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Can vitamin D boost production and circulating cathelicidin levels?

Jeremie Talvas, Guillaume Martinroche, Kassandra Lanchais, Stéphanie Rouge,
Nicolas Goncalves-Mendez, Marie-Paule Vasson

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PARIS - France
March 21-23, 2017

16th **F**at
Soluble
Vitamins



C O N G R E S S



*Société Française
Vitamines & Biofacteurs*

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WELCOMING MESSAGE



The French Society for Vitamins and Biofactors (SFVB) and the Scientific Committee invite you to join the XVIe Fat Soluble Vitamins Congress. Started in 1960 in the UK then touring Europe every 4-5 years, the last XVe FSV has been held in Kalabaka (Greece, 2012) and was organized by Dr. Anargyros Moulas. The present Committees followed the general guidelines of these meetings to present participants with an overview of the most recent knowledge on diverse aspects of Fat Soluble Vitamins. Since the discovery of these vitamins in the 1900s, many studies have been conducted to characterize their chemical structures, their metabolism and the mechanisms of their biological actions.

Today, the on-going studies still investigate their potential beneficial role on metabolic disorders, underlying some worldwide spread diseases such as obesity and related diseases. The present meeting precisely plans update the most recent data in this respect, and it is hopefully expected to bring new perspectives and extension of the acquired knowledge. The final schedule of the meeting will be built when all the participants' contributions are sent to the scientific committee.

Papers on improved analytical aspects, on new findings on absorption and bioavailability, and on the use of high throughput technologies for an integrated view are all welcome. Data on the recent strategies to alleviate deficiency of fat soluble vitamins in developing and emerging countries are also welcome. Modern societies are nowadays interested not only in the nutritional value of foods but also in disease prevention and health promotion. Under this perspective epidemiological and clinical studies on the health effects of fat soluble vitamins and papers about functional foods with fat soluble compounds are expected. The meeting will also attempt to open the question on whether some other fat soluble biofactors can exhibit vitamin-like effects. Besides some expected works recently undertaken, this topic will be illustrated with lutein-zeaxanthin, as described through their specific accumulation in the macula and their relationships with age-related macular degeneration. This open-mind proposals aims at targeting the young scientists who are particularly wished and expected to participate. Help to participate in the meeting and attractive poster awards will be offered to them.

With your contribution, the Scientific Committee will set up an attractive scientific program that will allow to listen to outstanding international speakers. We are delighted to already welcome you in France and to discover the romantic Paris capital during the wonderful spring season.

Edmond Rock
President of the congress



COMMITTEES

ORGANIZING



Agnès Dauvergne
Biochemistry Laboratory,
Beaujon Hospital, Paris, France



Anargyros Moulas
TEI of Thessaly, Larissa, Greece



Jocelyne Draï
Biochemistry Department,
Hospices Civils of Lyon,
France



Edmond Rock
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Institution, City, France



Stéphanie Lemaire
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SCIENTIFIC



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TEI of Thessaly, Larissa, Greece



Volker Böhm
Institute of Nutrition, FSU
Jena, Germany



Serge Rezzi
Nestlé Institute of Health Sciences,
Lausanne, Switzerland



Patrick Borel
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Marseille University, Marseille,
France



Edmond Rock
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Elina Hyppönen
University of South Australia,
Adelaide, Australia



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PROGRAM AT A GLANCE

TUESDAY MARCH 21, 2017

5.30-6.30pm	WELCOMING PARTICIPANTS
6.30-6.50pm	WELCOME & INTRODUCTION
6.50-7.30pm	OPENING CONFERENCE

WEDNESDAY MARCH 22, 2017

8.00-8.30am	WELCOMING PARTICIPANTS
8.30-10.40am	SESSION 1 - VITAMIN E
10.40-10.50am	FLASH POSTERS
10.50-11.20am	Coffee break
11.20-11.50am	FLASH POSTERS
11.50-12.40pm	SESSION 2 - VITAMIN K
12.40-1.00pm	Meeting for planning future network for H2020 call
1.00-2.15pm	Lunch
2.15-2.50pm	Posters session
2.50-4.50pm	SESSION 3 - VITAMIN D
4.50-5.20pm	Coffee break
5.20-7.10pm	SESSION 3 - VITAMIN D
7.30-9.00pm	SYMPOSIUM ON VITAMIN D - Round table & Dinner Venue: Restaurant «Au réveil Samaritain» - 3 Boulevard Saint-Jacques

THURSDAY MARCH 23, 2017

8.30-10.00am	SESSION 4 - FAT SOLUBLE VITAMINS
10.00-10.30am	Coffee break
10.30-11.20am	SESSION 4 - FAT SOLUBLE VITAMINS
11.20-12.20pm	POSTERS SESSION
12.20-2.00pm	Lunch
2.00-3.30pm	SESSION 5 - CAROTENOIDS
3.30-4.00pm	Coffee break
4.00-5.50pm	SESSION 6 - VITAMIN A
5.50-6.15pm	CLOSING SESSION - Edmond Rock, President



GENERAL INFORMATION

CONGRESS VENUE



FIAP JEAN MONNET

30 Rue Cabanis

75014 Paris

Metro: Line 6 > Nation/Charles de Gaulle-Étoile
Stop: Glacière

LUNCHES

You will have to present your ticket (distributed at the registration desk) to access the cafeteria.

COFFEE BREAKS

Enjoy coffee breaks to meet our quality partners and discover the posters.

POSTERS

The posters will be displayed in two spaces:

- | | | |
|--|--------|--|
| - VITAMIN E: Oslo room (Level -1) | Colour | |
| - VITAMIN K: Oslo room (Level -1) | Colour | |
| - VITAMIN D: Exhibition Hall (Hall 0) | Colour | |
| - VITAMIN A: Oslo room (Level -1) | Colour | |
| - FAT SOLUBLE VITAMINS: Oslo room (Level -1) | Colour | |
| - CAROTENOIDS: Oslo room (Level -1) | Colour | |

ROUND TABLE & DINNER

«Strengths and weakness» of supplemental vitamin D - Chair: Professor Simin Meydani (Boston, USA).
Venue: Restaurant «Au Réveil Samaritain» - 3 Boulevard Saint-Jacques - Price: 70€

SPEAKERS PRESENTATIONS

We will post speakers' presentations on the official website of the congress after the event (only those for which we have permission).

WIFI CONNECTION

You can have a free access to the FIAP WIFI. Name in the WIFI list: wifiap
You just have to give your email address when the internet page will open.



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SCIENTIFIC PROGRAM

■ TUESDAY MARCH 21, 2017

- 5.30-6.30pm WELCOMING PARTICIPANTS (Registration & Refresh)
- 6.30-6.50pm **WELCOME & INTRODUCTION**
Dr. Edmond Rock - President of the congress - INRA, Clermont-Ferrand, France
- 6.50-7.30pm **OPENING CONFERENCE**
Pr. Simin Meydani - USDA HNRCA at Tufts University, Boston, USA
Fat Soluble Vitamins: Where research has taken us, and where it is headed.

■ WEDNESDAY MARCH 22, 2017

- 8.00-8.30am WELCOMING PARTICIPANTS
- 8.30-10.40am** **SESSION 1 – VITAMIN E**
Chair: Pr. Simin Meydani & Serge Rezzi
- 8.30-9.00 **KEY NOTE – Pr. Manfred Eggersdorfer** - DSM Society, Kaiseraugst, Switzerland
Tocopherol – a systematic review of intake and status globally.
- ORAL COMMUNICATIONS**
- 9.00-9.20 **Francesco Galli** - University of Perugia, Perugia, Italy
Vitamin E metabolism and function.
- 9.20-9.40 **Lisa Schmölz** - Friedrich Schiller University Jena, Jena, Germany
Contribution of the structure of tocopherols and their long-chain metabolites to their biological effects.
- 9.40-10.00 **Jan Frank** - Institute of Biological Chemistry and Nutrition, Stuttgart, Germany
The long chain metabolite -tocopherol-13-COOH may be responsible for the induction of xenobiotic enzymes previously attributed to the parent -tocopherol.
- 10.00-10.20 **Ann Anderson Berry** - University of Nebraska Medical Center, Omaha, USA
Maternal and Infant Dynamics of Vitamin E Tocopherols.
- 10.20-10.40 **Corrine Hanson** - University of Nebraska Medical Center, Omaha, USA
Pro-vitamin A Compounds and Tocopherol Levels in Mother-infant Pairs from Midwest USA and Correlations with Fetal Growth.
- 10.40-10.50am** **FLASH POSTERS**
- VITAMIN E**
- Charlotte Cuerq** - Hospices Civils de Lyon, Pierre-Bénite, France
Abetalipoproteinemia and chylomicron retention disease: efficacy of two formulations of vitamin E in a randomized cross over clinical study.

Gaspar Kocharyan - Institute of Chemical Physics NAS RA, Yerevan, Armenia
Nonadditive antioxidant effect (synergy, antagonism) of bioflavonoid mixtures with trolox: water-soluble analogue of vitamin E.

Kimitaka Takitani - Osaka Medical College, Osaka, Japan
Dehydroepiandrosterone alters vitamin E status and prevents lipid peroxidation in vitamin E-deficient rats.

10.50-11.20am

Coffee break

11.20-11.50pm

FLASH POSTERS

Chair: Elina Hypponen & Patrick Sauvant

VITAMIN D

Poorya Shojai - MAZYAR, Ghaemshahr, Iran
Development and Evaluation of bone tissue engineering scaffolds capable of controlled release of vitamin D.

Ina Jasutiene - Kaunas University of Technology, Kaunas, Lithuania
Fortification of foodstuffs by cold water soluble vitamin D₃ preparation.

Natalia Davydova - U.S.Pharmacopeia, Rockville, USA
Comprehensive evaluation of Cholecalciferol (Vitamin D₃) Dietary Supplement Tablets.

Charlotte Lauridsen - Aarhus University, Tjele, Danmark
Bioavailability of vitamin D in pregnant and lactating pigs and the relationship to health biomarkers.

Argjira Juniku-Shkololli - University Clinical Center of Kosovo, Prishtina, Albania
Evaluation of the risk for developing colitis-associated cancer in patients with inflammatory bowel disease: the role of vitamin D.

Catherine Féart - INSERM, Bordeaux, France
Lower vitamin D concentrations and higher long-term risk of dementia and Alzheimer's Disease.

Ludmila Macova - Institute of Endocrinology, Prague, Czech Republic
Vitamin D and other steroids in autism.

VITAMIN A

Imar Djibrine Soudy - INSTA, Abéché, Tchad
Vitamin A status in non-pregnant women eating traditionally spirulina (Dihé) in Chad.

Ronald Corbee - Utrecht University, Utrecht, The Netherlands
Chronic vitamin A toxicosis in cats.

Pierre-Jacques Brun - Columbia University, New York, USA
The dual role of retinoic acid signaling in modulating insulin and glucagon secretion.

11.50-12.40pm

SESSION 2 - VITAMIN K

Chair: Omar Benzakour & Edmond Rock

11.50-12.20

Omar Benzakour - INSERM, Poitiers, France

Vitamin K: a vitamin like no other

12.20-12.40

Catherine Desoto - University of Northern Iowa, Cedar Falls, USA

Speculations of possible implications of Vitamin K genotype differences

12.40-1.00pm

Meeting for planning future network for H2020 call (Serge Rezzi)

Information will be provided at indoor registration

1.00-2.15pm

Lunch

2.15-2.50pm

Posters session

2.50-4.50pm

SESSION 3 - VITAMIN D

Chair: Elina Hypponen & Robert Winwood

ORAL COMMUNICATION

2.50-3.10

Jean-François Landrier - INRA, Marseille, France

Vitamin D modulates adipose tissue biology: possible consequences on obesity ?

3.10-3.30

Andrius Bleizgys - Vilnius University, Vilnius, Lithuania

Vitamin D Levels of Out-Patients: Variability by Age Groups and Seasons.

3.30-3.50

Augusto Litonjua - Harvard Medical School, Boston, USA

Vitamin D Supplementation in Pregnancy to Prevent Asthma in Offspring - Results from the Vitamin D Antenatal Asthma Reduction Trial (VDAART).

3.50-4.10

Emmanuelle Reboul - NORT - INRA - INSERM, Marseille, France

ABCB1 is involved in vitamin D intestinal efflux.

4.10-4.30

Charles Desmarchelier - NORT - INRA - INSERM, Marseille, France

A Combination of Single-Nucleotide Polymorphisms Is Associated with the Interindividual Variability in Vitamin D Bioavailability in Healthy Men.

4.30-4.50

Anargyros Moulas & Elisabeth Katsianidou - TEI of Thessaly, Larissa, Greece

- Fortification of food for addressing vitamin D deficiency.

- Educational material for promoting vitamin D awareness.

4.50-5.20

Coffee break

5.20-7.10pm

SESSION 3 - VITAMIN D

Chair: Elena Angeloudi & Edmond Rock

5.20-5.50

KEY NOTE - Elina Hypponen - University of South Australia, Adelaide, Australia

Vitamin D: is it beneficial or even safe?

