigned to one of the following 6 groups (20 animals/group): sham-operated, OVX-control, ONO-5334 1.2, 6 or 30 mg/kg, or alendronate (ALN) 0.05 mg/kg. ONO-5334 was orally administered once daily from the day following OVX surgery for 16 months. ALN was administered intravenously once every 2 weeks. After necropsy, lumbar vertebra and distal radius were scanned using pQCT to measure volumetric BMD (vBMD). Geometric parameters were analyzed in the distal radius. In the lumbar vertebra, OVX tended to decrease integral vBMD, but trabecular and cortical vBMD were not changed by OVX. ONO-5334 at 6 and 30 mg/kg significantly increased integral and cortical vBMD above sham level. ALN significantly increased integral vBMD to sham level, and tended to increase trabecular vBMD. In the distal radius, OVX significantly decreased trabecular vBMD, but there were no significant changes in integral and cortical vBMD, and geometric parameters. ONO-5334 significantly increased integral and cortical vBMD, and cortical thickness above sham level at 6 and 30 mg/kg, and increased trabecular vBMD at 30 mg/kg. ONO-5334 at 6 and 30 mg/kg significantly decreased endosteal perimeter, but did not affect periosteal perimeter. ALN did not affect any pQCT parameters in the distal radius. In summary, ONO-5334 increases BMD by affecting cortical bone predominantly as well as trabecular bone in the lumbar vertebra and distal radius.

P65

THE EFFECT OF SUPPLEMENTATION OF CA, VIT.D, BORON AND INCREASED FLOURIDE INTAKE ON BONE MECHANICAL PROPERTIES AND METABOLIC HORMONES IN RAT

M.R. Naghii[1], G. Ghanizadeh[2]
[1] *Nutrition Dept.;* [2]*Environmental Health, Baqiyattallah Univ. of Med Sciences, Tehran, Islamic Republic of Iran*

Evidence indicates that optimal nutrition plays a role in bone formation and maintenance. Besides major components of mineralization such as Ca, P and Vit. D, other nutrients like B and F have beneficial role, too. In this study, 34 male wistar rats were divided into five groups: Control diet, Flouride, Flouride+ Boron, Flouride+ Ca+D, and Flouride+B+Ca+D. Boron equal to 1.23 mg, Ca and Vit D 210 mg-55 IU and F, 0.7 mg/rat/day was added to their drinking water for 8 weeks. Plasma blood samples and bones were collected for analysis and mechanical testing. Findings are evidence that F+B intake revealed significant effects on bone mechanical properties and bone metabolic hormones. These findings suggest that combination intake of these two elements has beneficial effects on bone stiffness and breaking strength comparing to even Ca+Vit. D supplementation. This evidence dealing with health problems related

to bone and skeletal system in humans, should justify further investigation of the role of boron and fluoride with other elements in relation to bone.

P66

DYNAMICS OF CHANGE IN BONE MINERAL DENSITY IN WOMEN OF REPRODUCTIVE AGE WITH A DRUG – DEPENDED HYPOESTROGENIA

V. Novikova[1], G. Penzhoyan[1]
[1]*Obstetrics, Gynecology and Perinatology Faculty of Postgraduate Education, Kuban State Medical University, Krasnodar, Russian Federation*

One of the options for secondary osteoporosis is considered to be iatrogenic osteoporosis. The objective: to evaluate the change in bone mineral density in women of reproductive age with a drug – dependent hypoestrogenia. Materials and Methods: A comprehensive examination of 110 women of reproductive age with hyperplasic processes in reproductive sphere with a drug – depended hypoestrogenia was performed. I group - 20 women taking progestogens (Dydrogesterone 30 mg / day from 5th to 25th days of the menstrual cycle). Group II - 20 women receiving GnRH agonists (goserelin 3.6 mg / month). III women - 20 women taking an antagonist of gonadotropin (Gestrinone 2.5 mg twice a week for 6 months). The control, IV, group included 50 women without a drug – depended hypoestrogenia. The average age of women was 37 ± 2,5 years. The survey was conducted over two years: 6 months on the drug – depended hypoestrogenia therapy and 6 months after its implementation. The results: The women in group I initial level of the BMD (SD) was -0,7 ± 1,26 [1,5; -2,3]. After treatment was revealed an increase in BMD: 0,32 ± 1,2 [1,8; -1,8]; r = 0,49, p <0,5. In group II baseline BMD (SD) was -1,19 ± 1,3 [1,8; -2,8]. After treatment revealed a significant decrease in BMD: -1,6 ± 1,27 [1,5; -3,5];r = 0,98, p <0,001. In group III baseline BMD (SD) was -0,66 ± 1,12 [1,3; -2,5]. After treatment revealed a significant decrease in BMD: -0,97 ± 1,11 [1,3; -2,5]; r = 0,98, p <0,001. In group IV the initial level of the BMD (SD) was 0,65 ± 1, 21 [1.23, -1.5]. Revealed no change in BMD evaluated after a year: -0,24 ± 1,14 [1,8; -2,0]; r = 0,22, p <0,35. Conclusions: Drug – depended hypoestrogenia is at risk of changes in BMD in women of reproductive age. Intake of progestogens marked increase in bone mineral density (p <0,5). The use of GnRH agonists and antagonists of gonadotropins significantly reduces the BMD (p <0,001). Women with drug – depended hypoestrogenia is shown holding the prevention of abnormal decrease in BMD.

P67

BMP 2 EFFECT ON OSTEOPOROTIC SPINE FUSION IN ANIMAL STUDY

S.B. Park[1], C.K. Chug[2]
[1]*Neurosurgery Dept., Seoul Paik Hospital;* [2]*Neurosurgery Dept., Seoul National University Hospital, Seoul, Republic of Korea*

Bone morphogenetic proteins (BMPs) induce bone formation and many animal studies have been established the augmenting spinal fusion of BMPs. However, there is no sufficient knowledge about the effect of BMP in osteoporotic patient who needs a spine fusion. Therefore, we studied the effect of BMP on osteoporotic spinal arthrodesis. Female Sprague-Dawley rats (n=36) were ovariectomized (OVX) or sham-operated, and randomized into three groups: Group I (sham-operated + arthrodesis alone), Group II (OVX + arthrodesis alone) and Group III (OVX + arthrodesis + BMP 2, 90 μg). Eight weeks after ovariectomy, surgery as lumbar spinal arthrodesis was performed using autologous iliac bone. For analysis of mRNA expression, the half number of animals in three groups was killed 3 and 6 weeks after arthrodesis. The resting animals were checked bone formation status using micro-computed tomography per 3 weeks after surgery. Outcome assessment was done using radiological evaluation through micro-computed tomography and mRNA expression. Bone mass of G III increased significantly after 3 weeks surgery as compared to other groups. In mRNA analysis, the mean value of osteoblast markers as ALP, Osteocalcin, Runx2 and, Smad 1/ 5 increased significantly at postoperative 3 weeks. The changes of bone turnover markers in other groups were not significant The BMP2 in higher dose (90 μg) had shown efficacy in achieving spinal fusion in ovariectomized rats in early stage of bone formation. Therefore, the using of BMP2 in osteoporotic patients who need spinal arthrodesis would be promising.

P68

THE ENDOVANILLOID/ENDOCANNABINOID SYSTEM: A NEW POTENTIAL TARGET FOR OSTEOPOROSIS THERAPY

F. Rossi[1,2], G. Bellini[3], L. Luongo[3], M. Torella[4], S. Mancusi[1], L. De Petrocellis[5], D. Siniscalco[3], S. Perrotta[1], B. Nobili[1], V. Di Marzo[5], S. Maione[3]
[1]*Pediatrics Dept., Second University of Naples, Naples;* [2]*Haematology and Oncology, Children Hospital Bambino Gesù, Rome;* [3]*Experimental Medicine;* [4]*Department of Gynecology and Obstetrics, Second University of Naples, Naples;* [5]*Institute of Biomolecular Chemistry, Institute of Cybernetics and Institute of Protein Biochemistry, National Research Council, Italy*

Bone is a highly metabolically active tissue and its formation and resorption is at the base of bone remodeling. Removal of bone is task of osteoclasts (OCs), while its neo-formation relies on osteoblasts. The critical importance of a balanced remodeling is demonstrated by human diseases, i.e. osteoporosis, in which a net increase in bone resorption is responsible of skeleton weakening and fracture risk. Human OCs express functional TRPV1 vanilloid channels, CB1/CB2 cannabinoid receptors and endocannabinoid/endovanilloid synthetic/catabolic enzymes. Pharmacologic manipulation of this system can modulate osteoclast activity. Through multidisciplinary approaches, we demonstrate that enzymes and receptors of the endocannabinoid/endovanilloid system are differently expressed in OCs from menopausal women without or with osteoporosis. In OCs from osteoporotic patients, TRPV1 channels are up-regulated and, if persistently stimulated with resiniferatoxin (RTX), become clustered to the plasma membrane whilst inducing a massive over-expression of CB2 receptors, the counterpart receptor system for osteoclast inhibition. Accordingly, the CB2 agonist JWH-133 [5 μM] reduces TRAP levels in menopausal healthy and osteoporotic OCs. Moreover, TRPV1 silencing significantly reduces TRAP expression in osteoporotic OCs. By providing new evidence for a critical functional cross-talk between CB2 and TRPV1 receptors in osteoporosis, we speculate that TRPV1 desensitization, or its enhanced trafficking, together with TRPV1 agonist-induced CB2 receptor overexpression, might be critical to minimize calcium entry in OCs, which could be in turn responsible of cell over-activation and higher bone resorption. In this direction, drug cocktails or hybrid molecules, designed to simultaneously stimulate CB2 receptors and activate/desensitize or antagonize TRPV1 channels may prove useful in pathological conditions where an unbalanced osteoblast/osteoclast activity is observed. Our data pave the way to the use of TRPV1 agonist together with CB2 agonists in osteoporosis.

P69

ROLE OF TGFβ IN DEVELOPMENT OF OSTEOPOROSIS IN THALASSEMIA PATIENTS

K. Singh[1], R. Kumar[1], S. Agarwal[1]
[1]*Genetics Dept., Sanjay Gandhi Post Graduate Institute of Medical Sciences, Lucknow, India*

Background: Transforming growth factor plays an important role in bone turnover and therefore TGF-β1 gene is a candidate for mediating genetic influence on bone mass and risk of fracture. Aim: To find out the role of sequence variation: 713-8delC in the transforming growth factor-beta 1 gene in causing osteoporosis in thalassemia patients. Material and Methods: A total of 100 beta thalassemia major patients were recruited for the present study from Department of Genetics, Sanjay Gandhi Post Graduate Institute of Medical Sciences, Lucknow, India. Bone mineral density (BMD) was measured in beta thalassemia patients by Dual Energy X ray

Densitometry (DEXA). TGF beta gene sequence variation was analysed by PCR-RFLP method. Results: Z score of BMD of lumber spine and hips were -2.31±1.18 and -2.09±0.89. Osteoporotic lumber spine was observed in 42.5% cases of thalassemia. Out of 100, 52 patients had a one base deletion in the intron sequence 8 bases prior to exon 5 (713-8delC), which could influence splicing. We found no association of 713-8delC variant with the Z score of Lumbar Spine (P value=0.285) and Hips (P value=0.070) in thalassemia patients. But, previously it was reported by Langdhal et al (1998) in population of Denmark, sequence variation, 713-8delC, in the TGF-beta 1 gene is more frequent in patients with osteoporosis compared to normal controls. Conclusion: Tgf β has no significant role in development of osteoporosis in thalassemia.

P70

BACK PAIN IN PATIENTS WITH SEVERE OSTEOPOROSIS TREATED WITH TERIPARATIDE OR ANTIRESORPTIVES: A PROSPECTIVE, MULTICENTRIC, OBSERVATIONAL STUDY

S. Jasqui[1], T. Songpatanasilp[2], R. Malhotra[3], B. Dave[4], M. Mumatz[5], H. Chhabra[6], G. Bori[7], M. Yu[8], J. Blair[9], **S. Sorsaburu[10]**

[1]Bone and Joint Department, Hospital Angeles de las Lomas; [2]Bone and Joint Department, Phramongkutklao College of Medicine; [3]Bone and Joint Department, All India Institute of Medical Sciences, New Delhi, India; [4]Bone and Joint Department, Stavya Spine Hospital & Research Institute; [5]Bone and Joint Department, Island Hospital; [6]Bone and Joint Department, Indian Spinal Injuries Centre; [7]Bone and Joint Department, Instituto Mexicano del Seguro Social. Mexico; [8]Statistics, Eli Lilly Canada; [9]Medical Communications, Eli Lilly Australia Pty Ltd., Sydney, Australia; [10]Medicine, Eli Lilly and Company, USA

Aim: This 1-year study compared the effectiveness of teriparatide over antiresorptives on the relative risk of new/worsening back pain. Methods: This study in 9 countries enrolled 647 men and postmenopausal women (mean age 68.8 years), of whom 230 patients were prescribed and received teriparatide, and 322 patients were prescribed antiresorptives, for established severe osteoporosis under regular medical care for up to 12 months. The primary effectiveness measure was relative risk of new/worsening back pain at 6 months. Results: At baseline, more subjects on teriparatide versus antiresorptives had severe back pain (30.9% vs. 17.7%), extreme pain/discomfort (25.3% vs. 16.8%), extreme anxiety/depression (16.6% vs. 7.8%), and bed-confinement (10.0% vs. 5.3%). At study entry, patients treated with teriparatide differed from those treated with antiresorptives for VAS (5.82 vs. 5.05) and EQ-5D (37.7 vs. 45.5). With teriparatide and antiresorptives at 6 months, respectively, incidence of new/worsening back pain was 9.8% vs. 10.3% [relative risk (95% confidence interval) adjusted for propensity score, country, and baseline back pain severity in patients with severe baseline back pain was 0.99 (0.80, 1.23)]. At 12 months, incidence of severe back pain was 1.3% vs. 1.6%, respectively, EQ-5D scores were 46.1 vs. 55.4, VAS scores were 2.71 vs. 3.30, and more teriparatide-treated patients felt better (82.7% vs. 71.0%) and were at least very satisfied with their treatment (49.4% vs. 36.8%). Conclusions: Teriparatide-treated patients had a similar risk of new/worsening back pain as antiresorptive-treated patients at 6 months, though further research is needed for confirmation of results.

P71

EVALUATING ADDITIONAL RISK-FACTORS' INFLUENCE ON OSTEO-ARTICULAR DISORDERS FOR AN ELDERLY LOCAL-SPECIFIC TARGET GROUP

L.M. Susan[1], I. Mozos[2]

[1]Department of Internal Medicine; [2]Department of Physiology, Medical School: Medicine and Pharmacy University "Victor Babes", Timisoara, Romania, Timisoara, Romania

Hypothesis: Objectives: The etiology of osteoporosis and osteoarthritis contains two classes of factors: factors that generate biomechanical anomalies and general risk factors. Due to unalterable facts, the population from our county already presented 2 risk factors: the Caucasian race (99%) and the mild climate (100%). Our study researches the correlation of the other known risk factors and osteoporosis for the specific local population. Results: During the last year, we conducted a study in the IVth Medical Clinique, Timisoara, Romania. Osteoporosis was found at 73 patients, 67 women and 6 men. Their age varied between 61 and 86 years, with an average of 65.2 years. Another 56 patients (34 female, 22 male) had located degenerative joint disease. All the patients were diagnosed, by means of clinical and complex paraclinical exams, targeted on the musculoskeletal system with osteoarthritis and/or osteoporosis. With the increase of age, the presence of osteoporosis and/or osteoarthritis increased by 31.8% for every 10 years. A raise of 10 points in the BMI marked an increased risk of osteoporosis by 14.8%. An early menopause start-age marked 58% of all the women exhibiting osteoporosis. Each previous fracture after 50 years marked a 34.2% higher probability of developing either of the targeted disorders. Every cigarette smoked during a day added 0.88% to the probability of developing osteoporosis. Conclusion: Osteoarthritis and osteoporosis can lead to restricted movement and fractures therefore, to hospitalization and/or being homebound. By helping to determine high-risk persons, future problems and hospitalization may be avoided or at least expected.

P72

CLASSIC YIN AND YANG TONIC FORMULA FOR OSTEOPENIA: STUDY PROTOCOL FOR A RANDOMIZED CONTROLLED TRIAL

F. Yang

Spine Research Institute, Shanghai University of Traditional Chinese Medicine, Shanghai, China

Background: Osteoporosis is a growing worldwide problem, with the greatest burden resulting from fractures. Nevertheless, the majority of fractures in adults occur in those with "osteopenia" (bone mineral density (BMD) only moderately lower than young normal individuals). Since long-term drug therapy is an expensive option with uncertain consequences and side effects, natural herbal therapy offers an attractive alternative. The purpose of this study is to evaluate the effect on BMD and safety of the classic yin and yang tonic formula for treatment of osteopenia and to investigate the mechanism by which this efficacy is achieved. Methods/design: We propose a multicenter double-blind randomized placebo-controlled trial to evaluate the efficacy and safety of the classic yin and yang tonic formula for the treatment of osteopenia. Participants aged 55 to 75 with low bone mineral density (T-score between -1 and -2.5) and kidney deficiency in TCM will be included and randomly allocated into two groups: treatment group and control group. Participants in the treatment group will be treated with classic Yin and Yang Tonic Granule, while the controlled group will receive placebo. Primary outcome measure will be BMD of the lumbar spine and proximal femur using dual-energy X-ray absorptiometry. Secondary Outcomes will include pain intensity measured with visual analogue scales, quality of life, serum markers of bone metabolism, indices of Neuro-endocrino-immune network and safety. Discussion: If the classic Yin and Yang Tonic Formula can increase bone mass without adverse effects, it may be a novel strategy for the treatment of osteoporosis. Furthermore, the mechanism of the Chinese medical formula for osteoporosis will be partially elucidated.

Rheumatoid Arthritis

P73
A HIGH ECONOMIC AND SOCIAL IMPACT OF RHEUMATOID ARTHRITIS AT A LOW HUMAN DEVELOPMENT REGION OF BRAZIL

A.L. Borges Pinheiro[1], M. de Alencar[1], R. Pimentel[1], F. Klein Leitão[1], H. Forte[1], K. Botelho[1], M.V. Freitas[1]
[1]*Federal University of Ceará, Fortaleza, Brazil*

Introduction: Rheumatoid arthritis (RA) is a chronic inflammatory disease that may cause disabilities and requires a constant medical care and rehabilitation service. These factors can lead to an important economic and social impact on the patient lives. Objectives: To study the economic and social impact of RA among patients treated on a public hospital in a capital of the northeastern of Brazil, a region of low human development index according to the UN. Methods: Patients with RA treated at the Cesar Cals General Hospital, a public hospital in Fortaleza, Ceará, Brazil, were invited to answer an interview based on a pre-formulated questionnaire. Results: 54 patients were interviewed (90.7% female). The mean age was 53.5 years ± 11,2. The diagnosis was established before 2003 in 46.3% of them and 26.4% of all patients were retired because of incapacitating disability. Poverty help from the government was used by 27.8% and social welfare benefit by 42.6%. Thirty-nine percent live in families with at least 5 people, while other 27.8% live in families with 3 people. Eighty-nine percent have a family income between 1 to 3 minimum wages (about U$290.00 to U$870.00). Ninety-three percent did not attend any kind of rehabilitation service. The average cost of the disease for the patient was U$22±43. Conclusion: This study reassures the great financial and social impact of RA at a low human development region of Brazil.