ORAL COMMUNICATION

- 5.50-6.10 **Robert Winwood** - DSM Nutritional Products, Kaiseraugst, Switzerland
Unexpected, pervasive Vitamin D deficiency in people living in the Middle East.
- 6.10-6.30 **Wolfgang Herrmann** - Saarland University, Homburg, Germany
One-year B and D vitamins supplementation improves metabolic bone markers and homocysteine metabolism.
- 6.30-6.50 **Jeremie Talvas** - INRA - CRNH Auvergne - Clermont-Ferrand, France
Can vitamin D boost production and circulating cathelicidin levels?
- 6.50-7.10 **Lauriane Bonnet** - NORT - INRA - INSERM, Marseille, France
Kinetic effect of high fat diet on vitamin D metabolism in mice.
- 7.30-9.00pm **SYMPOSIUM ON VITAMIN D - ROUND TABLE & DINNER**
«Strengths and weakness» of supplemental vitamin D
Chair: Pr. Simin Meydani
Speakers: Elena Angeloudi, Elina Hypponen, Edmond Rock
Venue: Restaurant «Au Réveil Samaritain» - 3 Boulevard Saint-Jacques

THURSDAY MARCH 23, 2017

- 8.30-10.00am** **SESSION 4 - FAT SOLUBLE VITAMINS**
Chair: Edmond Rock & Anargyros Moulas
- 8.30-9.00 **KEY NOTE - Catherine Feart** - INSERM, Bordeaux, France
Nutrient biomarker patterns, including FSVs, and risk of neuro-generative diseases (dementia, Alzheimer's disease).
- ORAL COMMUNICATION**
- 9.00-9.20 **Marielle Margier** - NORT - INRA - INSERM, Marseille, France
Impact of pulses on fat-soluble vitamins bioavailability.
- 9.20-9.40 **Irene Pusceddu** - Hospital of Bolzano, Bolzano, Italy
The role of B and D vitamins in telomere length: results from the LURIC study and the Sud-Tyrolean study.
- 9.40-10.00 **Damien Prévéraud** - Adisseo France SAS, Commentry, France
Cholecalciferol (vitamin D3) and retinyl palmitate (vitamin A) display different solubilization capacities in mixed micelle solutions: effect of interactions with mixed micelle components and of cholecalciferol to self-associating properties.
- 10.00-10.30 Coffee break

10.30-11.20am**SESSION 4 - FAT SOLUBLE VITAMINS**

Chair: Patrick Borel & Patrick Sauvant

10.30-11.00

KEY NOTE - Adrian Franke - University of Hawaii Cancer Center, Honolulu, USA
Technology and methodology improvement of analytical approaches for FSV determination in biological samples.

ORAL COMMUNICATION

11.00-11-20

Serge Rezzi - Nestlé Institute of Health Sciences, Lausanne, Switzerland
A fast and simultaneous quantitative profiling of fat soluble vitamins and carotenoids in human plasma.

11.20-12.20

POSTER SESSION

12.20-2.00pm

LUNCH

Dedicated tables for participants willing to prepare a scientific project for H2020 call.

2.00-3.30pm**SESSION 5 - CAROTENOIDS**

Chair: Volker Böhm & Patrick Borel

2.00-2.30

KEY NOTE - Mr. Torsten Bohn - Luxembourg Institute of Health, Strassen, Luxembourg
Carotenoids - From Occurrence to Bioavailability to Bioactivity.

ORAL COMMUNICATION

2.30-2.50

Judith Hempel - University of Hohenheim, Stuttgart, Germany
Food sources of macular pigments: studies into the bioaccessibility and physical deposition form of carotenoids from goji berries (*Lycium barbarum* L.).

2.50-3.10

Emmanuelle Reboul - NORT - INRA - INSERM, Marseille, France
Canned spinach matrix does not significantly affect lutein bioavailability.

3.10-3.30

Ilya Vasilyev - Kazan Federal University, Kazan, Russia
First identification of C₅₀ carotenoids biosynthesis gene cluster in nematode-associated bacterium *Agreia bicolorata* strain VKM AC-1804 and its abundance in coryneform actinobacteria group.

3.30-4.00pm

Coffee break

4.00-5.50pm**SESSION 6 - VITAMIN A**

Chair: Patrick Borel & Edmond Rock

4.00-4.30

KEY NOTE - Mr. Patrick Sauvant - Bordeaux Sciences Agro, Bordeaux, France
Seeing through the dark: vitamin A from deficiency in developing countries to retinoic acid as a powerful and promising drug.

ORAL COMMUNICATION

4.30-4.50

Consuelo Macias-Matos - National Institute of Hygiene, La Habana, Cuba
CUBA-UNICEF: 18 years working together against vitamin A deficiency.

4.50-5.10

Georg Lietz - Newcastle University, Newcastle upon Tyne, United Kingdom

Influence of nutritional and physiological factors on total body vitamin A stores using the isotope dilution technique.

5.10-5.30

Maria Vaiou - Technological Education Institute TEI of Thessaly, Larissa, Greece

Comparative effects of Retinoic Acid and cytostatic drugs on arterial smooth muscle cell proliferation.

5.30-6.15pm

CLOSING SESSION - Edmond Rock, President



18th International Symposium on Carotenoids

9-14 JULY 2017 | LUCERNE, SWITZERLAND

OPEN FOR REGISTRATION & ABSTRACT SUBMISSION

The International Carotenoid Society and the symposium organizing team are very pleased to invite you to register to the ICS Symposium 2017.

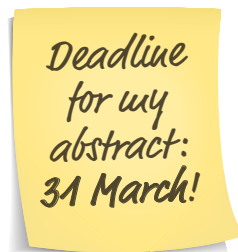
We encourage you to submit your abstract as soon as possible. The research topics are:

- Nutrition and health
- Chemistry: analytics and synthesis
- Industrial production, extraction, synthesis
- New methods in carotenoid research
- Photochemistry and Phytophysics
- Carotenoids in the eye
- Emerging carotenoid science
- Apo-carotenoid and retinoid metabolism and function
- Risk reduction of chronic disease
- Plant biology and plant genetics
- Carotenoid metabolism
- Brain and cognition
- Industrial production and commercial application
- Food science and technology

Please register at www.icslucerne2017.org/registration.html and submit your abstract!
For abstract guidelines and template visit: www.icslucerne2017.org/program/abstract-submission.html

We look forward to welcoming you to Lucerne and to an exciting and well-attended conference!

The International Symposium on Carotenoids is a triennial event of the International Carotenoid Society hosted in collaboration with its partners in Academy and Industry.



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The “vitamins” SFVB–ASQUALAB External Quality Assessment schemes (EQAS)

The SFVB is a non-profit organization involving searchers, physicians and manufacturers developing studies on the role and metabolism of the vitamins. Since 2002, a survey has been organized by SFVB, with currently 57 participant laboratories (41 French and 16 European or non-European laboratories). To meet ISO 9001 and 17043 requirements, SFVB teamed up with ASQUALAB, a French EEQ organizer, in order to improve organization of EQAS surveys. This partnership is intended to increase the level of reliability of the results provided by the laboratories through improvement of analytical methods used and practices. Furthermore this work could facilitate the development of standard methods.

The annual program is composed of 6 surveys of 2 samples. The 12 lyophilized of pooled human serum vials are sent once in the beginning of the year. They can be kept at -20°C until reconstitution with 3 mL water. The serum are spiked or not with

- vitamin A (retinol)
- vitamin E (alpha tocopherol)
- vitamin C (ascorbic acid)
- vitamin D (25 OHvitamin D₃)
- vitamin B6 (pyridoxal phosphate)
- vitamin B9 (methyl tetrahydrofolic acid)
- vitamin B12 (cyanocobalamine)
- homocysteine
- beta-carotene

The number of participants varies according to the compound considered (46 for vitamin A, 14 for beta-carotene)

The final report includes the following information:

- a summary report (all the results, all the methodologies)
- an histogram for each sample with the distribution of all methodologies, the distribution of the peer group, the value of the laboratory
- an individual report with mean, CV, bias, Z-score and comment for all methodologies and for peer if possible (number of participants > 6)

The price of the program is 330€ excluding shipping cost.
The inscription could be done by e-mail or postal mail at:
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Web : www.asqualab.com - e-mail : asqualab@wanadoo.fr



ABSTRACT BOOK

SESSION 1 - VITAMIN E

Manfred Eggersdorfer - KEY NOTE - E1	page 17
Francesco Galli - ORAL COMMUNICATION - E2	page 19
Lisa Schmölz - ORAL COMMUNICATION - E3	page 21
Jan Frank - ORAL COMMUNICATION - E4	page 23
Ann Anderson Berry - ORAL COMMUNICATION - E5	page 25
Corrine Hanson - ORAL COMMUNICATION - E6	page 27
Charlotte Cuerq - FLASH POSTER - E7	page 29
Gaspar Kocharyan - FLASH POSTER - E8	page 31
Kimitaka Takitani - FLASH POSTER - E9	page 33

SESSION 2 - VITAMIN K

Omar Benzakour - ORAL COMMUNICATION - K1	page 35
Catherine Desoto - ORAL COMMUNICATION - K2	page 37

SESSION 3 - VITAMIN D

Jean-François Landrier - ORAL COMMUNICATION - D1	page 39
Andrius Bleizgys - ORAL COMMUNICATION - D2	page 41
Augusto Litonjua - ORAL COMMUNICATION - D3	page 43
Emmanuelle Reboul - ORAL COMMUNICATION - D4	page 45
Charles Desmarchelier - ORAL COMMUNICATION - D5	page 47
Anargyros Moulas & Elisabeth Katsianidou - ORAL COMMUNICATION - D6/D7	page 49
Elina Hypponen - KEY NOTE - D8	page 51
Elina Hypponen - POSTER - D9	page 53
Robert Winwood - ORAL COMMUNICATION - D10	page 55
Wolfgang Herrmann - ORAL COMMUNICATION - D11	page 57
Jeremie Talvas - ORAL COMMUNICATION - D12	page 59
Lauriane Bonnet - ORAL COMMUNICATION - D13	page 61
Poorya Shojai - FLASH POSTER - D14	page 63
Ina Jasutiene - FLASH POSTER - D15	page 65
Natalia Davydova - FLASH POSTER - D16	page 67
Charlotte Lauridsen - FLASH POSTER - D17	page 69
Argjira Juniku-Shkololli - FLASH POSTER - D18	page 71

Catherine Féart - FLASH POSTER - D19	page 73
Ludmila Macova - FLASH POSTER - D20	page 75
Sharif Elham - POSTER - D21	page 77
Marie-Christine Carlier - POSTER - D22	page 79
Tarek Chaabouni - POSTER - D23	page 81

SESSION 4 - FAT SOLUBLE VITAMINS

Catherine Feart - KEY NOTE - FSV1/FSV2/FSV3	page 83/87
Marielle Margier - ORAL COMMUNICATION - FSV4	page 89
Irene Pusceddu - ORAL COMMUNICATION - FSV5	page 91
Damien Prévéraud - ORAL COMMUNICATION - FSV6	page 93
Adrian Franke - KEY NOTE - FSV7	page 95
Adrian Franke - POSTER - FSV8	page 97

SESSION 5 - CAROTENOIDS

Torsten Bohn - KEY NOTE - C1	page 99
Judith Hempel - ORAL COMMUNICATION - C2	page 101
Emmanuelle Reboul - ORAL COMMUNICATION - C3	page 103
Ilya Vasilyev - ORAL COMMUNICATION - C4	page 105

SESSION 6 - VITAMIN A

Patrick Sauvart - KEY NOTE - A1	page 107
Consuelo Macias-Matos - ORAL COMMUNICATION - A2	page 109
Georg Lietz - ORAL COMMUNICATION - A3	page 111
Maria Vaiou - ORAL COMMUNICATION - A4	page 113
Simone Frey - ORAL COMMUNICATION - A5	page 115
Imar Djibrine Soudy - FLASH POSTER - A6	page 117
Ronald Corbee - FLASH POSTER - A7	page 119
Pierre-Jacques Brun - FLASH POSTER - A8	page 121

SESSION 1 - VITAMIN E - KEY NOTE

Manfred Eggersdorfer - Abstract n° E1

City: Kaiseraugst Country: Switzerland
Institution: DSM Speciality: Vitamins
Email: manfred.eggersdorfer@dsm.com

Title of abstract: Tocopherol – a systematic review of intake and status globally

Authors and addresses: Manfred Eggersdorfer, PhD
Professor for Healthy Ageing University Medical Center Groningen
DSM Nutritional Products, Wurmisweg 576. 4303 Kaiseraugst, Switzerland
Coauthors: Peter Weber, PhD, MD, DSM Nutritional Products, 4303 Kaiseraugst, Switzerland
Szabolcs Peter, PhD, MD, DSM Nutritional Products, 4303 Kaiseraugst, Switzerland

Key words: Vitamin E intake, serum concentration, optimal level

Abstract: Vitamin E is essential for human health and achieving an optimal status is associated with beneficial health outcomes. Dietary recommendations are established in many countries around the world and refer to the role of vitamin E in preserving the integrity of the cell membrane. We reviewed the published literature reporting vitamin E intake levels and serum concentrations in order to obtain a global overview of vitamin E status.

A search in the Pubmed/Medline database focused on population based studies published between January 1st 2000 and July 30th 2012 resulted in 176 articles referring to 132 single studies with reported intake and/or serum concentration.