P74
EFFICACY OF RITUXIMAB RETREATMENT IN REFRACTORY JUVENILE IDIOPATHIC ARTHRITIS

E. Alexeeva[1], S. Valieva[1], **R. Denisova**[1], T. Bzarova[1], T. Sleptsova[1], E. Mitenko[1], K. Isaeva[1]
[1]*Rheumatology Dept., Scientific Center of Children's Health of Russian Academy of Medical Sciences, Moscow, Russian Federation*

Background: Chimeric monoclonal anti-CD20 B-cell antibody (rituximab) is promising drug for the treatment of JIA refractory to immunosuppressive drugs and TNF-α-blockers. Objectives: To evaluate clinical efficacy of rituximab retreatment in patients with severe juvenile idiopathic arthritis (JIA). Methods: 75 patients were enrolled in the study, 36 boys and 39 girls with JIA. Range of age was from 2,3 to 17 years; mean disease duration was 5,32 (0.6; 7,0) years. Rituximab was administered at a mean dose of 375 mg/m^2/administration according to the following regimen: 1 dose once a week for 4 consecutive weeks every 24 weeks. The next course of Rituximab was administrated if patients had systemic manifestations, active joints, increasing level of CRP and ESR in 24 weeks after Rituximab treatment. 75 patients have received one treatment course (24 weeks), 72 children have received 2 courses (48 weeks), 55 children have received 3 courses (72 weeks), 38 – 4 courses (96 weeks), 23 – 5 courses (120 weeks). Results: The ACR Pedi 30, 50, 70 were achieved by 85%,45%, 40% of patients at Week 24, and by 90%, 75%, 70% of patients at Week 48, respectively. At week 72 ACR pedi 50 and 70 were achieved by 75% and 70% of patients. The remission was achieved by 25% of patients at Week 24, by 48% of patients at Week 48, by 65% of patients at Week 72 and by 80% and 90% of patients at Week 96 and 120. Conclusion: Rituximab is effective drug of treatment in patients with severe juvenile idiopathic arthritis. The remission was achieved by 90% of patients at Week 120.

P75
SERUM ANTI CYCLIC CITRULLINATED PEPTIDE ANTIBODIES MAY PREDICT DISEASE ACTIVITY IN RHEUMATOID ARTHRITIS

K. Esalatmanesh[1], R. Jamali[1], Z. Soleimani[1]
[1]*Internal Medicine, Kashan University of Medical Sciences, Kashan, Islamic Republic of Iran*

Objective: To define the relationship between serum anti cyclic citrullinated peptide antibodies (anti-CCP) and disease activity, and to construct a new disease activity index by using anti-CCP in Rheumatoid Arthritis (RA). Methods: One hundred and five RA patients included. Disease activity based on DAS28-ESR, and serum anti-CCP were measured. Results: There was correlation between serum anti-CCP and DAS28-ESR. (R2 = 0.71, P value < 0.01). New disease activity index was developed by replacing anti-CCP with ESR in DAS28-ESR. There was correlation between new model and DAS28-ESR. (R2 = 0.91, P value < 0.01) The new composite index best cut off values corresponding to DAS28-ESR values of 2.6, 3.2, and 5.1 were 3.21, 3.38, and 4.74 respectively. There was agreement between new model and DAS28-ESR for determination of patients in different disease activity categories. (Kappa = 0.71, P value < 0.01). Conclusion: The new disease activity index that applies serum anti-CCP may predict disease activity in RA.

P76
SAFETY PROFILE OF INFLIXIMAB INFUSIONS IN A REGION OF LOW HUMAN DEVELOPMENT INDEX

H. Forte[1], F. Klein Leitão[1], M. de Alencar[1], R. Pimentel[1], A.L. Borges Pinheiro[1], K. Botelho[1], M.V. Freitas[1]
[1]*Federal University of Ceará, Fortaleza, Brazil*

The northeast of Brazil is characterized as a demographic and socio-economic region that is classified as low human development according to the UN. The aim of this study was to evaluate the safety profile of infliximab infusions in the city of Fortaleza, capital of a state in northeastern Brazil, in a center of public attention, Cesar Cals General Hospital. It was reviewed the medical records of 16 patients (10 women) treated with infliximab for rheumatoid arthritis or ankylosing spondylitis, in the period from March 2008 to May 2010, with 128 infusions analyzed. The parameters evaluated were: occurrence of reactions infusion, blood pressure (BP), heart rate (HR) and respiratory rate (RR), axillary temperature, weight, AST, ALT, ESR, creatinine, number of swollen and tender joints and infliximab dosage. All infusions are preceded by dexclorfeniramina 4mg orally. No serious infusion reaction was observed. One patient developed herpes zoster after the tenth infusion. The average of BP was 123mmHg systolic and 79mmHg diastolic before, 117mmHg and 77 mmHg during, 118mmHg and 76 mmHg after the infusions. The HR and RR did not change (average = 74bpm and 19rpm, respectively) and temperature (average = 36oC). The average weight was 62kg. The average number of joints affected was four. Creatinine was 0.8mg/dL, AST: 26.1mg/dL, ALT:26.0 and ESR: 23mm/1a hours. Finally, the average dose of infliximab was 229mg, giving average dose per patient 3.7mg/Kg. This study demonstrates that the use of biological drugs are safe even for lower socio-economic profile.

P77
NON-INVASIVE METHODS TO ASSESS CARDIOVASCULAR PROFILE IN RHEUMATOID ARTHRITIS PATIENTS

L. Gianturco[1], M. Turiel[1], D. Stella[1], P. Sarzi-Puttini[2], F. Atzeni[3], C. Ricci[4], V. De Gennaro-Colonna[5]
[1]*Cardiology Unit, University of Milan, IRCCS Galeazzi Orthopedic Institute, Milan;* [2]*Rheumatology Dept., L. Sacco University Hospital, Italy;* [3]*Experimental Medicine and Rheumatology, Queen Mary University, London, UK;* [4]*Clinical Epidemiology and Biometry Uni, IRCCS Policlinico San Donato;*
[5]*Pharmacology Dept., University of Milan, Milan, Italy*

Rheumatoid arthritis (RA) is characterized by an excess of cardiovascular (CV) morbidity and mortality mainly due to chronic inflammation that promotes the development of endothelial

dysfunction and enhanced atherosclerosis. Our goal was to evaluate the relationship between coronary flow reserve (CFR), carotid intima-media thickness (cIMT) and inflammation indexes in RA patients. We enrolled 120 adult patients in order to ACR classification criteria [M 20 (16.6%), F 100 (83.4%)], mean age 61±13 years) without clinical evidence of CV disease underwent dipyridamole stress-echo to evaluate CFR in the left descending coronary artery. Common cIMT was calculated by ultrasound. Furthermore, a blood sample was collected to measure plasma ADMA levels, ESR, CRP. 72/120 patients (60%) had CFR<2.5 of which 14/120 (12%) had CFR<2. All patients had normal wall motion at rest and during stress. Common cIMT was in normal range (0.73±0.13 mm) while plasma ADMA levels were increased (0.72±0.10 vs. 0.63±0.08; P<0.001). Linear regression analysis showed a significant negative correlation between CFR and common cIMT (P<0.001), plasma ADMA levels (P<0.001) and patient's age (P=0.019). Moreover, CFR resulted negatively related with rheumatoid factor levels (P=0.0009) and visual analogue score (VAS) (P=0.0092). RA patients without clinical evidence of CV diseases showed an early impairment of coronary microcirculation and endothelial dysfunction before structural changes of large vessels occur. This suggests that reduced CFR is an early marker of enhanced atherosclerosis in a preclinical stage and it is associated with endothelial dysfunction. Moreover, indexes of disease activity resulted negatively associated with coronary microcirculation function.

P78

COMPARISON OF THE PROTECTIVE EFFECT OF GENISTEIN AND DIADZEIN ON COLLAGEN-INDUCED ARTHRITIS (CIA) RATS

F. Haidari[1], M. Mohamad Shahi[1], M.R. Rashidi[2], S. Mahboob[3], B. Rashidi[4]

[1]Nutrition Dept., Ahvaz Jondishapour University of Medical Science, Ahvaz; [2]Drug Applied Research Center; [3]Nutrition Dept., Nutrition Research Center, Ahvaz; [4]Schools of Medicine, Esfahan University of Medical Sciences (ANATOMY), Esfahan, Islamic Republic of Iran

Introduction: Genistein and daidzein, two isoflavones from soy have been previously shown to possess anti-inflammatory properties. We have analyzed the effects of these two isoflavones on rheumatoid arthritis prognosis and prevention in rats and compared them with dexamethasone. Method: Collagen type II was used to induce arthritis in rats. Rats were divided randomly into 5 groups: healthy control, CIA (collagen-induced arthritis) control, dexamethasone (1mg/kg), genistein (25mg/kg) and daidzein(25mg/kg) ant treated for 30 days. Clinical symptoms were recorded using standard protocols day by day. Serum concentration of TNF-α, IL-6, adiponectin and leptin were taken. Tarsal and tibiotarsal joints of animals cut for histopathologic analyses. Result: Day of onset arthritis for genistein and daidzein treated rats were delayed significantly with comparison CIA group .TNF-α and IL-6 serum concentrations as well as adiponectin and leptin reduced significantly (p<0.05) after treatment with genistein and daidzein compared to CIA control. Soy isoflavones protect tarsal and tibiotarsal joints damages when compared to dexamethasone. Conclusion: Soy isoflavones, daidzein and especially genistein could significantly improve arthritis manifestations in rats. The structural similarity of isoflavones to estrogen could be the possible underlying mechanism involved in the function.

P79

IMPORTANCE OF ANTI-CCP IN RHEUMATOID ARTHRITIS

G. Kavaja[1], X. Ceka[2], O. Mustafaraj[1], S. Tonuzi[1]

[1]Hospital of Durres, Durres; [2]Department of Genetics, Cell- and Immunobiology, University of Tirana, Tirana, Albania

Background: Rheumatoid Arthritis is a chronic, autoimmune and multisystemic disease. It is characterized by a gradual progression and an unexpected prognosis. RA affects all ages, races and both sexes. RF (rheumatoid factor), anti-CPP2 antibodies and ANA (antinuclear antibody), and the indicators of acute inflammation phase are very important in establishing diagnosis, monitoring the evolution and prognosis of the disease. Objectives: To study the relationship between the immunological tests (RF, anti-CCP2 and ANA) and other inflammation indicators of the connective tissue diseases with their stage of advancement, the link between disease of connective tissue and positivity of the immunologic tests (RF, anti-CPP2 antibodies, ANA), relationship between disease progression and the change of indicators of acute phase of inflammation (fibrinogen, ESR test). Methods: The study included 86 patients which were 78 women (90.7%) and 8 males (9.3%). Age ranged from 22 years to 77 years. The patients met the ACR criteria for connective tissue diseases. Patients did not suffer from diseases that can alter tests for which we were interested. Patients have been in treatment with disease-modifying antirheumatic drug, corticosteroids and NSAIDs. Patients were followed in three stages with 6-months period. In every visit was performed: immunological tests (RF, anti-CPP2 antibodies, ANA) and the analysis of peripheral blood, ESR test and fibrinogen. Results: Anti-CCP2 resulted positive in 68 of patients with RA or 87% of cases. Statistical study showed a statistically important relation (r = 0.255, p 0.017). Rheumatoid factor resulted positive in 61 patients with the AR or 78% of cases. In the study appeared a statistically important relation (r = 0.113, p = 0.017). 27 patients with AR with positive FR, resulted positive for ANA test and they belonged to the stage II-III and III of the disease. Tests of inflammation improved under the effect of therapy regardless the stage of disease (there is a statistically important alteration in time of the values of HB, fibrinogen and ESR test between consecutive controls (t1, t2, T3) p <0.05. Conclusions: RA is a chronic disease with a long performance which predominates mainly in female sex. Specific immunologic tests have a particular importance in establishing diagnosis, in determining the prognosis of the disease and their performance. In this study we found a strong relation between RF test and anti-CCP2 antibodies for the diagnosis of AR. The presence of a positive test for anti-CCP2 antibodies in a patient with RA and a positive FR shows an aggressive performance of serious illness and prognosis. Indicators of acute inflammation phase (ESR test and fibrinogen) are important elements in determining disease activity and effectiveness of therapy used for their treatment.

P80

ASSOCIATION OF LEFLUNOMIDE AND INFLIXIMAB IN THE TREATMENT OF RHEUMATOID ARTHRITIS IN A PUBLIC HOSPITAL IN FORTALEZA, BRAZIL

F. Klein Leitão[1], H. Forte[1], R. Pimentel[1], M. de Alencar[1], A.L. Borges Pinheiro[1], K. Botelho[1], M.V. Freitas[1]

[1]Federal University of Ceará, Fortaleza, Brazil

Many studies with biological drugs demonstrated their efficacy and superiority when combined with methotrexate. However, the toxicity of methotrexate may limit its use. According to the Rheumatology Brazilian Society, leflunomide is an option that can be used in combination with the biological drugs in the treatment of rheumatoid arthritis (RA). In order to evaluate the safety of concomitant use of leflunomide and infliximab, medical records of nine patients with RA in a public hospital were reviewed (six women and three men). Blood pressure, heart and respiratory rate, axillary temperature (all before, during and after each infusion), occurrence of infusion reactions, weight, AST, ALT, ESR, creatinine, number of painful and swollen joints and infliximab dosage were evaluated. All infusions were preceded by premedication with dexchlorpheniramine 4mg orally. In total, 84 infliximab infusions were evaluated. All patients were taking leflunomide 20mg/day. The average systolic blood pressure was 126mmHg and diastolic 80mmHg before, 119mmHg and 79mmHg during, and 119mmHg and 77mmHg after the infusions. The heart and respiratory rate and the temperature did not vary between infusions (average=76 bpm, 20bpm and 36.2°C respectively). The average weight was 63kg. The average number of painful and swollen joints was 5.2. The creatinine was 0.8mg/dL, AST 25.3mg/dL, ALT 26.7mg/dL and ESR 26mm/1st hour. The average dose used in infusions of infliximab was 209mg (3.3mg/kg). Therefore the use of leflunomide in combination with infliximab is safe in the treatment of

rheumatoid arthritis. It was not observed any increase in adverse reactions with leflunomide or infliximab alone.

P81

BIOLOGICAL THERAPY COULD BE MONITORED BY A RHEUMATOLOGY NURSE-LED CLINIC WITHOUT ANY DIFFERENCES IN OUTCOME – A RANDOMISED CONTROLLED STUDY

I. Larsson[1], B. Arvidsson[2], B. Fridlund[1], A. Teleman[4], S. Bergman[3]
[1]School of Health Sciences, Jönköping University, Jonkoping , Sweden; [2]School of Social and Health Sciences, Halmstad University, Halmstad; [3]Research and Development Centre; [4]Spenshult Hospital for Rheumatic Diseases, Oskarström, Sweden

Background: Patients with rheumatic diseases treated with biological therapy are usually followed up by rheumatologists. Rheumatology nurse-led clinics have been proposed for patients who are in low disease activity or remission. Objectives: To compare treatment outcomes from a rheumatology nurse-led clinic and a rheumatologist clinic for patients treated with biological therapy with low disease activity or in remission. Methods: In a prospective controlled study 107 patients were randomised into two groups with six months follow up to a rheumatology nurse (intervention group; n=53) or to a rheumatologist (control group; n=54). Inclusion criteria were ongoing biological therapy and Disease Activity Score 28 (DAS28) ≤3.2. All patients met the rheumatologist at inclusion and after 12 months. In the rheumatology nurse-led clinic the patients´ disease activity was assessed by examination of tender or swollen joints and laboratory tests. The rheumatology nurse also had a dialogue concerning the patient's needs with regard to drug therapy, smoking habits and psychosocial aspects. After 12 months 97 patients completed the study. Main outcome was disease activity measured by DAS28. Results: Patients had mean age of 55.4 years and disease duration of 16.7 years. DAS28 was 2.1. At inclusion there were no significant differences in DAS28 between the groups. There were no differences (p=0.67) in change of DAS28 between the intervention group (0.14) or control group (0.20) from inclusion to 12 months. Conclusions: In patients with low disease activity biological therapy could be monitored by a rheumatology nurse-led clinic without any differences in outcome as measured by DAS28.

	Intervention group		Control group	
	Inclusion	12 months	Inclusion	12 months
Numbers	53	47	54	50
Male/Female	23/30	21/26	23/31	22/28
Age (mean)	55,0		55,8	
Disease duration (mean)	16,2		17,3	
DAS28 (mean)	1,96	2,10	2,14	2,34

P82

EFFECTS OF A YOGA PROGRAM ON PAIN RELIEF, REDUCING ANXIETY AND EXTENDED RANGE OF MOTION OF KNEE IN RHEUMATOID ARTHRITIS PATIENTS

S. Mahidashtizad[1], A. Salajegheh[1]
[1]Department of Nursing, Islamic Azad University, Tehran Medical Unit, Tehran, Islamic Republic of Iran

Background: Positive effects of exercise both in water environment (hydrotherapy) and out, on decreasing pain and stress and increasing range of motion of joints have been demonstrated in many studies. The present study was designed to investigate the effects of a Yoga program, a gentle form of physical activity which can integrate and bring balance to the body, mind and spirit, on pain decline, reducing anxiety, and improvement of RoM of knee joint in RA patients. Material and Methods: In a clinical trial, a total of 40 adult females were equally assigned in experimental and control groups. At baseline, demographic data and disease history were asked then the severity of pain were assessed by the use of pain visual-analog scale, level of anxiety by STAI-I and STAI-II anxiety inventory and knee joint range of motion by a goniometer. Then the experimental group was advised to participate in a yoga program for 12 weeks. By the end of yoga program, both groups were reassessed. Results: The mean pain severity was reduced in both groups, however, experiments showed a statistical significant differences ($p<0.001$). The mean level of anxiety had a noticeable decline with statistical significant differences in experimental group ($p<0.001$). The controls did not show significant changes in level of anxiety. Knee joint range of motion was also significantly increased in yoga group, when compared with controls ($p<0.05$). Conclusion: Yoga could effectively decrease pain severity as well as level of anxiety and improve RoM of knee in patients with rheumatoid arthritis.