Applying an RDA (Recommended Daily Allowance) of 15 mg/d and EAR (Estimated Average Requirement) of 12 mg/d to all populations with a minimum age of 14 years, 82% and 61% of mean and median data points were below the RDA and EAR, respectively. Regarding serum concentrations, globally 13% of the included data points were below the functional deficiency threshold concentration of 12 µmol/L (F.a.N. Board 2000), mostly newborns and children. Several prospective observational studies suggest that a serum α-tocopherol concentration of ≥30 µmol/L has beneficial effects on human health. Of the reported study populations and subpopulations, only 21% reached this threshold globally.

The systematic review suggests that the vitamin E status is inadequate in a substantial part of the studied populations. This review could be a useful stepping stone for researchers to combine existing data, fill in data gaps and to understand more about the complex field of vitamin E and its impact on human health.

SESSION 1 - VITAMIN E - ORAL COMMUNICATION

Francesco Galli - Abstract n° E2

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Country: Italia

Speciality: Biochemistry and Nutrition

Title of abstract: Vitamin E metabolism and function.

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Key words: Vitamin E; CYP4F2; ω -hydroxylase activity

Abstract: Discovered in 1922 as a factor essential for rat fertility and soon after characterized for its properties of fat-soluble antioxidant, vitamin E was identified to have signalling and gene regulation effects that are still poorly characterized. Recent times, the cellular metabolism of this vitamin was characterized and suggested to have roles alternative to catabolism. Endogenous metabolites, such as α -tocopheryl phosphate and the long-chain metabolites formed by the ω -hydroxylase activity of cytochrome P-450, have been suggested to behave as physiological bioactive molecules with gene modulation and homeostatic effects that include the control of inflammatory pathways and lipid metabolism, and cell cycle regulation. The molecular mechanisms underlying these responses to vitamin E metabolites are under investigation in several laboratories and side-glances to research on other fat soluble vitamins may help to move faster in this direction. The results of this emerging research are expected to shed light in the mechanisms of reduction of the cardiovascular risk, as well as in the other health-promoting effects of this vitamin that are currently under investigation, such as its immunomodulation and antiallergic properties, and the neuroprotection properties observed in models of glutamate excitotoxicity and spino-cerebellar damage, or in the hepatoprotection and prevention of liver toxicity by different causes that include non-alcoholic steatohepatitis. These aspects will be discussed in this presentation providing an overview on the emerging literature and lines of research.

SESSION 1 - VITAMIN E - ORAL COMMUNICATION

Lisa Schmözl - Abstract n° E3

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Title of abstract: Contribution of the structure of tocopherols and their long-chain metabolites to their biological effects

Authors and addresses: Lisa Schmözl 1,2, Maria Wallert 2,3, Nicolò Rozzino 4, Andrea Cignarella 5, Francesco Galli 6, Michael Glei 2,7, Oliver Werz 8, Andreas Koeberle 8, Marc Birringer 9, Stefan Lorkowski 1,2 / 1 Department of Nutritional Biochemistry and Physiology, Institute of Nutrition, Friedrich Schiller University Jena, Germany / 2 Competence Center for Nutrition and Cardiovascular Health (nutriCARD), Halle-Jena-Leipzig, Germany / 3 Baker IDI Heart and Diabetes Institute, Melbourne, Australia / 4 Department of Pharmaceutical and Pharmacological Sciences, University of Padova, Italy / 5 Department of Medicine, University of Padova, Italy / 6 Department of Pharmaceutical Sciences, Laboratory of Nutrition and Clinical Biochemistry, University of Perugia, Italy / 7 Department of Nutritional Toxicology, Institute of Nutrition, Friedrich Schiller University Jena, Germany / 8 Department of Pharmaceutical/Medicinal Chemistry, Institute of Pharmacy, Friedrich Schiller University Jena, Germany / 9 Department of Nutritional, Food and Consumer Studies, University of Applied Sciences Fulda, Germany

Key words: Vitamin E, α -13'-OH, α -13'-hydroxychromanol, α -13'-COOH, α -13'-carboxychromanol, long-chain metabolites of Vitamin E

Abstract: The cytochrome P-450 dependent metabolism of vitamin E forms initially the long-chain metabolites (LCM) 13'-hydroxychromanols (13'-OH) and 13'-carboxychromanols (13'-COOH), which can also be found in blood. Further oxidation steps result in water-soluble, short-chain metabolites (carboxyethylhydroxychromanols, CEHC). Due to sparse knowledge about the regulatory effects of the LCM, we conducted a comparative study to unravel the contribution of substructures of the LCM molecules to their regulatory actions. We compared the effects of α - and δ -tocopherols (TOH) as metabolic precursors and the respective LCM, α - and δ -13'-OH as well as α - and δ -13'-COOH, with compounds representing either the chromanol system (α -CEHC) or the oxidative modified aliphatic side-chain (pristanic acid). We analyzed the effects of the different molecules on the expression of the scavenger receptor CD36 and the inflammatory inducible nitric oxide synthase (iNos), both of which have been previously shown to be affected by the LCM. The effects were prominent for the LCM-treated cells with induction of CD36 expression and inhibition of the lipopolysaccharide (LPS)-induced iNos expression or nitric oxide release, while their precursors or the molecules resembling substructures were less or not effective. Our results clearly show that the entire LCM molecule, comprised of chromanol ring, aliphatic side-chain and terminal oxidation of the side-chain is required to exert the effects, which could be explained by the existence of a specific, so far unknown receptor for the LCM. Furthermore, our study provides further evidence for the relevance of LCM as a highly interesting new class of regulatory metabolites of vitamin E.

SESSION 1 - VITAMIN E - ORAL COMMUNICATION

Jan Frank - Abstract n° E4

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Title of abstract: The long chain metabolite α -tocopherol-13'-COOH may be responsible for the induction of xenobiotic enzymes previously attributed to the parent α -tocopherol.

Authors and addresses: Jan Frank, University of Hohenheim, Institute of Biological Chemistry and Nutrition, 70599 Stuttgart, Germany

Abstract: All eight vitamin E congeners are metabolized by xenobiotic enzymes to the short-chain carboxyethyl hydroxychromanol metabolites (CEHC). The rate-limiting step in the sidechain degradation of vitamin E is thought to be catalyzed by cytochrome P450 (CYP). As CYP enzymes are substrate-inducible, it was suggested that high-dose supplementation with vitamin E (predominantly α -tocopherol) may induce CYP and other xenobiotic enzymes. This notion was supported by studies demonstrating induction of CYP and certain membrane efflux transporters, including P-glycoprotein (P-gp), in rodents injected with high doses of α -tocopherol (α T). Our own experiments in cells incubated with α T and mice, rats, and guinea pigs fed high doses of α T, on the other hand, did not confirm changes in the mRNA and protein expression or activities of CYP and efflux transporters. Both, CYP and P-gp are under the control of the nuclear receptor pregnane X receptor (PXR). During the metabolism of α -tocopherol to the water-soluble short-chain metabolite α CEHC, the long-chain metabolite α -tocopherol-13'-COOH (α T-13'-COOH) is formed. In order to gain a deeper understanding of the biological activities of the α T metabolites, we analyzed the activation of PXR and the subsequent protein expression and activity of its target P-gp in LS 180 cells incubated with α T, α T-13'-COOH, and α CEHC. Neither α T nor the short chain metabolite α CEHC activated PXR or altered the expression or activity of P-gp in the cells. α T-13'-COOH, on the other hand, activated PXR and induced the protein expression of P-gp and the efflux of the Pgp substrate rhodamine 123. In conclusion, the long chain metabolite α T-13'-COOH and not the parent compound α T appears to facilitate the induction of xenobiotic enzymes reported in animal experiments using injection of very high-doses of α T. α T injection results in the accumulation of long chain α T metabolites in vivo, which is unlikely to occur upon intake of high oral doses of the vitamin and may explain the contradicting data from animals injected or fed with high doses of α T. Further studies to elucidate these phenomena are underway in our laboratory.

SESSION 1 - VITAMIN E - ORAL COMMUNICATION

Ann Anderson Berry - Abstract n° E5

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Title of abstract: Maternal and Infant Dynamics of Vitamin E Tocopherols

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Presenting author: Ann L Anderson Berry

Key words: alpha-tocopherol, gamma-tocopherol, Maternal, Infant

Abstract: Objective: Vitamin E is of critical importance in early infancy, and deficiency in this population has devastating consequences such as severe intracranial hemorrhage. Vitamin E occurs naturally in several different isoforms, including alpha and gamma tocopherol. New evidence indicates that vitamin E isoforms have different roles in influencing inflammation. In contrast to the anti-inflammatory properties of the alpha-tocopherol isoform, the gamma-tocopherol isoform has been shown to demonstrate pro-inflammatory properties. It is known that placental transfer of alpha tocopherol to the fetus is limited, and the maternal levels have little influence on the delivery of this substance to the fetus. However, much less is known about maternal-fetal transfer or impacts of other tocopherol isoforms.

Methods: Samples of maternal and infant cord blood were collected on 189 mother-infant pairs at delivery. Concentrations of alpha and gamma tocopherol were measured using high-performance liquid chromatography. Descriptive statistics were calculated and Spearman correlations coefficients were used to look at the association of maternal and cord tocopherol measurements. Independent sample t-tests were used to compare continuous measures between dichotomous groups. $P < 0.05$ was considered statistically significant.

Results: Maternal tocopherol levels at delivery were 12,501.7 (+4661.9) and 1,456.8 (+727.6) ug/L for alpha and gamma tocopherol, respectively; cord alpha and gamma tocopherol levels were 2,035.7 (+1020.4) and 243.7 (+186.5) ug/L. Maternal and cord serum tocopherol concentrations were positively correlated for gamma tocopherol ($r=0.31$, $p < 0.001$). In contrast, maternal alpha tocopherol concentrations were not associated with cord concentrations. Cord blood levels of gamma tocopherol were inversely associated with birth weight ($r=-0.20$, $p=0.007$) and birth length ($r=-0.20$, $p=0.009$). Higher levels of gamma tocopherol were also associated with a C-section delivery ($p=0.03$) a diagnosis of pre-eclampsia ($p=0.006$), and admission to the NICU ($p=0.04$).

Conclusion: As opposed to alpha tocopherol, serum gamma tocopherol levels were correlated between mothers and infants. Maternal-fetal transfer of gamma tocopherol is mediated by either different or more efficient methods than transfer methods for alpha tocopherol. Maternal and infant levels of gamma tocopherol at delivery were negatively associated with growth and adverse pregnancy and neonatal outcomes. As maternal tocopherol levels are modifiable by diet, further research into maternal-fetal transfer and impacts on maternal-infant outcomes are warranted.

SESSION 1 - VITAMIN E - ORAL COMMUNICATION**Corrine Hanson - Abstract n° E6**

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Title of abstract: Pro-vitamin A Compounds and Tocopherol Levels in Mother-infant Pairs from Midwest USA and Correlations with Fetal Growth

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Key words: vitamin A, fetal growth

Abstract: Background: Poor fetal growth leads to higher risk of neonatal morbidity and mortality. Fetal growth restriction and SGA are predictors of impaired neurodevelopment and adult chronic disease. Risk factors for poor growth include primiparity, low pre-pregnancy body mass index (BMI), smoking and preeclampsia. Free radicals and maternal antioxidant defenses may be involved in fetal growth. Nutritionally derived antioxidants represent potentially modifiable exposures, and it has been hypothesized that higher levels of antioxidants in maternal blood may provide protection from poor growth. Objective: Evaluate correlations between maternal and cord blood levels of pro-vitamin A compounds and vitamin E isoforms with newborn growth variables (weight, length, and head circumference). Method: Samples of maternal and infant cord blood were collected on 189 mother-infant pairs at delivery. Concentrations of alpha and beta-carotene, beta-cryptoxanthin, lycopene, retinols, lutein and tocopherols were measured using high-performance liquid chromatography. Descriptive statistics were calculated and Spearman correlations coefficients were used to look at the association of maternal and cord pro-vitamin A compounds and tocopherol measurements. Independent sample t-tests were used to compare continuous measures between dichotomous groups. $P < 0.05$ was considered statistically significant. Results: 72.8% of infants had retinol levels of 0.35-0.70 $\mu\text{mol/L}$ (deficient), 17.9% had levels of 0.70-1.05 $\mu\text{mol/L}$ (inadequate) and 7.5% had low levels $< 0.35 \mu\text{mol/L}$ (severely deficient). No statistically significant difference was present between retinol levels and growth variables. Significant correlations were observed between birth weight and length with maternal levels of lutein + zeaxanthin ($p < 0.0001$ for both), beta-cryptoxanthin ($p = 0.01$ and $p = 0.006$), cis-lycopene ($p = 0.01$ and $p = 0.04$), alpha-carotene ($p = 0.002$ and $p = 0.02$), and cis-beta-carotene ($p = 0.02$ and 0.03). Newborn head circumference was statistically associated with maternal levels of trans-, cis-, and total-lycopenes ($p = 0.04$, $p = 0.02$, $p = 0.03$, respectively). Maternal alpha- and beta-carotene levels also correlated significantly with infant head circumference ($p = 0.002$ and $p = 0.02$, respectively). Maternal levels of alpha- and gamma-tocopherol were also statistically associated with birth growth variables, with alpha tocopherol having a positive association with birth weight, head circumference and length ($p = 0.02$, 0.03 , and 0.04 , respectively) while cord levels of the pro-inflammatory isomer gamma-tocopherol showed inverse associations with newborn growth ($p = 0.007$ and 0.009 for birth weight and length, respectively).