P83

CIRCULATING ANTIBODIES DIRECTED AGAINST TRYPTOPHAN DERIVATIVE COMPOUNDS LINKED TO PROTEIN IN RHEUMATOID ARTHRITIS

S. Duleu[1], G. Ferran[1], J. Sibilia[2], J. Goetz[2], **A. Mangas**[3], M. Geffard[4,1]
[1]IDRPHT; [2]Hautepierre Hospital; [3]Gemacbio, Saint Jean d'Illac, France; [4]Laboratoire IMS, ENSCPB-EPHE

The main objective of our study was to indirectly evaluate for the first time the activation of the 2 tryptophan metabolic pathways in Rheumatoid Arthritis (RA) patients by identification of specific circulating antibodies directed against conjugated tryptophan derivative (TD) compounds. The second objective was to assay the immunoglobulin (Ig) G, M, A isotypes of these circulating antibodies. For the antibody binding, we synthesized several TD linked to protein carrier (bovine serum albumin, BSA) in order to mimic antigenic modifications induced during the pathogenic processes. Each TD of tyrosine hydroxylase (THO) and 2,3 indoleamine dioxygenase (IDO) pathways was bound to BSA using carbodiimide coupling reaction. Then, TD-protein carrier conjugates were purified and tested using ELISA assays. The THO and IDO molecules were respectively: tryptophan, 5-hydroxytryptophan, serotonin, 5-methoxytryptamine, 5-hydroxyindol acetic acid, melatonin, 5-hydroxytryptophol, 5-methoxytryptophol; kynurenine, 3-hydroxykynurenine, and kynurenic, quinaldic, quinolinic, xanthurenic, anthranilic, 3-hydroxyanthranilic, picolinic acids. For these circulating antibody assays, 56 patients with RA: 42 women and 14 men were compared to 19 healthy controls. All TD-protein carrier conjugates were coated on well plates. High significant circulating antibody levels were found in IgA on: 3-hydroxykynurenine, 3-hydroxyanthranilic, quinaldic, kynurenic, 5-hydroxytryptophol conjugates, and in IgG on tryptophan and serotonin conjugates. The specific binding of A and G circulating Ig in RA patient sera directed against chemically defined TD-protein carrier shows the THO and IDO pathways are specifically activated during the RA pathological processes. More, these results open new perspectives for the treatment of RA.

P84

UMBILICAL CORD MATRIX MSC (UCMMSC) AS THERAPEUTIC AGENTS FOR TREATING RHEUMATOID ARTHRITIS

J.M. Santos[1], S.I. Simões[2], M.M. Gaspar[2], S. Calado[2], J. Almeida[1], M. Filipe[1], M. Teixeira[1], J.P. Martins[1], R.N. Bárcia[1], P.Cruz[1], M.E.M. Cruz[2], H. Cruz[1]
[1]ECBio – Investigação e Desenvolvimento em Biotecnologia S.A., Amadora; [2]Research Institute for Medicines and Pharmaceutical Sciences (iMed.UL), Faculty of Pharmacy, University of Lisbon. Lisbon, Portugal

Mesenchymal stem cells (MSCs) display immunosuppressive and anti- inflammatory properties and their putative therapeutic role in a variety of inflammatory autoimmune diseases are currently under investigation. Joint destruction, caused by persistent inflammation, renders rheumatoid arthritis (RA) a possible clinical target for cartilage

and bone repair using MSCs. MSCs from umbilical cord matrix, or Whaton's jelly (ucmMSCs), have been shown to be able to be safely used in allogeneic applications due to both their lack of immunogenicity when compared to other MSC, and their marked capacity for localized immunosuppression. Furthermore, ucmMSCs have advantages over other MSCs due to their non-invasive ease of access, higher expansion potential and overall higher potency to differentiate into more diverse specialized cells originating from the three germ layers, including chondrocytes and osteoblasts. ECBio has developed proprietary technology to consistently isolate, expand, and cryopreserve well-characterized populations of ucmMSC ready to be used in cell-therapy protocols (MatrixStemR – www.ecbio.com). Quality results by ECBio show that ucmMSCs maintain MSC phenotype upon expansion namely, the capacity to adhere to plastic, their fibroblast-like shape, are positive for CD44, CD73, CD90 and CD105, and negative for CD14, CD31, CD34, CD45, CD19 and HLA-DR surface markers, are capable to differentiate into adipocytes, chondrocytes and osteoblasts. Karyotype analysis has demonstrated that expansion up to passage 15 does not affect genome stability, and unlike embryonic stem cells, there were no signs of teratoma formation in mice, even at higher passages. An animal adjuvant arthritis model treated with human ucmMSC has shown faster remission of Rheumatoid arthritis when compared to controls, as seen by a statistically relevant 20% lower Arthritic Index (AI) in the groups where ucmMSC were administered by either intra articular (i.a.) or intraperitoneal (i.p.) injections. These results were confirmed by macroscopic observations of treated groups that appeared full symptomatic recovery 30 days after treatment. In summary, ucmMSC seem to be an effective and promising new approach for treating arthritic symptoms.

P85

PROTECTIVE EFFECT OF SOY PROTEIN ON COLLAGEN-INDUCED RHEUMATOID ARTHRITIS IN RAT

M. Mohamad Shahi[1], F. Haidari[1], M.R. Rashidi[2], S. Mahboob[3], B. Rashidi[4]

[1]Nutrition Dept., Ahvaz Jondishapour University of Medical Science, Ahvaz; [2]Drug Applied Research Center; [3]Nutrition Dept., Nutrition Research Center, Ahvaz; [4]Schools of Medicine, Esfahan University of Medical Sciences (ANATOMY), Esfahan, Islamic Republic of Iran

Objective: To evaluate preventive and therapeutic effects of soy protein on collagen-induced Rheumatoid arthritis (RA) rats. Methods: Sprague-Dawley rats immunized with bovine type II collagen emulsified in adjuvant and treated with soy protein (7 g/kg), dexamethasone (1 mg/kg) and casein (in control groups) by daily gavages feedings for 30 days. Score of arthritis recorded every day for each paws of animal. TNF-α, IL-6, leptin and adiponectin were measured in serums. Results: Treatment with soy protein resulted in significant delay in time to onset of arthritis as well as significantly decreased arthritis incidence, clinical arthritis severity score, histopathological arthritis severity score, and in vivo cell mediated immunity to collagen ($p<0.05$). Administration of soy protein significantly suppressed the progression of collagen II- induced arthritis (CIA) and inhibited the production of TNF-α, IL-6, leptin and adiponectin. Conclusion: Soy protein appeared to be a potent immunomodulatory inhibitor of CIA in rats. It could delay onset of RA and reduced cartilage erosion and synovitis inflammation. Therefore, it may be a useful protein in the prevention and treatment of RA patient.

P86

VARIATIONS IN DOSES OF INFLIXIMAB USED IN PUBLIC SERVICE IN NORTHEASTERN BRAZIL

A.L. Borges Pinheiro[1], **R. Pimentel**[1], M. de Alencar[1], H. Forte[1], F. Klein Leitão[1], K. Botelho[1], M.V. Freitas[1]

[1]Federal University of Ceará, Fortaleza, Brazil

The cost of treatment with immunobiological may vary the dose for each patient. In order to evaluate the variations in the doses used in infusions of infliximab in the treatment of rheumatoid arthritis (RA) were reviewed medical records of 13 patients (9 women) followed at the Hospital Geral César Cals. All patients underwent at least four infliximab infusions (mean = 8.8, SD = 4.8). The average dose of infliximab administered was 220mg, while the average weight of patients was 61.4 kg (SD = 10.3), giving relationship dose / weight equal to 3.6 mg / kg. In the first infusion the average dose was 3.5 mg / kg and at the last infusion evaluated was 3.7 mg / kg, so there was no significant variation between the average dose infused in the begin of the treatment and after, at least, four infusions of infliximab. The observation of the relative change of doses during the treatment revealed that three patients (23%) were unchanged in their doses, six (46%) required dose escalation to achieve clinical improvement and four (31%) had their dose reduced during treatment. Only one patient required a reduction of time between infusions ranges from eight to seven weeks, maintaining the administered dose. It can be concluded that although there was a need for increased dose of infliximab for the clinical management in nearly half of patients with RA, the impact of this change in average dose was insignificant because the dose was reduced on about one-third of the treated patients.

P87

THE EFFECT OF BEVACIZUMAB TREATMENT ON A MODEL OF RHEUMATOID ARTHRITIS (RA)

C. Tomos[1], S. Tsartsalis[1], N. Siskos[1], C. Emmanouilides[3], K. Kallaras[2], M. Mironidou-Tzouveleki[1]

[1]A' Laboratory of Pharmacology; [2]Department of Physiology, Medical School, Aristotle University of Thessaloniki; [3]Interbalkan Medical Cente, Thessaloniki, Greece

Introduction: Understanding the role of vascular endothelial growth factor (VEGF) in the pathogenesis of RA suggests new horizons in the treatment of RA. Aim: To investigate the therapeutic effects of intra articular (ia) injection of bevacizumab, a humanized anti-VEGF monoclonal antibody, in an animal model of RA in vivo. We used rabbits with antigen-induced arthritis (AIA), a well-known experimental model of RA. Methods: Pre-immunized female New Zealand white rabbits weighing 4-5 Kg were used in the study. 24h after arthritis induction using ovalbumin, the animals (N=10) were anesthetized and randomized into two groups. One group (N=5) served as the disease control and was subjected to two ia injections of 0.05 mL of 0.9% NaCl on days 1, 14. Second treatment group (N=5) was also subjected to the same dosing regimen using ia injections of 1.25 mg/0.05 mL of bevacizumab. All animals were sedated and sacrificed 28 days after arthritis onset. To evaluate the grade of arthritis/inflammation, we measured the joint swelling, defined as increase in extended knee diameter from normal, using caliper and observed the grade of pannus formation as follows: 0, no involvement;1, mild; 2, moderate; and 3, severe. Statistical analysis was performed in SPSS-19, $p<0.05$. Results: Treatment with bevacizumab significantly decreased pannus formation ($p<0.05$, *t*-Student) and reduced joint swelling in rabbits with AIA ($p<0.05$, ANOVA) compared to control group. Conclusion: Arthritis is ameliorated by ia injections of bevacizumab. However further research is necessary in order to prove its efficacy and establish its usefulness in the treatment of RA.

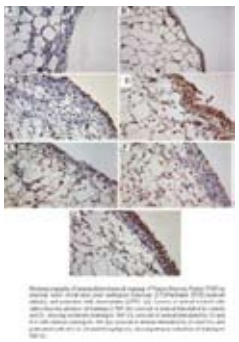
Translational Science

P88

ATORVASTATIN ATTENUATES INFLAMMATORY AND NOCICEPTIVE RESPONSE IN AN EXPERIMENTAL ARTICULAR INCAPACITATION MODEL POTENTIATED BY PACLITAXEL

V. Alencar[1], H. Forte[2], M. Cardoso[1], A. Braga[1], G.A. Brito[1], M. Vale[1], R. Ribeiro[1]
[1]*Universidade Federal do Ceara;* [2]*Federal University of Ceará, Fortaleza, Brazil*

Paclitaxel (PCX) is an important and wide broad antineoplastic agent used in chemotherapy of various solid tumors. Fatigue and musculoskeletal symptoms, including joint pain and myalgia, are common side effects of PCX-treatment in up to 68% of the patients, 8% of which present severe symptoms with potential impairment to physical function and quality of life. The involvement of TNF-α in the pathogenesis of these affections has been demonstrated and provides potential therapeutic target. It has been shown that Atorvastatin, a largely used statin, attenuates plasma levels and mRNA expression of TNF-α in myocardial ischemia-reperfusion injury in rats. In the present study, initially we demonstrate that the intraperitoneal injection of Paclitaxel (8mg/kg) significantly potentiates the inflammatory and nociceptive response induced by injection of Zymosan (250 µg/animal) in rat knee joint. The methods used to demonstrate these effects were the paw elevation time in a rat knee joint incapacitation model and the expression of TNF-α, IL-1β, IL-6 and CINC-1 in the synovial fluid and of TNF-α in the immunohistochemical staining. Afterwards, the pretreatment of the animals with Atorvastatin (3, 10, 30 mg/kg, oral, 3 days) significantly attenuates TNF-α levels in the synovial fluid and its immunoexpression in synovial tissue. The rat knee joint incapacitation induced and potentiated by Zymosan and Paclitaxel treatment, respectively, is also significantly inhibited by Atorvastatin pretreatment. Therefore, these results show, for the first time, an animal model of the articular nociceptive response potentiated by Paclitaxel, with TNF-involvement, and provides a possible therapeutic agent for its management with Atorvastatin.



P89

LOW LEVEL LASER THERAPY INDUCES DIFFERENTIAL EXPRESSION OF OSTEOGENIC GENES DURING BONE REPAIR IN RATS

P. Bossini[1], E. Fávaro-Pípi[2], J. Ribeiro[2], P. Oliveira[2], N. Parizotto[2], C. Tim[2], H. Araújo[2], D. Ribeiro[1], A.C. Rennó[1]
[1]*Department of Biosciences, Federal University of São Paulo, Santos;*
[2]*Department of Physiotherapy, Federal University of São Carlos, São Carlos, Brazil*

The aim of this study was to measure the temporal pattern of the expression of osteogenic genes after low level laser therapy during the process of bone healing. We used quantitative real-time polymerase chain reaction (qPCR) along with histology to assess gene expression following laser irradiation on created bone defects in tibias of rats. The animals were randomly distributed into two groups: control or laser-irradiated group. Noncritical size bone defects were surgically created at the upper third of the tibia. Laser irradiation started 24 h post-surgery and was performed for 3, 6, and 12 sessions, with an interval of 48 h. A 830 nm laser, 50 J/cm^2, 30 mW, was used. On days 7, 13, and 25 post-injury, rats were sacrificed individually by carbon dioxide asphyxia. The tibias were removed for analysis. The histological results revealed intense new bone formation surrounded by highly vascularized connective tissue presenting slight osteogenic activity, with primary bone deposition in the group exposed to laser in the intermediary (13 days) and late stages of repair (25 days). The quantitative real-time PCR showed that laser irradiation produced an upregulation of BMP-4 at day 13 post-surgery and an upregulation of BMP4, ALP and Runx-2 at day 25 after surgery. Our results indicate that laser therapy improves bone repair in rats as depicted by differential histopathological and osteogenic genes expression, mainly at the late stages of recovery.

P90

LOW LEVEL LASER THERAPY ASSOCIATED WITH A BIOSILICATE® INCREASE IN BONE DEPOSITION AND INDENTATION BIOMECHANICAL PROPERTIES OF CALLUS IN RATS

P. Bossini[1], R. Fangel[2], D. Ribeiro[1], C. Wang[2], K. Nonaka[2], P. Driusso[2], N. Parizotto[2], J. Oishi[2], A.C. Rennó[1]
[1]*Department of Biosciences, Federal University of São Paulo, Santos;*
[2]*Department of Physiotherapy, Federal University of São Carlos, São Carlos, Brazil*

We investigate the effects of a novel bioactive material (Biosilicate®) and low level laser therapy (LLLT), at 120 J/cm^2, on bone fracture consolidation in rats. The animals are randomly divided into four groups, with 10 animals each: bone defect control group; bone defect filled with Biosilicate group; bone defect irradiated with laser at 120 J/cm^2 group; bone defect filled with Biosilicate and irradiated with LLLT, at 120 J/cm^2 group. Laser irradiation is initiated immediately after surgery and performed every 48 h for 14 days. Histopathological analysis points out that bone defects are predominantly filled with the biomaterial in specimens treated with Biosilicate. In the 120 J/cm^2 laser plus Biosilicate group, the biomaterial fills all bone defects, which also contained woven bone and granulation tissue. Also, the biomechanical properties are increased in the animals treated with Biosilicate associated to laser therapy. Our results indicate that laser therapy improves bone repair process in contact with Biosilicate as a result of increasing bone formation as well as indentation biomechanical properties.

P91

PARTICIPATION OF NITRIC OXIDE (NO) AND ATP-SENSITIVE POTASSIUM CHANNELS (KATP) ON THE ANTINOCICEPTIVE EFFECT OF ZOLEDRONIC ACID IN EXPERIMENTAL MODELS

H. Forte[1], V. Alencar[1], A. Araújo[1], C. Amaral[1], R. Ribeiro[1], M. Vale[1]
[1]*Universidade Federal do Ceara, Fortaleza, Brazil*

Zoledronic acid (ZA), a bisphosphonate used on the treatment of bone metastasis, has been noticed a possible analgesic agent. The aim of this study was to evaluate the antinociceptive effect of ZA upon zymosan-induced writhing test (WT) in mice and zymosan-induced articular incapacitation (AI) on rat knee joint. Male Wistar rats were pretreated with saline, ZA(10-300µg/kg; i.p.) or ZA(20ug/cavity; intraarticular), 30 min after they received Zymosan (intrarticular,1mg/animal) and were evaluated during 1 min every hour until the 4th hour for the AI. The effect of postreatment with ZA was also evaluated. The number of migrating cells was also investigated. Male Swiss mice were pretreated with saline or ZA (10-100µg/kg) 30 min before zymosan (1mg/animal, i.p.) and the number of writhes were counted. Mice were also pretreated with L-NAME, L-arginine, Glibenclamide and diazoxide before ZA. Either i.p. or i.a. ZA inhibited AI (52,7%,i.p and 41% i.a. $p<0.05$) when compared to Sal group but did not inhibit cell migration to articular cavity. The ZA postreatment

enhanced Zymosan nociceptive activity by 123%. In WT, ZA demonstrated antinociceptive effect (-72%, p<0.05). L-NAME reverted ZA antinociceptive activity (99,09%, p<0.05) which was prevented by L-arginine (75%, p<0.05). Glibenclamide also reverted the ZA antinociceptive effect in the WT(71% p<0.05) which was prevented by diazoxide (100%, p<0.05). We suggest that ZA has preventive antinociceptive activity rather than an anti-inflammatory effect. The antinociceptive effect did not occur with the postreatment protocol. Probably the antinociceptive activity is linked with nitric oxide production and subsequent opening of potassium channels.