Conclusion: These findings suggest a possible influence of low levels of pro-vitamin A compounds and of vitamin E tocopherols in newborn growth outcomes. Whether diet modification to produce higher levels of these substances would be protective of poor growth is still unknown.

SESSION 1 - VITAMIN E - FLASH POSTER

Charlotte Cuerq - Abstract n° E7

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Speciality: Nutrition

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Title of abstract: Abetalipoproteinemia and chylomicron retention disease: efficacy of two formulations of vitamin E in a randomized cross over clinical study

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Key words: Alpha-tocopherol. Abetalipoproteinemia. Chylomicron retention disease

Abstract: Objective: Hypobetalipoproteinemias (HBL) represent a heterogeneous group of rare diseases characterized by reduced plasma levels of LDL-cholesterol and apolipoprotein B. Abetalipoproteinemia (ABL) and chylomicron retention disease (CMRD) are rare recessive forms of HBL. They are characterized by an intestinal lipid malabsorption and a severe vitamin E deficiency leading to disabling neuro-ophthalmologic sequelae. Despite early initiation of treatment with high doses of vitamin E, fundoscopic and retinal changes may appear. Finding the most efficient formulation and dose of tocopherol for treatment is of major interest. Tocofersolan, a water-soluble derivative of RRR- α -tocopherol, is a commercially available vitamin E supplement which has proven its efficiency in chronic cholestasis but it has never been evaluated in hypobetalipoproteinemias. Therefore, the aim of this study was to assess its interest in the treatment of ABL and CMRD. Methods: 3 patients with ABL and 4 with CMRD were included. The intestinal absorption of tocofersolan and alpha-tocopherol acetate was studied in a pharmacokinetic (PK) assay by measuring the plasma concentrations of α -tocopherol at baseline and 4, 8, 12, 24, 36, 48, 60, 72, 84 and 96h after a single oral load compared to 5 healthy control subjects. The efficiency of these 2 molecules to restore vitamin E storage were evaluated by the concentrations of α -tocopherol in plasma, red blood cells (RBC) and adipose tissue (AT) after a 4 months period treatment in a randomized cross-over clinical study. Results: In the PK assay, tocofersolan was significantly better absorbed in CMRD compared to α -tocopherol acetate ($p < 0.05$); but the absorption was almost nil with both molecules in ABL. However, in plasma, RBC and AT, α -tocopherol concentrations were not significantly different whether ABL and CMRD children have been treated with one or the other formulation. CMRD patients were better corrected after 4 months of treatment than ABL with the same dose of α -tocopherol ($p < 0.05$). Conclusion: Although tocofersolan does not improve significantly vitamin E storage after 4 months of treatment compared to tocopherol acetate in patients with hypocholesterolemia, this study provides new insights about the vitamin E status in ABL and CMRD diseases.

SESSION 1 - VITAMIN E - FLASH POSTER

Gaspar Kocharyan - Abstract n° E8

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Title of abstract: NONADDITIVE ANTIOXIDANT EFFECT (SYNERGY, ANTAGONISM) OF BIOFLAVONOID MIXTURES WITH TROLOX: WATER-SOLUBLE ANALOGUE OF VITAMIN E

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Key words: Flavonoid, Vitamin E, nonadditive effect, trolox

Abstract: Nonadditive effects (synergy and antagonism) are often observed in the biological systems during lipid peroxidation at simultaneous presence of antioxidants. The study of synergistic and antagonistic effects in the mixtures of antioxidants is among urgent problems, as in the real aerobic biological systems the antioxidant protection is realized exactly by several antioxidants. So revealing the mechanism of nonadditive action of antioxidants is of important point.

In this research joint antioxidant action of flavonoids in the mixture with trolox in the aqueous medium was studied by the methods of determining the absorption capacity in relation to oxygen-centered radicals (ORAC) and square-wave voltammetry (SWV). At that flavonoids containing glycoside in the molecular structure (rutin, naringin) and not containing this group (morin, quercetin) were considered. Comparison of the antiperoxyradical capacity for individual antioxidants and their mixtures with trolox demonstrates that the pairs rutin-trolox and naringin-trolox exhibit synergistic effect of the antiperoxyradical capacity (17.5%; 7.2%, respectively), while the pairs quercetin-trolox and morin-trolox exhibit antagonistic effect (-40.7% and -15.0%, respectively).

Kinetic studies by the SWV method have shown that introduction of trolox into the rutin-containing reaction mixture resulted in deceleration in the rutin consumption, that is reduction of phenoxil radicals of rutin by the trolox molecule took place yielding its phenolic form with higher antioxidant capacity. This leads to the synergistic effect. In case of the structural analogue of quercetin, not containing glycoside group, addition of the co-antioxidant, trolox, resulted in acceleration in the quercetin consumption. This fact testified that the molecule of a flavonoid with higher antiradical capacity (quercetin, morin) leads to trolox regeneration, which has a significant small value of the antiradical capacity. As a result, consumption of flavonoids with high antiradical capacity is accelerated and the antagonistic effect was observed.

Based on the data obtained it was established that in aqueous medium, the mixtures of trolox with flavonoids having carbohydrate side chains (rutin, naringin) exhibit synergistic effect of the antiperoxyradical activity, while the mixtures of the flavonoids without glycoside substituents in the side chain (quercetin, morin) exhibit antagonistic effect. It may be concluded additionally that the same effect will be observed for the liposoluble analogue of trolox, vitamin E, which may be present with flavonoids in the interphase dipolar medium of cell membranes.

SESSION 1 - VITAMIN E - FLASH POSTER

Kimitaka Takitani - Abstract n° E9

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Title of abstract: Dehydroepiandrosterone alters vitamin E status and prevents lipid peroxidation in vitamin E-deficient rats.

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Key words: vitamin E, dehydroepiandrosterone, oxidative stress

Abstract: In humans, dehydroepiandrosterone (DHEA) and its sulfate ester metabolite DHEA-S are secreted predominantly from the adrenal cortex, and DHEA is converted to steroid hormones, including androgens and estrogens, and neurosteroid. DHEA exerts protective effects against several pathological conditions. Although there are reports on the association between DHEA and vitamins, the exact relationship between DHEA and vitamin E remains to be determined. Therefore, we attempted to elucidate the effect of DHEA on vitamin E status and the expression of various vitamin E-related proteins, including binding proteins, transporters, and cytochrome P450 (CYP), in vitamin E-deficient (VED) rats.

Plasma α -tocopherol levels in VED rats increased in response to DHEA administration. The expression of hepatic α -tocopherol transfer protein was repressed in VED rats compared to that in control rats; however, DHEA administration significantly upregulated this expression. Hepatic expression of CYP4F2, an α -tocopherol metabolizing enzyme, in VED rats was decreased by DHEA administration, whereas hepatic expression of ATP-binding cassette transporter A1, an α -tocopherol transporter, was not altered following DHEA administration. DHEA repressed lipid peroxidation in the liver of VED rats. Therefore, adequate DHEA supplementation may improve lipid peroxidation under several pathological conditions, and DHEA may modulate α -tocopherol levels through altered expression of vitamin E-related protein

SESSION 2 - VITAMIN K - ORAL COMMUNICATION

Omar Benzakour - Abstract n° K1

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Speciality: pediatrics

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Title of abstract: Vitamin K: a vitamin like no other

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Abstract: Vitamin K or vitamin “Koagulation” (German spelling for coagulation) was discovered by the 1943 Nobel Prize winners Henrik Dam and Edwards A. Doisy, as a fat soluble substance, the deficiency of which caused bleeding disorders. Vitamin K in its reduced form, vitamin K hydroquinone, is required as a cofactor for the γ -glutamyl carboxylase enzyme that catalyses the γ -carboxylation of specific glutamyl residues to γ -carboxyglutamic acid residues. The γ -carboxylase reaction generates γ -carboxyglutamate and vitamin K 2,3,-epoxide which is then recycled back to the hydroquinone form by a vitamin K reductase system. Vitamin K-dependent proteins (VKDP) are a family of proteins characterized by such vitamin K-dependent post-translational modifications. Warfarin and its derivatives inhibit the vitamin K epoxide reductase, blocking thereby the gamma-carboxylation reaction. VKDP synthesized in the presence of warfarin are under-gamma-carboxylated and are either not secreted but degraded intracellularly or have impaired biological activities. Since VKDP are mainly secreted factors most of which regulate blood coagulation, the specificity and efficiency of warfarin in inhibiting the gamma-carboxylation reaction, has led to its widespread use in oral anticoagulant therapy. Processes regulated by VKDP are referred to as vitamin K-dependent mechanisms and warfarin treatment as anti-vitamin K therapy or AVK. Until recently, interest in vitamin K- was mostly restricted to the field of hematology. However, the discovery that some VKDPs are ligands for a family of related tyrosine kinase receptors has opened up a new area of research. Moreover, the phenotypes associated with the invalidation of genes encoding VKDP or their receptors revealed the implication of VKDP in regulating retinogenesis, neurogenesis, osteogenesis, and spermatogenesis. Therefore, the elucidation of the molecular mechanisms underlying the role of vitamin K and VKDP in regulating apoptotic cell phagocytosis may lead could form the framework of new therapeutic strategies aiming at a selective targeting of VKDP associated pathologies.

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SESSION 2 - VITAMIN K - ORAL COMMUNICATION

Catherine Desoto - Abstract n° K2

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Title of abstract: Nature, Nurture and Vitamin K: Speculations regarding neurodevelopmental effects of VK genotype.

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Key words: Epigenetics, Vitamin K, VKORC1, autism

Abstract: It is well-known that humans vary in the gene that encodes for Vitamin K epoxide reductase complex (VKORC1) and recent research has documented the protective effect of Vitamin K (VK) on neural cells. It is now clear that VK plays an important role in maintaining normal neural development and protecting against toxic exposures. It is speculated that a paucity of VK during development could contribute to key brain development aberrations, including those associated with developmental disorders. Preliminary data from a small sample of severely autistic children of Somali ancestry showed these children had a higher than expected genetic substitution that results in reduction in the efficiency of the Vitamin K cycle. Broadly, the possibility that this genetic variation could play an etiological role in the development of developmental disorders is discussed, with emphasis on the importance of additional research. Discussion of the importance of recent research on epigenetics and a proper understanding of environment/gene interactions will be included.

SESSION 3 - VITAMIN D - ORAL COMMUNICATION

Jean-François Landrier - Abstract n° D1

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Title of abstract: Vitamin D modulates adipose tissue biology : possible consequences on obesity ?

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Key words: adipose tissue, vitamin D, adipocyte, inflammation, obesity

Abstract: Cross-sectional studies have depicted an inverse relationship between vitamin D status, reflected by plasma 25-hydroxyvitamin D and obesity. In agreement, recent studies in vitro and in animal models tend to demonstrate an impact of vitamin D and Vitamin D Receptor on adipose tissue and adipocyte biology, that could support at least in part a causal role of vitamin D insufficiency on obesity and associated physiopathological disorders such as adipose tissue inflammation and consecutive insulin-resistance. However, clinical and genetic studies are far less convincing, with results highly contrasted, which do not permit to conclude for the moment. Nevertheless, prospective studies provide interesting data supporting the hypothesis of a preventive role of vitamin D on onset of obesity. The aim of the present presentation is to summarize data available regarding relationships between vitamin D, adipose tissue / adipocytes physiology and obesity, and to shed some light on key points that will need to be address in a near future to gain insight on this controversial relationship.

SESSION 3 - VITAMIN D - ORAL COMMUNICATION

Andrius Bleizgys - Abstract n° D2

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Institution: VILNIUS UNIVERSITY Speciality: LECTOR, FAMILY PHYSICIAN

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Title of abstract: Vitamin D Levels of Out-Patients: Variability by Age Groups and Seasons

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(affiliation of both authors - FACULTY OF MEDICINE, VILNIUS UNIVERSITY).

Key words: seasons, vitamin D, sex factors, age factors

Abstract: The aim of the study. Data on prevalence of vitamin D deficiency in Lithuania are still scarce. The aim was to assess the reserves of vitamin D in different age groups of in-patients regarding the season of the year.

Material and Methods. Data on serum 25-hydroxyvitamin D levels from blood tests (made in 2012-2014) were obtained from the "Medicina Practica" laboratory and a retrospective cross-sectional analysis was performed.

Results. 9581 unique subjects were enrolled in the final analysis. The mean age of the participants was 33±23 yrs. The mean levels of vitamin D were higher in males than in females, $p < 0,001$. The highest mean vitamin D levels were in 0-9 yrs. age group, the lowest were in 10-19 yrs. age group and in the group of 70 yrs. and older, $p < 0,001$. The lowest reserves of vitamin D have been found to be in January ($59,0 \pm 49,6$ nmol/l), February ($63,3 \pm 49,0$ nmol/l), March ($57,1 \pm 40,7$ nmol/l) and April ($60,1 \pm 42,0$ nmol/l). The highest reserves have been found to be in August ($86,2 \pm 46,2$ nmol/l) and September ($82,8 \pm 47,1$ nmol/l). Overall, low vitamin D was detected in 67% of the cases; 12% cases (mainly those of the group up to 2 years of age) had an excess of vitamin D, and normal values were found only in 21% of the cases.