P92

HIGH ARTICULAR LEVELS OF THE ANGIOGENETIC FACTORS VEGF AND VEGF-RECEPTOR 2 AS TISSUE HEALING BIOMARKERS AFTER SINGLE BUNDLE ANTERIOR CRUCIATE LIGAMENT RECONSTRUCTION

L. De Girolamo[1], P. Randelli[2], P. Volpi[1], G. Dogliotti[3], A. Quaglia[1], G. Banfi[1,4], P. Cabitza[2], M.M. Corsi[3], M. Denti[1], **E. Galliera[3]**
[1]IRCCS IStituto Ortopedico Galeazzi; [2]Dipartimento di Scienze Medico-Chirurgiche; [3]Dipartimento di Morfologia Umana e Scienze Biomediche-Città Studi; [4]Dipartimento di Tecnologie per la Salute, Università Degli Studi di Milano, Milano, Italy

Meniscal repair and anterior cruciate ligament reconstruction can be positively correlated by the modulation of healing response of meniscal fibrochondrocytes by growth factors released with intra-articular bleeding analysis of vascular endothelial growth factor (VEGF) and its receptors, VEGFR1 and VEGFR2, may be useful in the clinical assessment of bone and soft-tissue remodeling.. We measured systemic and local levels of VEGF (VEGF165), VEGFR1 and VEGFR2 after either arthroscopic partial meniscectomy (APM) or single-bundle anterior cruciate ligament reconstruction (ACLR) in order to determine the local effect of bone tunneling and notchplasty on the release of these growth factors. At the end of the operation, knee joint fluid and blood samples were collected and VEGF, VEGFR1 and VEGFR2 concentrations were determined by enzyme-linked immunosorbent assay (ELISA). No significant differences in VEGF, VEGFR1 or VEGFR2 concentrations in the venous blood were observed between the two groups. In contrast, VEGF and VEGFR2 levels were significantly higher in the knee joint fluid of the ACLR group; furthermore, VEGF and VEGFR1 were significantly higher in the knee joint fluid than in the venous blood, whereas VEGFR2 was lower in the knee joint fluid than in the venous blood. Local release of VEGF and its angiogenetic receptor VEGFR2, but not its negative regulator VEGFR1, was significantly higher after ACLR than after APM, indicating a better vasculogenic potential for enhanced bone-graft and meniscus healing. These results could suggest that VEGF and VEGFRs could be considered good biomarkers of tissue healing after knee joint surgery

P93

MOLECULAR STUDY OF PORPHYROMONAS GINGIVALIS-DERIVED LIPOPOLYSACCHARIDE ON PERIODONTAL BONE DISEASE

T-I. Kim[1], K.M. Woo[2], T. Seo[3]
[1]Department of Periodontology; [2]Department of Cell and Developmental Biology, Seoul National University; [3]Department of Life Science, Dongguk University, Seoul, Republic of Korea

Periodontal bone disease is caused by detachment of periodontal ligament from the surrounding alveolar bone and finally leads to the loss of teeth. Periodontal ligament has an important function in maintaining alveolar bone. Previous studies showed that PDL fibroblasts (PDLFs) have the potential to differentiate into osteoblasts. Porphyromonas gingivalis (P.g.), which has pathogenicity for periodontal bone destruction, contains lipopolysaccharide (LPS). However, P.g.-derived LPS-induced PDLFs responses are not well characterized. Therefore we selectively cultured human PDLFs with P.g.-derived LPS and investigate their various responses through proteome profiling, real-time PCR, alkaline phosphatase (ALP) activity test, and bone mineralization assay. Proteome profiling results showed that p38, ERK, JNK, STAT, p53, RSK, and MSK levels were affected by P.g.-derived LPS treatment. Increased phosphorylation of ERK and p38 was prominent. The level of Cytochrome c was increased following LPS exposure. P.g.-derived LPS also resulted in the alteration of caspase-3 to its active form. Morphological changes and apoptosis were observed in LPS-treated PDLFs. Finally, when PDLFs were cultured with differentiation media, P.g.-derived LPS reduced the expression of differentiation marker genes, as well as reducing ALP activity and mineralization. Consequently, we have confirmed that P.g.-derived LPS regulated levels of signaling pathway proteins, as well as cytokines and apoptotic proteins. Moreover, P.g.-derived LPS suppressed the capacity of PDLFs to differentiate into osteoblasts. These results provide new information regarding the mechanisms by which P.g. can induce periodontal bone diseases.

P94

THE USE OF IONISING RADIATON IN THEATRES – ARE WE OVER EXPOSING OUR PATIENTS AS ORTHOPAEDIC SURGEONS?

C. Lamb[1], N. Unnikrishnan[1], P. Pidikiti[1], N. Emms[1]
[1]Orthopaedics Dept., Whiston Hospital, Liverpool, UK

The use of ionizing radiations (X-rays) in orthopaedic theatre has increased with the advent of newer fixation techniques. X-rays in high dose are harmful to tissues. The objective of this study was to correlate the radiation exposure incurred by trauma patients undergoing surgery to the experience of the operating surgeon and to identify if the radiation exposure was compliant with national guidance of annual patient radiation exposure (IRR 1999). Data was prospectively collected during August 2010 to September 2011. The procedures included fractures of the distal radius, neck of femurs, nailing of femurs and tibia, ankle fractures, manipulations under anaesthesia of the distal radius and dislocated total hip replacements. The data was tabulated for the procedure, the grade of the surgeon operating, the time and total exposure dose of the radiation. The time and radiation dose was retrieved for the fluoroscopy machines. Out of the 140 patients who underwent any of the procedures 70 were operated by the trainee and the rest by an orthopaedic consultant. Out of all the procedures except for intramedullary tibial nailing and ankle fixation the consultants used more radiation doses when compared to the trainee. The mean radiation dose for any given procedure was 0.35 milli Sievert (0.01 – 0.70) and the mean time was 24.6 seconds (0.9 – 139.89 seconds). Our results showed the experienced surgeons seem to use more time and radiation doses compared to the orthopaedic trainee possibly because they tend to take up the more complex cases. Nevertheless, the amount of radiation exposure is still well under the national accepted guidance. This suggests that the operating surgeon can be free from judgment for risk of excessive radiation to the patient and to use the image intensifiers judiciously to ensure the best possible clinical outcome.

P95

OPTIMAL SERUM 25-HYDROXYVITAMIN D3 LEVELS ON PHYSICAL FITNESS IN COMMUNITY-DWELLING PRE-FRAIL WOMEN

J. Okuno[1], S. Tomura[3], H. Yanagi[1], T. Fukasaku[2], T. Okura[2], K. Tanaka[2]
[1]Institute of Medical Science; [2]University of Tsukuba, Tsukuba; [3]University of Urawa, Urawa, Japan

Aim: The aim of this study was to evaluate the optimal level of serum 25-hydroxyvitamin D_3 ($25(OH)D_3$) on mobility, balance, and muscle strength in community-dwelling pre-frail elderly women in Japan. Methods: A longitudinal survey was conducted in a town (latitude 36 degrees north). Eighty women aged 65 years and over attended a 3-month exercise class. A face-to-face interview was conducted based on a questionnaire. The serum levels of $25(OH)D_3$, intact parathyroid hormone (iPTH), were measured. Nine physical fitness tests were

performed at baseline and at the end of a 3-month follow-up period. Results: Among 80 subjects, 56.3% experienced falls, and 71.3% experienced stumbling more than once during the past year. The prevalence of $25(OH)D_3$ < 50 nmol/l or $25(OH)D_3$ < 75 nmol/l were 27.5% and 88.8%, respectively. Significantly greater improvements in alternate step: muscle strength, functional reach (FR): balance, "timed up & go" (TUG), and 5-m walk: mobility, and superior functional capacity for the subjects with $25(OH)D_3$ levels greater than 67.5 nmol/l (highest quartile) was observed at the end of the class. In contrast, the subjects with $25(OH)D_3$ levels < 47.5 nmol/l (lowest quartile) did not improve their physical fitness. Conclusions: A serum $25(OH)D_3$ level of greater than 47.5 nmol/l may therefore be necessary to maintain mobility and balance. Greater than 67.5 nmol/l appears to be preferable for lower-extremity muscle strength in Japanese pre-frail elderly women.

P96

COMPARATIVE STUDY OF THE EFFECTS OF LOW INTENSITY PULSED ULTRASOUND AND LOW LEVEL LASER THERAPY ON BONE DEFECTS IN TIBIAS OF RATS

P. Bossini [1], E. Fávaro-Pípi[2], S. Feitosa[1], D. Ribeiro[1], P. Oliveira[2], N. Parizotto[2], **A.C. Rennó[1]**

[1]Department of Biosciences, Federal University of São Paulo, Santos; [2]Department of Physiotherapy, Federal University of São Carlos, São Carlos, Brazil

The aim of this study was to investigate and to compare the effects of low intensity ultrasound (LIPUS) and low level laser therapy (LLLT) during the process of bone healing by means of histopathological and morphometric analysis. The animals were randomly distributed into three groups of 30 animals each: the control group (bone defect without treatment); the laser-treated group: (bone defect treated with laser), and the LIPUS-treated (bone defect treated with ultrasound). Each group was further divided into three different subgroups (n = 10) and on days 7, 13, and 25 post-injury, rats were killed with an intra-peritoneal injection of general anesthetic. The rats were treated with a 30 mW/cm^2 low intensity pulsed ultrasound and a 830 nm laser at 50 J/cm^2. The results showed intense new bone formation surrounded by highly vascularized connective tissue presenting a slight osteogenic activity, with primary bone deposition being observed in the group exposed to laser in the intermediary (13 days) and late stages of repair (25 days). This was confirmed by morphometric analysis in which significant statistical differences ($p < 0.05$) were noticed when compared to the control. No remarkable differences were noticed in the specimens treated with ultrasound with regard to the amount of newly formed bone in comparison to the control group. Taken together, our results indicate that laser therapy improves bone repair in rats as depicted by histopathological and morphometric analysis, mainly at the late stages of recovery. Moreover, it seems that this therapy was more effective than US to accelerate bone healing.