Conclusions. There was established that vitamin D status demonstrated clear seasonality. There were also determined statistically significant sex-related differences of vitamin D statuses. According to the study, some age groups are at a higher risk of vitamin D deficiency. It is assumed, that these persons should be examined for vitamin D levels, especially during the cold season, and, if necessary, an appropriate treatment should be prescribed. In addition, for small children, a proper dose should be chosen in order to avoid vitamin D excess.

SESSION 3 - VITAMIN D - ORAL COMMUNICATION

Augusto Litonjua - Abstract n° D3

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Title of abstract: Vitamin D Supplementation in Pregnancy to Prevent Asthma in Offspring – Results from the Vitamin D Antenatal Asthma Reduction Trial (VDAART)

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Key words: Vitamin D, Clinical Trial, Prenatal Supplementation, Asthma

Abstract: Background: Vitamin D insufficiency and deficiency are prevalent worldwide, and pregnant women and infants are at highest risk for having deficiency. Epidemiologic studies have shown contradictory results, likely due to the fact that deficiency is widespread. We have hypothesized that vitamin D deficiency has contributed to the asthma and allergy epidemic in Western countries.

Rationale: To test whether supplementation with vitamin D in pregnancy could lead to prevention of asthma and recurrent wheeze in the offspring by age 3 years.

Methods: The Vitamin D Antenatal Asthma Reduction Trial (VDAART) was a randomized, double-blind, placebo-controlled trial between October 2009 and January 2015 in 3 centers across the United States. 881 pregnant women between the ages of 18 and 39 years at high risk for having children with asthma were randomized at 10-18 weeks gestation. Five participants were deemed ineligible shortly after randomization and were discontinued. Women were randomized to either daily 4,000 IU vitamin D plus a prenatal vitamin containing 400 IU vitamin D (n=440) or a placebo plus a prenatal vitamin containing 400 IU vitamin D (n=436). The main outcome of the trial was parental report of physician-diagnosed asthma or recurrent wheezing through 3 years of age in the offspring.

Results: Eight-hundred and ten infants were born in the study, and 806 were included in the analyses for the 3-year outcomes. Two hundred eighteen children developed asthma/recurrent wheeze – 98 (24.3%, 95% CI, 19-29) in the 4,400 IU/day group vs. 120 (30.4%, 95% CI, 26-73) in the 400 IU/day group, which resulted in a 20% decreased risk for asthma/recurrent wheeze among children born to mothers in the treatment arm (hazard ratio = 0.8, 95% CI = 0.6-1.0, p=.051).

Because of the growing recognition that nutrient trials are different from drug trials, mainly due to the fact that participants have varying levels and intakes of the nutrient, we performed secondary analyses based on the initial and achieved 25OHD levels. Both maternal baseline 25OHD levels (OR = 0.89, 95%CI = 0.82-0.97, p = 0.006) and third trimester 25OHD levels (OR = 0.91, 95%CI = 0.86-0.96, p = 0.002) were inversely associated with asthma/recurrent wheeze by age 3 years. Children born to mothers who had 25OHD levels both above 30 ng/ml at early pregnancy and at the 3rd trimester had the lowest risks for developing asthma/recurrent wheeze by age 3 years (OR = 0.54, 95%CI = 0.30-0.98).

Conclusions: This is the first trial to show that supplementation of vitamin D in pregnancy decreases the incidence of asthma and recurrent wheeze in the mothers' offspring. Our secondary analyses show that the greatest reduction in asthma and recurrent wheeze in the children occurred when their mothers had high levels throughout pregnancy. Our results have important public health implications for the respiratory health of young children.

SESSION 3 - VITAMIN D - ORAL COMMUNICATION

Emmanuelle Reboul - Abstract n° D4

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Title of abstract: ABCB1 is involved in vitamin D intestinal efflux

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Key words: Cholecalciferol, 25-hydroxycholecalciferol, intestine, excretion

Abstract: Recently, a new pathway for cholesterol elimination has been discovered: the transintestinal cholesterol excretion (TICE). This phenomenon involves ABCB1 (ATP-binding cassette B1). Vitamin D₃ (cholecalciferol) has been shown to be absorbed by enterocytes via cholesterol transporters. It may thus be excreted by pathways similar to those of cholesterol. As vitamin D is essential for calcium and phosphate homeostasis, immune system and vascular risk prevention, this situation should be considered for patients whose TICE would be activated. The aim of this study was thus to assess the contribution of ABCB1 to the intestinal efflux of vitamin D (cholecalciferol and its metabolite 25-hydroxyvitamin D (25(OH)D). Cholecalciferol and 25(OH)D efflux by cells transfected either stably or transiently with the ABCB1 gene was measured. 25(OH)D status in *abcb1*-deficient mice was compared to that of wild mice. Their postprandial plasma cholecalciferol response was then assessed following cholecalciferol gavage. Besides, the intestine ability to excrete cholecalciferol and 25(OH)D was estimated using Ussing chambers and via in situ perfusion experiments. Finally, 39 healthy adult men were genotyped using whole-genome microarrays. The association between SNPs in genes involved in vitamin D and lipid metabolism and the 25(OH) status was analyzed by partial least squares regression (PLS regression). The data collected showed that cells overexpressing ABCB1 had a better capacity to excrete cholecalciferol and 25(OH)D compared to control cells (+167% for cholecalciferol and +150% for 25(OH)D; $p < 0.05$). These results were confirmed by Ussing chambers ($p < 0.05$). In vivo, *Abcb1*-deficient mice displayed fasting plasma 25(OH)D concentrations 30% higher than wild type mice ($p < 0.05$). The postprandial cholecalciferol response in *abcb1*-deficient mice was also twice higher than in wild mice ($p < 0.05$). In situ perfusion analyses are still ongoing. In humans, a significant ($p = 3.94 \times 10^{-7}$) PLS regression model, which comprised 29 SNPs in 10 genes (including 3 SNPs in ABCB1), was associated with 73% of the interindividual variability in fasting plasma 25(OH)D concentration. These results suggest that an apical efflux of newly-absorbed cholecalciferol and a trans-epithelial efflux of 25(OH)D exists, and that the ABCB1 transporter is likely to be involved in the intestinal excretion of vitamin D and in its homeostasis.

SESSION 3 - VITAMIN D - ORAL COMMUNICATION

Charles Desmarchelier - Abstract n° D5

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Title of abstract: A Combination of Single-Nucleotide Polymorphisms Is Associated with the Interindividual Variability in Vitamin D Bioavailability in Healthy Men.

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Key words: vitamin D, 25-hydroxycholecalciferol, absorption, nutrigenetics

Abstract: Background – A significant part of vitamin D present in the human body is synthesized in the skin following UV light exposition. However, to obtain or maintain an adequate vitamin D status, most individuals have to consume vitamin D, either as part of their diet or as supplements. The blood response to vitamin D supplementation has been shown to exhibit a large interindividual variability. Moreover, vitamin D intestinal transport depends, at least partly, on proteins and we have shown that the bioavailability of other lipid micronutrients (tocopherol, lutein, lycopene and beta-carotene), which share common absorption mechanism with cholecalciferol (D_3), was partly modulated by single nucleotide polymorphisms (SNPs) in genes involved in the intestinal transport of these micronutrients and in the metabolism of chylomicrons. The main objective of this study was thus to identify SNPs associated with the interindividual variability in the bioavailability of D_3 . Methods – Thirty nine healthy adult men were genotyped using whole-genome microarrays. They consumed a meal that contained 5g D_3 as a supplement. D_3 and calcifediol (25(OH)D) concentration in plasma chylomicrons was measured at regular time intervals up to 8h after meal intake. The association between SNPs in genes involved in vitamin D and lipid metabolism (61 candidate genes representing 3791 SNPs) and the D_3 response (calculated as the area-under-the-curve of the postprandial chylomicron D_3 concentration) was analysed by partial least squares regression (PLS regression).

Results – The postprandial chylomicron D_3 concentration peaked 5.4 h after meal intake. There was no significant variation in the postprandial chylomicron 25(OH)D concentration. The D_3 response displayed a large interindividual variability (CV=47%). It correlated positively with the postprandial chylomicron triglyceride response ($r=0.60$, $P<0.001$) but not with the fasting 25(OH) D plasma concentration (a marker of vitamin D status) ($r=0.04$, $P=0.83$). A significant ($P=1.32\times 10^{-4}$) PLS regression model, which included 17 SNPs in 13 genes (LPL, ISX, SLC10A2, GC, SCARB1, PNLIP, DHCR7, ABCA1, ABCB1, APOB, MAPRE2, BET1, NAT2), was associated with the variance in the D_3 response. Five of these genes (ABCA1, APOB, BET1, LPL and NAT2) have been associated in another study with the postprandial chylomicron triglyceride response in the same subjects.

Conclusions – In a group of healthy men, we observed a high interindividual variability in D_3 bioavailability which was associated with a combination of SNPs located in/near genes involved in both vitamin D and lipid metabolism.

Desmarchelier et al., A Combination of Single-Nucleotide Polymorphisms Is Associated with Interindividual Variability in Cholecalciferol Bioavailability in Healthy Men, Journal of Nutrition, In Press.

SESSION 3 - VITAMIN D - ORAL COMMUNICATION

Anargyros Moulas & Elisabeth Katsianidou - Abstract n° D6

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Title of abstract: Fortification of food for addressing vitamin D deficiency

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Key words: Vitamin D, food fortification, cholecalciferol, bioavailability

Abstract: Vitamin D is the only essential nutrient that is not contained in adequate amounts even in a well-balanced healthy diet. Most foods do not contain nutritionally significant amounts of vitamin D with the exception of few foods like oily fish. In persons not receiving supplements, solar exposure accounts for approximately 90% of the vitamin D in the body. Vitamin D insufficiency is common in many countries, even in the sunny countries of the European South and has been associated with serious health conditions. Maintaining vitamin D status is important for prevention of diseases. However, extended exposure to UV radiation has been associated with increased risk for skin cancer while supplements, besides their cost, are not generally accepted by the population. For the above reasons, vitamin D fortification of food can be the option of choice for maintaining vitamin D status in the general population. For this purpose, several vitamin D fortified foods that are usually consumed need to be available. We have developed and studied for bioavailability and efficiency a series of everyday use foods, such as bread, juice, dairy products and pasta. Vitamin D fortified foods are effective in addressing vitamin D deficiency and for maintaining vitamin D status. Fortification of more foods should be considered for addressing vitamin D deficiency. This research was co-financed by the European Union and by Greek funds through the Research Project Archimedes III, Investment in the Society of knowledge

Abstract n° D7

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Title of abstract: Educational material for promoting vitamin D awareness.

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Key words: Vitamin D, education. Awareness

Abstract: The frequency of vitamin D deficiency is high in modern societies and constitutes a major health problem. Awareness of the health professionals and the public is essential for addressing deficiency and maintaining vitamin D status. For the promotion of awareness on vitamin D we have developed educational tools including informational material, a website, quizzes and interactive games. This research was co-financed by the European Union and by Greek funds through the Research Project Archimedes III, Investment in the Society of knowledge.

SESSION 3 - VITAMIN D - KEY NOTE

Elina Hypponen - Abstract n° D8

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Title of abstract: Vitamin D: Is it beneficial or even safe ?

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Key words: Vitamin D, cognition, memory, mendelian randomisation

Abstract: Recent years have seen an explosion in the proposed health effects of vitamin D, with this pro-hormone suggested to have benefits far beyond the classical effects on bone health and calcium metabolism. For long much of the enthusiasm was powered by observational studies, which are helpful for creating hypotheses, but less so when aiming to demonstrate true causal associations. More recently, re-analyses of randomised controlled trials using vitamin D supplementation to improve bone health, have provided support for beneficial influences on some of the outcomes, including a meta-analysis showing reduced mortality risk following modest dose vitamin D supplementation. However, there has also been some observations for unexpected adverse effects, with at least two large scale trials reporting increases, rather than decreases in the risk of falls following vitamin D supplementation with bolus dosages. This talk discusses the proposed benefits and adverse effects of vitamin D on various health outcomes. It summarises findings from randomised trials using vitamin D supplementation, and emerging data from large scale genetic studies, to make a case that there may be a strive towards «too much of a good thing».

SESSION 3 - VITAMIN D - POSTER

Elina Hyppönen - Abstract n° D9

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Title of abstract: Investigating the effect of vitamin D status on cognitive function using a Mendelian randomisation approach

Authors and addresses: Hyppönen E1,2, Maddock J1, Zhou A2, A Cavadino A1, Power C, Llewellyn D2 for the Vitamin D – Cognition collaboration.

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Key words: vitamin D, cognition, mendelian randomisation, causality

Abstract: Background: Epidemiological studies have linked vitamin D deficiency to reduced cognitive function in mid- to later life, however, due to the observational nature those evidence are prone to confounding and reverse causality. We used a genetic Mendelian randomization approach, also called “the nature’s randomized trial”, to explore the causal relationship between 25(OH)D and cognitive function in mid- to later life.

Methods: This study included data from 17 cohorts, including up to 172,357 participants. DHCR7 (rs12785878), CYP2R1 (rs12794714) and their combined “synthesis” score were chosen to act as a proxy (“instrument”) for 25(OH)D. To harmonize cognitive outcomes between cohorts, composite scores that capture global and memory cognition were derived using cognitive tests available for each cohort. Coefficients from phenotypic and genetic associations between 25(OH)D concentrations and cognitive function were first calculated in each cohort and then meta-analysed to obtain the pooled estimates.

Results: DHCR7, CYP2R1, and the synthesis score were strongly associated with 25(OH)D ($p < 0.001$), indicating robust instruments for serum 25(OH)D. In observational analyses, both low and high 25(OH)D concentrations were associated with lower scores in global and memory cognition (p value for curvature < 0.003 for both). In contrast, there was no evidence for causal association with cognitive outcomes using the genetic ‘instruments’ ($p > 0.2$ for all comparisons). There was also no genetic evidence for an association when stratified by thirds of 25(OH)D concentrations nor when stratifying by age or gender ($p > 0.1$ for all).

Conclusions: Despite support from observational studies, we found no genetic evidence for 25(OH)D concentrations acting as a causal factor for cognitive performance in mid- to later life. While this meta-analysis involved over 170,000 participants in the main analyses, our study may have been underpowered to detect small causal effects operating at the extremes of 25(OH)D distribution.

SESSION 3 - VITAMIN D - ORAL COMMUNICATION

Robert Winwood - Abstract n° D10

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Title of abstract: Unexpected, pervasive Vitamin D deficiency in people living in the Middle East

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Key words: Vitamin D Middle East deficiency

Abstract: Vitamin D deficiency can lead to serious medical conditions, such as rickets, osteoporosis and cardiomyopathy. Recent studies have shown that Vitamin D deficiency is not just a problem in extreme northern and southern latitudes, but is also now pervasive in many sun-rich countries such as those found in the Middle East.

Typically Vitamin D insufficiency, deficiency and severe deficiency as defined as 50-75 nmol/L, 27.5-50 nmol/L and <27.5 nmol/L respectively. The results of a recent study on young women aged 11 -18 years in the United Arab Emirates (1) produced the following results for each category respectively were 1%, 19.8% and 78.8% respectively i.e. over three quarters of the girls had severe deficiency which is likely to lead to problems for them and their offspring in later life.

A recent study of 10,735 adults from the Kingdom of Saudi Arabia that took place during the spring/summer of 2013 demonstrated that 63% of females and 41 of males were deficient in Vitamin D (i.e. plasma levels less than 28 ng/mL as defined by the Saudi Ministry of Health. Unfortunately, processed foods manufactured in KSA are not routinely fortified with Vitamin D and as the population is only likely to spend more time indoors in the future, it seems prudent for "at risk" groups, such as females over the age of 50 years to consume fortified food or consume daily supplements.

This paper will review the Vitamin D blood plasma status of the residents of the Middle East. It will assess dietary intake levels and sunlight exposure patterns. The contrasting effects of traditional local culture and adoption of westernized behaviors will be examined.

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SESSION 3 - VITAMIN D - ORAL COMMUNICATION

Wolfgang Herrmann - Abstract n° D11

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Title of abstract: One-year B and D vitamins supplementation improves metabolic bone markers and homocysteine metabolism.

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Key words: Vitamin D, B vitamins, homocysteine, bone markers

Abstract: BACKGROUND: Vitamin D and vitamin B deficiency are common in elderly subjects and are important risk factors for osteoporosis and age-related diseases. Supplementation with these vitamins is a promising preventative strategy. The objective of this study was to evaluate the effects of vitamins D₃ and B supplementation on bone turnover and metabolism in elderly people.

METHODS: Healthy subjects (n=93; >54 years) were randomly assigned to receive either daily vitamin D₃ (1200 IU), folic acid (0.5 mg), vitamin B12 (0.5 mg), vitamin B6 (50 mg), and calcium carbonate (456 mg) (group A) or only vitamin D₃ plus calcium carbonate (group B) in a double blind trial. We measured at baseline and after 6 and 12 months of supplementation vitamins, metabolites, and bone turnover markers.

RESULTS: At baseline mean plasma 25-hydroxy vitamin D [25(OH)D] was low (40 or 30 nmol/L) and parathormone was high (63.7 or 77.9 pg/mL). 25(OH)D and parathormone correlated inversely. S-Adenosyl homocysteine and S-adenosyl methionine correlated with bone alkaline phosphatase, sclerostin, and parathormone. One year vitamin D₃ or D₃ and B supplementation increased plasma 25(OH)D by median 87.6% (group A) and 133.3% (group B). Parathormone was lowered by median 28.3% (A) and 41.2% (B), bone alkaline phosphatase decreased by 2.8% (A) and 16.2% (B), osteocalcin by 37.5% (A) and 49.4% (B), and tartrate-resistant-acid-phosphatase 5b by 6.1% (A) and 36.0% (B). Median total homocysteine (tHcy) was high at baseline (group A: 12.6, group B: 12.3 μmol/L) and decreased by B vitamins (group A) to 8.9 μmol/L (29.4%). tHcy lowering had no additional effect on bone turnover.

CONCLUSIONS: One-year vitamin D₃ supplementation with or without B vitamins decreased the bone turnover significantly. Vitamin D₃ lowered parathormone. The additional application of B vitamins did not further improve bone turnover. The marked tHcy lowering by B vitamins may modulate the osteoporotic risk.

SESSION 3 - VITAMIN D - ORAL COMMUNICATION

Jeremie Talvas - Abstract n° D12

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Title of abstract: Can vitamin D boost production and circulating cathelicidin levels?

Authors and addresses: Jeremie Talvas(1), Guillaume Martinroche(1), Kassandra Lanchais(1), Stéphanie Rougé(1), Nicolas Goncalves-Mendes(1), Marie-Paule Vasson(1,2)

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Key words: vitamin D, cathelicidin, immunity, nutrition

Abstract: Introduction :The vitamin D deficiency (vitD) is widespread in France, especially in the elderly, causing in addition to osteoskeletal disorders, an increase of the infectious risk. VitD exerts immunomodulatory effects after binding to its receptor (VDR) expressed by certain immune cells including peripheral blood mononuclear cells (PBMC). These effects could be explained in part by the ability of vitD to stimulate the production of antimicrobial peptides, such as human cathelicidin, which has vitD response elements in its promoter (VDRE). The aim of this work was to determine whether vitD can induce the expression and production of cathelicidin in circulating immune cells both by i) ex vivo and ii) in vivo approaches. Methods: i) PBMCs collected from healthy donors were incubated ex vivo for 24 h and 48 h in the presence of different doses of vitD (0 ng/ml: control; 25 ng/ml: deficiency; 75 ng/ml: physiological; 125 ng/ml : suprphysiological) and then stimulated or not by a bacterial agent (extract of Escherichia coli Lipopolysaccharides (LPS): 100 ng / ml); or a viral mimetic agent(synthetic double-stranded RNA Poly (I: C) (PIC): 10 µg / ml). ii) Leukocytes and serum from healthy volunteers (> 65 years) were collected after randomization (V1), then 3 months after vitD or placebo supplementation (V2), and then 28 days later after influenza vaccination (V3). Gene expression was assessed by quantitative PCR and protein expression by western blot. Cathelicidin concentrations were determined by ELISA. Results:;i) Ex vivo, vitD significantly induced cathelicidin gene expression at t24 h with a maximum effect at 125 ng / ml in either unstimulated (x9) or stimulated LPS (x37) and PIC (x23). This intracellular overexpression is found significantly at the protein level at t48h under unstimulated conditions (x 1.5, D125) and stimulated at LPS (x1.7, D125). The excretion of the peptide in the supernatant is induced significantly by LPS and PIC with a tendency to a dose effect of vitamin D. ii) In vivo, a significant overexpression of cathelicidin is observed in the supplemented vs placebo group at V3 after vaccination (x9.15, p <0.05). The circulating rate of cathelicidin remained unchanged throughout the study, while vitamin D levels were significantly increased in the supplemented group (x 2.1, V2 vs V1, x 1.8, V3 vs V1) Conclusion: Intracellular expression of human cathelicidin in circulating leukocytes is induced by vitD in a dose-dependent manner, whereas extracellular production appears to be less influenced by vitD but more by stimulation of the immune system. These results suggest that vitamin supplementation in people with deficiencies may enhance the intracellular availability of cathelicidin that will be required in case of infections.

SESSION 3 - VITAMIN D - ORAL COMMUNICATION

Lauriane Bonnet - Abstract n° D13

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Title of abstract: Kinetic effect of high fat diet on vitamin D metabolism in mice.

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Key words: obesity, vitamin D, metabolism

Abstract: Low serum 25(OH)D concentrations, the major plasma form of vitamin D (VD), and low free 25(OH)D (1% of total circulating form) have been largely reported in obese subjects. Several hypotheses have been emitted to explain these observations: a sequestration of VD and/or its metabolites in adipose tissue (AT) which is their main storage site, or a dilution volumetric that occurs in obese subjects. We hypothesized that modifications of VD metabolism under high fat diet effect could explain a modification of VD plasma observed in obesity.

Male C57BL6j mice were fed with diet containing 10% (control group, HF10) and 60% (obese group, HF60) energy from fat for 7 and 11 weeks. VD and its metabolites have been quantified in plasma by LC-MS/MS. Free 25(OH)D plasmatic has been measured by ELISA. Gene expression of 25-hydroxylation (CYP2R1, CYP27A1 and CYP2J6) and 1 α hydroxylation (CYP27B1) enzymes, involved in 25(OH)D and 1,25(OH)₂D production respectively, have been quantified by qPCR in liver and AT.

As expected, the HF60 group had significantly higher body weight and white AT compared with HF10 group, more pronounced at 11 weeks than at 7 weeks. No discrepancies of energy or VD intake was observed between the 2 groups. Total 25(OH)D concentration was more important in HF60 than HF10 (1.2 and 1.2 fold respectively) that could be explain by a constant VD intake and/or by an increase of 25-hydroxylation enzymes (CYP2R1 (1.8 fold for 7 weeks and 1.5 fold for 11 weeks), CYP2J6 (1.5 fold for 7 weeks) and CYP27A1 (1.3 fold for 7 weeks)) mRNA levels in the liver of HF60 mice. Conversely, in agreement with literature, free 25(OH)D concentration decreased in HF60 only for 11 weeks (0.9 fold). These results do not support the dilution volumetric hypothesis since, at 7 weeks of HF60 diet, the fat mass was increased without modification of free 25(OH)D. Interestingly, cholecalciferol concentration was decrease in HF60 compared to HF10 (0.5 and 0.6 fold respectively at 7 and 11 weeks). This could be explained by the increase of CYP2R1 (2 fold for 7 weeks and 3.1 fold for 11 weeks) mRNA expression and a decrease of CYP27B1 (0.5 fold for 11 weeks) mRNA expression which could be lead to a possible storage of VD in AT under 25(OH)D form and participated to the decrease of plasma cholecalciferol concentration.

A high fat diet in mice, for 7 or 11 weeks, with the same VD intake between groups, leads to a modification of VD metabolism in liver and AT and could explain biologic modification observed. A dosage of the different forms of VD in TA is necessary to validate our different hypotheses.

SESSION 3 - VITAMIN D - FLASH POSTER

Poorya Shojai - Abstract n° D14

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Title of abstract: Development and Evaluation of bone tissue engineering scaffolds capable of controlled release of vitamin D

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poorya shojaee: ghaemshahr, iran

Key words: vitamin D, gelatin, drug delivery, bone tissue engineering

Abstract: Vitamin D has a key role in metabolism and bone turn over and many researchers reported the correlation between vitamin D deficiency and prevalency of complex diseases such as osteoporosis and diabetes. In this work we loaded vitamin D in gelatin carrier for bone tissue engineering applications. First, gelatin water based solution was prepared then vitamin D has been loaded in to gelatin via dual emulsion technique using acetone as secondary solvent. Afterword, to improve mechanical stability and diffusion behavior, crosslinked using glutar aldehyde 1% . in order to study micro structure and loading, the fourier transform infrared spectroscopy (FTIR) was conducted. Then to investigate the bioactivity of samples, simulated body fluid (SBF) was synthesized and samples were soaked in it for 21 days. The formation of secondary hydroxyl apatite was studied using X-ray diffraction (XRD) technique. Than, the drug release profile was studied through PBS solution in defined time points. More over, the degradation behavior of samples were studied in DW in defined time points (via pH and mass measurement). After word, the cytotoxicity of samples extracts were observed compared to control sample using MTT. Further more, the osteoblast activity of samples were studied via ALP activity measurement. The results showed that vitamin D improved the viability and osteoblasts activity and increased the degradation rate. More over, the dual emulsification method is an appropriate technique for vitamin D loading in hydrophobic systems.