P97

HUMAN PLATELET RICH PLASMA AS A XENOGENIC PLATELET-RICH PLASMA EFFECTS ON CRITICAL SIZE BONE DEFECT HEALING IN RABBIT MODEL: CLINICAL, RADIOLOGICAL AND BIOMECHANICAL EVALUATION

Z. Shafiei-Sarvestani[1], A. Bighamsadegh[1]

[1]Department of Veterinary Surgery and Radiology, Shahrekord University, Faculty of Veterinary Medicine, Shahrekord, Islamic Republic of Iran

A lot of studies have been performed to investigate the effect of Platelet-rich plasma (PRP) upon bone defect regeneration. Platelet-rich plasma is clinically used as an autologous blood product to stimulate bone formation *in vivo*. The aim of the present study was to assess the effects of human PRP (xenogeneic PRP) on new bone formation in a critical diaphyseal long bone defect in rabbit model. A critical size defect (10 mm) in the radial diaphysis of 12 rabbit was created and then supplied with human PRP (treatment group) or the defect left empty (control group). Platelets in the PRP were about 10.1 fold compared to normal blood. Radiographs of each forelimb was taken postoperatively on 1st day and at the 2nd, 4th, 6th and 8th weeks post injury to evaluate bone formation, union and remodeling of the defect. The operated radiuses were removed on 56th postoperative day and were evaluated for gross signs of healing. In addition, biomechanical test was conducted on the operated forearms of the rabbits. This study demonstrated that human PRP (hPRP), as a xenogeneic PRP, could promote bone regeneration in critical size defects with a high regenerative capacity. The results of the present study demonstrated that hPRP could be an attractive alternative for reconstruction of the major diaphyseal defects of the long bones in animal models.

P98

THE STUDY OF NUTRITIONAL KNOWLEDGE OF TYPE 2 DIABETIC PATIENTS ATTENDING AHWAZ GOLESTAN HOSPITAL IN 2009

E. Shirbeigi

Medical Specialities, Ahvaz Jondishapour University of Medical Science, Ahvaz, Islamic Republic of Iran

Background & Objective: One of the basic principles in prevention of complications in diabetic patients is promotion of patients' knowledge level with regard to treatment method, signs, complications and nutrition. The goal of the present study was to determine knowledge level of type 2 diabetic patients who attended endocrine clinic of Golestan Hospital. Method: By a cross-sectional study, 130 known type 2 diabetic patients who had referred to endocrine clinic of Golestan Hospital were assessed through convenience sampling. Method of collecting data was a questionnaire with 2 parts filled out by interview. In part one, demographic characteristics and in part two, nutritional knowledge level of patients was studied. SPSS version 16 was used for data analysis. Findings: Average score of knowledge with regard to types of dietary subgroups was: 16.2 out of 21 for bread and cereals, 15.2 out of 21 for meat, 12.4 out of 20 for dairy products, 11.5 out of 21 for lipids, 11.8 out of 15 for vegetables, 11.6 out of 17 for fruits, and 15.8 out of 21 for others. Overall mean of knowledge was 94(±12) out of 130. Conclusion: Nutritional knowledge level of diabetic patients in this study was average. Considering this result, control of diabetes complications with proper education can be useful.

P99

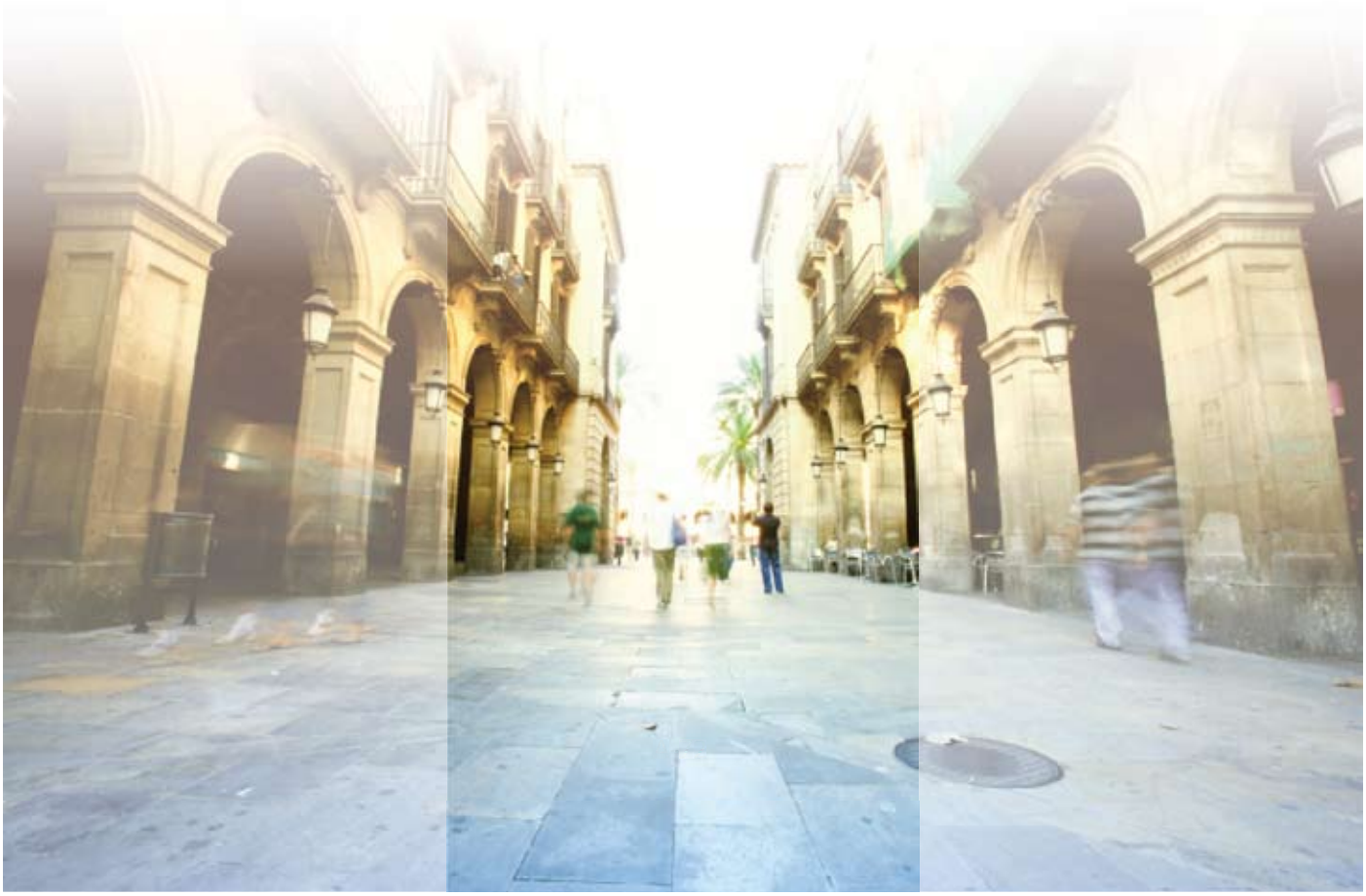
EFFECTS OF LOW LEVEL LASER THERAPY AND SCAFFOLD OF BIOSILICATE® IN THE PROCESS OF BONE REPAIR

C. Tim[1], K. Zambone Pinto[2], B. Rossi[1], M. Crovace[3], O. Peitl-Filho[3], A.C. Rennó[4]

[1]Department of Physiotherapy; [2]Department of Pathology; [3]Department of Materials Science and Engineering, Federal University of São Carlos, São Carlos; [4]Department of Biosciences, University Federal of São Paulo, Brazil

Several resources have been studied in order to accelerate the process of bone repair. Among these resources, bioactive materials and low level laser therapy (LLLT) have gained prominence. Within this context, this project aimed to assess the effects of LLLT (λ = 830nm), with the fluencies of 120J/cm² and scaffold Biosilicate®, used associated or not, on consolidation of induced tibial bone defects in the rats. In this study it was used 40 male Wistar rats divided into four groups: group control bone defect without any treatment (GC), group bone defect irradiated with LLLT (GL); group bone defect treated with implantation of scaffolds Biosilicate® (GB); group bone defect treated with implantation of scaffolds Biosilicate® and LLLT (GBL). The animals were submitted to laser irradiation (830nm, 100mW) at a single point on the bone defect for eight sessions, on alternate days. The euthanasia of animals occurred at day 15 after surgery, 24 hours after the last laser treatment session. Morphological analysis revealed that the laser group, showed better tissue organization in relation to other groups. Furthermore, morphometric analysis revealed that the irradiated animals showed a higher amount of newly formed bone compared to the other groups. The expression of COX-2 and RUNX-2 were higher in GB and GBL groups. Our findings indicate that both

treatments had osteogenic potential 15 days after surgery, but the LLLT was more effective in bone repair when compared to the biomaterials, or even when the two treatment modalities were associated.



WORLD CONGRESS

on Debates & Consensus

in Bone, Muscle & Joint Diseases

INDEX

BMJD

World Congress

on Debates & Consensus

BMJD

World Congress

on Debates & Consensus

BMJD

World Congress

on Debates & Consensus

BMJD

World Congress
on Debates & Consensus

in Bone, Muscle & Joint Diseases

BMJD

2nd WORLD CONGRESS

on Debates & Consensus

in Bone, Muscle & Joint Diseases

Mark Your Calendar

Brussels, Belgium

October 3-6 2013

GL events | CongressMed

GL events | CongressMed
20 Lincoln St. | 67134 Tel Aviv | Israel
Tel. +972 73 706 6950 | Fax: +972 73 706 6959

Contact Information
www.congressmed.com/bmjd

bmjd@congressmed.com
www.facebook.com/bmjd