SESSION 3 - VITAMIN D - FLASH POSTER**Ina Jasutiene - Abstract n° D15**

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Title of abstract: Fortification of foodstuffs by cold water soluble vitamin D₃ preparation

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Key words: hydrosoluble vitamin D₃, food fortification, stability

Abstract: Limited number of foods naturally contains vitamin D. Therefore it is important to find the best ways for the addition of vitamin D into food products. The recovery of added vitamin in the final product, depending on the fortification method used, remains a challenge for the food manufactures. Usually for the fortification of food vitamin D in liposoluble form is used. However, sometimes food manufacturers need the hydrosoluble vitamin D. In the current study we examined the possibility to employ the commercial cold water soluble vitamin D₃ preparation 100 CWS/AM (DSM Nutritional Products, Netherlands) for the fortification of food products. Apple juice and two dairy products - curd and condensed milk, were enriched by this vitamin D preparation. Vitamin D₃ content in food products was determined by reverse phase HPLC after overnight saponification at room temperature, extraction with hexane, evaporation and dry residual dissolving in mobile phase.

Apple juice was fortified by cold water soluble vitamin D₃ before and after pasteurization. Heat treatment had no effect on the recovery of vitamin in the product – in both cases it was 85.5%. No changes in the vitamin content were recorded during juice storage in the dark at 4°C for one month. However, vitamin D content decreased more than 2 times after storage of juice at 4°C for one month in the illuminated place (4187 lx). The recorded decrease of vitamin D was from 7.6 µg/100g in freshly prepared juice to 2.7 µg/100g after storage. Two samples of curd were produced by acid and acid-enzymatic coagulation methods in the small-scale laboratory conditions. Products were enriched by water soluble 100 CWS/AM preparation and lipid soluble crystalline cholecalciferol. It was found that the solubility of added vitamin had no effect on the recovery of vitamin D₃ in curd. The differences in vitamin recovery were caused by the method of curd production. In the curd samples made by acid-enzymatic method the vitamin D₃ recovery was 83% and in curd produced by acid fermentation the recovery was considerably smaller - 63%. Industrial trial was performed with the condensed milk enriched by the cold water soluble vitamin preparation. Vitamin preparation 100 g was added to the 10252 kg condensed milk before sterilization (D₃ 2.44 µg/100g). Determination of vitamin content in the beginning, middle and end of the production line showed, that vitamin distribution was equal – 2.45±0.31 µg/100g. After two months of storage, no decrease of vitamin was observed in the fortified condensed milk.

SESSION 3 - VITAMIN D - FLASH POSTER

Natalia Davydova - Abstract n° D16

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Title of abstract: Comprehensive evaluation of Cholecalciferol (Vitamin D₃) Dietary Supplement Tablets

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Key words: Vitamin D, dietary supplements

Abstract: Purpose: Dietary supplements containing cholecalciferol are available in different dosage forms, including capsules, liquids, chewable gels and tablets. However, there is no official compendial monograph with quality specifications for cholecalciferol in tablet form. Assay and dissolution tests are typical requirements in compendial monographs that help ensure the strength and quality of the finished products. Accordingly, a novel reverse-phase based HPLC method and a reliable and sensitive dissolution procedure were developed and validated for a comprehensive quality evaluation of dietary supplement tablets containing cholecalciferol in a wide range of doses.

Methods: The new reversed-phase HPLC procedure was developed on the Agilent Poroshell 120 SB-AQ brand column. Acetonitrile and water (70:30) was used as the mobile phase with UV detection at 265 nm. Cholecalciferol was extracted from the powdered tablets by sonication with a small volume of water followed by sonication with dimethylformamide and dilution with isopropyl alcohol (5:10:35). Dissolution test was performed in a dissolution medium that consisted of 500 mL of 0.1% (w/v) Triton X-100 in water using USP Apparatus 2 at 50-75 rpm. Dissolution profiles were generated over 120 min.

Results: The HPLC method separated cholecalciferol, ergocalciferol (vitamin D₂), and their vitamin D precursors. The typical retention times for cholecalciferol and ergocalciferol were 11.5 min and 12.1 min, respectively. The dissolution medium was found to assure sink conditions and chemical stability of cholecalciferol. The dissolution procedure generated suitable profiles to allow for discrimination among batches of product from the same manufacturer and among products from different manufacturers. Complete dissolution could be achieved within 45 minutes. The dissolution results varied between 95% and 175% of the labeled claim. The results from the dissolution tests were consistent with the Assay results.

Conclusion: A simple and sensitive isocratic HPLC method and a dissolution test for comprehensive evaluation of cholecalciferol dietary supplement tablets were developed and validated. These methods will be used in the new U. S. Pharmacopeia (USP) monograph proposal for cholecalciferol tables. These methods could be used to monitor manufacturing processes, as well as the quality of tablets used in clinical trials, or moving in the market as finished dietary supplements.

SESSION 3 - VITAMIN D - FLASH POSTER**Charlotte Lauridsen - Abstract n° D17**

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Title of abstract: Bioavailability of vitamin D in pregnant and lactating pigs and the relationship to health biomarkers

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Key words: 25-hydroxyvitamin D₃, piglet, bone health, reproduction

Abstract: From research in other animal species and humans, it is known that vitamin D has several biologically functions related to reproduction, bone health and immune modulation. Pigs are reared without exposure to sun light, at the main form of vitamin D is dietary supplementation of D₃ or its metabolite, 25(OH)D₃. Little knowledge is available on the effect of dietary forms and doses on the vitamin D status in body fluids and tissues, and the relationship to health of the pigs. Recently, the official vitamin D requirement for pregnant and lactating pigs was increased from 200 to 800 IU vitamin D/kg feed. The purpose of the present paper is to review the main findings of a published study, which has contributed to the basis for this establishment. In this study, a dose-response trial with 4 doses of both D₃ and 25(OH)D₃ was performed with reproducing pigs and consisted of 2 experiments: In Exp. 1, 160 pigs from first estrus until day 28 of gestation were fed diets containing four concentrations of one of two vitamin D sources (i.e., 200, 800, 1,400, and 2,000 IU/kg from cholecalciferol or corresponding levels of 5, 20, 35, or 50 µg/kg from 25(OH)D₃ [Hy-D]). Concurrently in study 2, the same eight dietary treatments were fed to 160 sows from the first day of mating until weaning. The results of this study addressed the nutritional benefits of vitamin D dose and forms for pregnant and lactating sows and their offspring in terms of vitamin D status, reproduction, transfer to the neonate, and bone health. Based on the plasma vitamin D status it was concluded that the potency of the dietary 25(OH)D₃ in relation to vitamin D₃ depended on the amount tested, but above 200 IU, the metabolite was a more bioavailable source than vitamin D, and as such, could be considered an equivalent or even more advantageous source of vitamin D. Tissue levels reflected the dietary forms of vitamin D, i.e., the tissue 25(OH)D₃ level was higher in pigs provided the 25(OH)D₃ compared with those fed vitamin D₃, while the tissue vitamin D₃ level was higher in the pigs fed vitamin D₃ compared with those fed 25(OH)D₃. The lactation stage of the sows and the age of the suckling pigs influenced the bone status markers measured. Reproductive performance was not influenced by dietary vitamin D treatments, except for a decreased number of stillborn piglets with the larger doses of vitamin D compared with the smaller levels of vitamin D. Irrespective of the dietary dose and form of vitamin D provided the sows, very little vitamin D was transferred to the piglets. Suckling piglets without exposure to sunlight may need a vitamin D supplement. The results are put into context with the existing literature including the importance of vitamin D in relation to human health considering the pig as an animal model.

SESSION 3 - VITAMIN D - FLASH POSTER

Argjira Juniku-Shkololli - Abstract n° D18

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Title of abstract: Evaluation of the risk for developing colitis-associated cancer in patients with inflammatory bowel disease: the role of vitamin D

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Key words: Vitamin D, immune mechanisms, inflammatory bowel disease, colorectal cancer

Abstract: Inflammatory bowel disease (IBD) is a chronic gastrointestinal disease, associated with an increased risk for the development of colorectal cancer (CRC). Although colitis-associated cancer (CAC) develops in a small number of IBD-patients (1%), it has a high mortality, accounting for about 20% of deaths in IBD. Risk factors for CAC development are: duration of the disease, family history for CRC, extent of colitis and the presence of co-existent primary sclerosing cholangitis. Results from recent studies have shown that bowel strictures and post-inflammatory polyps should be considered as important risk factors for CRC development. Data from case-control studies suggest that high degree of inflammation (colonoscopic or histologic) has an increased risk for CAC. Colectomy is strictly recommended for patients diagnosed with high grade dysplasia or CRC. Multifocal low grade dysplasia is a strong indication for colectomy. It is proven that mesalazine has a protective role against CRC and dysplasia. Surveillance of IBD in the future involves new endoscopic techniques. Over the past decade an increasing emphasis has been given to the anti-inflammatory and immunomodulatory actions of vitamin D, as well as its antitumoral action. These effects have led towards investigations of vitamin D implications in the pathophysiology of IBD and its role in the development of CRC in IBD patients.

SESSION 3 - VITAMIN D - FLASH POSTER

Catherine Féart - Abstract n° D19

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Title of abstract: Lower vitamin D concentrations and higher long-term risk of dementia and Alzheimer's Disease

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Key words: Vitamin D, Dementia, Alzheimer, Prospective Cohort

Abstract: IMPORTANCE: Hypovitaminosis D is highly prevalent worldwide, and particularly among the aged population. In addition to its effects on bone metabolism, it has been associated with several chronic conditions, such as cardiovascular diseases which are risk factors for dementia; yet, association of hypovitaminosis D to risk of dementia has been inconsistent.

OBJECTIVE: To analyze the relation between plasma 25(OH)D concentration and the risk of dementia and Alzheimer's Disease (AD) in French elderly community-dwellers.

DESIGN, SETTING, AND PARTICIPANTS: The study population consisted of 916 participants from the Three-City-Bordeaux cohort aged 65 years and over, non-demented at baseline, who provided blood samples for assessment of vitamin D status and were followed for up to 12 years. The baseline concentration of plasma 25(OH)D (corrected for season of blood draw) was categorized as < 25 nmol/L (deficiency), 25 to 50 nmol/L (insufficiency), or > 50 nmol/L (sufficiency). Incident cases of dementia and AD were diagnosed by an independent committee of neurologists every 2 years during follow-up.

MAIN OUTCOME AND MEASURES: Associations between plasma 25(OH)D concentrations and risk of dementia or AD were estimated using multivariate Cox models.

RESULTS: A total of 177 dementia cases, including 124 AD, occurred over 10.8 years, on average. The prevalence of plasma 25(OH)D deficiency and insufficiency at baseline were 23.8% and 59.7%, respectively. After adjustment for socio-demographic variables, cardiovascular risk factors, smoking status, physical activity, depressive symptomatology, Apolipoprotein E genotype, and diet quality, compared to individuals with 25(OH)D sufficiency, participants with both 25(OH)D deficiency and insufficiency had a significantly increased risk of dementia (Hazard ratio (HR)=2.12, 95% Confidence Interval (95%CI) 1.21-3.71 and HR=1.98, 95%CI 1.17-3.36, respectively; P for trend across the three categories of 25(OH)D status = 0.02). Stronger associations were observed with AD risk (HR=2.85, 95%CI 1.37-5.97 and HR=2.78, 95%CI 1.36-5.68 for participants with 25(OH)D deficiency and insufficiency, respectively; P for trend 0.02).

CONCLUSIONS AND RELEVANCE: This large prospective study of French older adults suggests that maintaining adequate vitamin D status in older age could contribute to delay or prevent the onset of dementia, especially of AD aetiology.

SESSION 3 - VITAMIN D - FLASH POSTER

Ludmila Macova - Abstract n° D20

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Title of abstract: Vitamin D and other steroids in autism

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Key words: autism, vitamin D, neurosteroids

Abstract: Introduction: Autism or autistic spectrum disorder (ASD) is a serious neuropsychiatric disorders with constantly increasing incidence. Its diagnosis is based predominantly on psychiatric questionnaire. There are so far lacking laboratory markers which could confirm or at least contribute to its early diagnosis. In accordance with the extreme male brain theory of ASD (Baron-Cohen 1999), boys are more likely than girls to be diagnosed with an ASD. At the same time, an association exists between ASD and a steroid biosynthesis disorder known as Smith-Lemli-Opitz syndrome. Vitamin D deficiency has been often mentioned as an environmental trigger for ASD. However the connection of the disease to steroids remains unclear.

Methods and Results: We investigated Vitamin D - as a representative of neurosteroids - and other steroids as potential markers involved in ASD development. Cohort of 45 autistic pediatric patients (4-7 y) and 40 age matched controls were included into the study. Serum Vitamin D (25(OH) D) was measured by commercially available ELISA kit. Data was adjusted to period of the sample collection to avoid the influence of vitamin D seasonal changes. Mean levels of 25(OH)D in ASD patients were 65.07 ± 25.9 nmol/L and 70.35 ± 20.7 nmol/L in controls, respectively. 69% of the patients and 62% of control group had non-optimal levels of vitamin D (less than 75 nmol/L). Despite a higher proportion of low values among autistic patients, the difference was not statistically significant.

More than 100 steroids and their metabolites were determined by a unique GC-MS/MS method. Preliminary results show elevated levels of 19C steroids and their metabolites which indicates raised activity of zona reticularis in autistic patients.

Conclusion: Opposite to other studies, we found no significant difference in levels of serum vitamin D between group of autistic patients and healthy controls. It indicates that low levels of vitamin D may be a risk factor for autism, but it is also a non-specific parameter that is needed to be viewed from a broad perspective.

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SESSION 3 - VITAMIN D - POSTER

Elham Sharif - Abstract n° D21

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Title of abstract: THE ASSOCIATION BETWEEN VITAMIN D DEFICIENCY AND ENDOTHELIAL DYSFUNCTION IN ASYMPTOMATIC SUBJECTS

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Key words: vitamin D deficiency, Endothelial dysfunction, biomarkers

Abstract: Endothelial dysfunction is the earliest stage of several types of diseases related to cardiovascular system. The endothelial dysfunction, is characterized by several changes such as upregulation of adhesion molecules and elevation of chemokine production and endothelial permeability. Several studies suggested that vitamin D deficiency could accelerate the endothelial dysfunction process.

Aim:

This study was performed to investigate the possible effect of vitamin D status on endothelial function in asymptomatic subjects.

Results:

The current study showed that subjects with low vitamin D level have a significantly higher level of Plasminogen Activator Inhibitor-1 (PAI-1) and soluble Intercellular Adhesion Molecule (sICAM) than control subjects. However, significantly lower levels was detected for adiponectin hormone in subjects with low vitamin D level than control subjects. No significant differences in P-selectin level and inflammatory biomarkers were observed between the two studied groups. Aging effect in increasing the level of endothelial dysfunction biomarkers has been hindered by sufficient level of vitamin D.

Conclusion:

Findings of present study suggested that there is an association between vitamin D deficiency and endothelial dysfunction biomarkers elevation in asymptomatic subjects.

SESSION 3 - VITAMIN D - POSTER

Marie-Christine Carlier - Abstract n° D22

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Title of abstract: Measured free 25OH vitamin D levels in chronic kidney disease

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Key words: free 25 vitD CKD

Abstract: Most chronic kidney disease patients suffer from 25OH vitD deficiency which might contribute to adverse health outcomes. It has been proposed that serum free 25 OHvitamin D better reflects vitamin metabolism.

We aim to evaluate whether serum free 25 OH VitD varies regarding the different stages of CKD, in comparison with total 25 OH vitD

Methods: For 86 CKD patients with a glomerular filtration rate measurement (GFR) by inulin clearance, serum free 25OHvitD by ELISA (DiaSource, Leuven, Belgium) and total 25OHvitD by immunoluminometry (DiaSorin, Italy) was measured

Results: Patients were aged 54.8 (43-66,7) yr, 41 men and 45 women. Mean GFR by inulin was 61.7 (57.9–65.6) ml/min/1.73m², serum total 25OHvitD was 67.8 (61.6-73.9) nmol/L and serum free 25OHvitD 5.8 (5.4-6.3) ng/L. We found a strong association between free 25OHvitD and total 25OHvitD ($r=0.86$, $p<0.001$). There was no correlation between free 25OHvitD and GFR ($r = -0.04$, $p=0.69$). The ratio free/total 25OHvitD strongly decreased with the decline of kidney function ($r=0.4$, $p<0.001$). We did not find any relationship between free 25OHvitD nor total 25OHvitD and measures of mineral metabolism.

Conclusion: Free 25 OH vitD is not influenced by the level of renal function and the bioavailability may be reduced in advanced CKD

SESSION 3 - VITAMIN D - POSTER**Tarek Chaabouni - Abstract n° D23**

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Title of abstract: Analytical and clinical evaluation of the automated Fujirebio Lumipulse®G non-competitive assay for 25(OH)-vitamin D, a comparison with LC-MS/MS and the automated Isys IDS competitive assay.

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Key words: vitamin D, automated method, LC-MS/MS

Abstract: Introduction: The clinical interest for vitamin D exploded during the last decade and, in 2016, 4327 references concerning this subject appeared in PubMed. Over the same period the availability of automated methods for the measurement of 25-OH vitamin D in blood increased considerably. Except for one, all are competitive assays. The recent method proposed by Fujirebio on the Lumipulse G is the first sandwich immunoassay for the quantification of 25-OH vitamin D. Here, we compare results obtained with this non-competitive assay, with those obtained using an automated competitive immuno-assay on Isys (IDS) and those generated with an LC-MS/MS reference method.

Methods: Forty nine samples with only endogenous 25-OH vitamin D, used in a previous study (Denimal et al. Clin Chem Lab Med, 2013), were analyzed. Between the first study and this one a new version (version S) of the Isys kit was commercialized. So we compare the two versions of the competitive immuno-assay. The fully automated Fujirebio technology is an innovative non-competitive two step chemiluminescence enzyme immuno-assay (CLEIA).

- for all assays, the 25-OH vitamin D must be released from its transport protein, the vitamin D binding protein (VDBP). The extraction is done by a proprietary competitive steroid compound and not by a physico-chemical condition as reported for other assays. - the detection of 25-OH vitamin D, which is a very small molecule, is done by sandwich immunoassay on the basis of antimetatype antibodies. Briefly, an immobilised sheep monoclonal antibody captures the 25-OH vitamin D. A second recombinant chicken monoclonal antibody labeled with alkaline phosphatase recognizes the 25-OH vitamin D/sheep monoclonal antibody immuno-complex. Finally, luminescence is generated by dephosphorylation of a substrate. The luminescence signal reflects the amount of 25-OH vitamin D in the sample. Sandwich assays are known to offer generally better sensitivity and specificity than competitive immuno-assays. The limits of detection are respectively, for Isys and Lumipulse assays, 6.5 nmol/L and 2.7 nmol/L, and the limits of quantification are respectively 17.5 nmol/L and 8.9 nmol/L. The accuracy of the sandwich method far better than with the competition assays. The within-run CV for low concentrations of 25-OH vitamin D (around 25 nmol/L) is respectively, for Isys and Lumipulse, 6.4% and 3.8%, and for high concentrations (around 275 nmol/L) 5.1% and 0.8%. The total CV (n = 80, adapted from CLSI EP 5A-2) is respectively 10.6% and 5.6% for low 25-OH vitamin D concentrations and 7.2% and 2.2% for high concentrations. Results: The correlation between the two versions of the Isys competitive immuno-assay (Passing-Bablok "Isys" = $0.8875 \times \text{"Isys S"} + 8.95$ $R^2=0.9846$) conforms to the results announced by IDS ("Isys" = $0.91 \times \text{"Isys S"} + 2.8$ $R^2=0.884$ n=283). This confirmed that the conservation of the samples was good and that they could be used for further investigations. The correlation between the Isys version S and LC-MS/MS gives "LC-MS/MS" = $0.8518 \times \text{"Isys S"} + 15.374$ $R^2=0.941$. This correlation is in accordance with the correlation obtained with the external quality control scheme DEQAS between the mean result of LC-MS/MS (n=154 to 159) and mean result of Isys S (n = 88 to 91) in four different control schedules (20 samples, 486-505) "LC-MS/MS" = $0.872 \times \text{"Isys S"} + 5.271$ $R^2=0.9628$. This is also in accordance with the data from IDS with 95% confidence interval "LC-MS/MS" = 0.86 to 1.04 \times "Isys S" - 3.2 to +7.8 $R^2=0.8556$. The correlation between the Fujirebio and LC-MS/MS is excellent "LC-MS/MS" = $1.00001 \times \text{"Lumipulse"} - 6.992$ $R^2=0.9849$.

Conclusion: The non-competitive Fujirebio assay for 25-OH vitamin measurement in blood correlates well with our LC-MS/MS reference method. The intra and inter assay CV is more than two times lower than the 5% required by the Vitamin D Standardization Program (VDSP). From the clinical point of view, compared to LC-MS/MS results, there is no misclassification of vitamin D deficiency, insufficiency and sufficiency.

SESSION 4 - FAT SOLUBLE VITAMINS - KEY NOTE

Catherine Féart - Abstract n° FSV1

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Title of abstract: Nutrient biomarker patterns and risk for frailty among 4 European cohorts of older adults

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Key words: Pattern, Nutrients, frailty

Abstract: Importance: With the aging population worldwide, frailty has become a public health challenge. At the same time, micronutrient deficiencies are common among older adults. Previous studies reported an increased risk of frailty in people with low vitamin D status while others have observed an association between low levels of carotenoids and an increased risk of becoming frail. To our knowledge, no studies have focused on patterns of fat-soluble micronutrients. This study was designed to investigate the relationship of blood nutrient patterns with frailty, cross-sectionally and over 2 years, in four large European population-based cohorts of older adults. Methods: We included 1324 participants from four cohorts of older adults from France (Three-City and AMI), Spain (Toledo Study for Healthy Aging) and Italy (InChianti) and with blood measurements of 9 fat-soluble nutrients (alpha and beta-carotene, lycopene, cryptoxanthin, lutein and zeaxanthin, 25(OH)D, alpha and gamma tocopherols, and retinol) at baseline, and who were followed for up to 2 years. Frailty was defined as having at least three out of the following five criteria: unintentional weight loss; exhaustion; slowness; muscle weakness and low energy expenditure. A principal component analysis (PCA) was used to derive the patterns on the basis of the serum concentration of the nine fat-soluble vitamins and carotenoids. Multivariate logistic models, controlled for socio-demographic and clinical characteristics, were performed to test the association between each pattern of nutrients and prevalence of frailty or risk of frailty 2-y later. Results: Three nutrient patterns have been identified, explaining 29.8%, 15.6% and 12.8% of the variance respectively. The cross-sectional analysis consisted of 1324 participants. Among the 3 nutrient patterns, only the pattern characterized by high retinol and vitamin E levels and low carotene levels was significantly associated with frailty at baseline: the quartile 1 was associated with a higher prevalence of frailty (Odds Ratio =2.2, 95% Confidence Interval 1.3-3.8, P=0.001) compared with quartile 4. The prospective association was performed on 915 non frail participants at baseline, among whom 84 became frail at 2-y of follow-up. We observed no significant association between each nutrient pattern and the risk for frailty 2 years later, in fully adjusted models. Conclusion: A blood nutrient pattern reflecting high retinol and vitamin E levels and low carotene levels in older adults appeared associated with the presence of frailty but not with the risk for frailty in 4 European large cohorts. This analysis suggested that these dietary characteristics were marker of the frailty status but not predictor of frailty.

The research leading to these results has received funding from the European Union's Seventh Framework Programme (FP7/2007-2013) under grant agreement n°305483, FRAILOMIC Project

SESSION 4 - FAT SOLUBLE VITAMINS - KEY NOTE

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Title of abstract: Lower vitamin D concentrations and higher long-term risk of dementia and Alzheimer's Disease

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Key words: Vitamin D, Dementia, Alzheimer, Prospective Cohort

Abstract: IMPORTANCE: Hypovitaminosis D is highly prevalent worldwide, and particularly among the aged population. In addition to its effects on bone metabolism, it has been associated with several chronic conditions, such as cardiovascular diseases which are risk factors for dementia; yet, association of hypovitaminosis D to risk of dementia has been inconsistent.

OBJECTIVE: To analyze the relation between plasma 25(OH)D concentration and the risk of dementia and Alzheimer's Disease (AD) in French elderly community-dwellers.

DESIGN, SETTING, AND PARTICIPANTS: The study population consisted of 916 participants from the Three-City-Bordeaux cohort aged 65 years and over, non-demented at baseline, who provided blood samples for assessment of vitamin D status and were followed for up to 12 years. The baseline concentration of plasma 25(OH)D (corrected for season of blood draw) was categorized as < 25 nmol/L (deficiency), 25 to 50 nmol/L (insufficiency), or > 50 nmol/L (sufficiency). Incident cases of dementia and AD were diagnosed by an independent committee of neurologists every 2 years during follow-up.

MAIN OUTCOME AND MEASURES: Associations between plasma 25(OH)D concentrations and risk of dementia or AD were estimated using multivariate Cox models.

RESULTS: A total of 177 dementia cases, including 124 AD, occurred over 10.8 years, on average. The prevalence of plasma 25(OH)D deficiency and insufficiency at baseline were 23.8% and 59.7%, respectively. After adjustment for socio-demographic variables, cardiovascular risk factors, smoking status, physical activity, depressive symptomatology, Apolipoprotein E genotype, and diet quality, compared to individuals with 25(OH)D sufficiency, participants with both 25(OH)D deficiency and insufficiency had a significantly increased risk of dementia (Hazard ratio (HR)=2.12, 95% Confidence Interval (95%CI) 1.21-3.71 and HR=1.98, 95%CI 1.17-3.36, respectively; P for trend across the three categories of 25(OH)D status = 0.02). Stronger associations were observed with AD risk (HR=2.85, 95%CI 1.37-5.97 and HR=2.78, 95%CI 1.36-5.68 for participants with 25(OH)D deficiency and insufficiency, respectively; P for trend 0.02).

CONCLUSIONS AND RELEVANCE: This large prospective study of French older adults suggests that maintaining adequate vitamin D status in older age could contribute to delay or prevent the onset of dementia, especially of AD aetiology.

SESSION 4 - FAT SOLUBLE VITAMINS - KEY NOTE

Catherine Féart - Abstract n° FSV3

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Title of abstract: Nutrient biomarker patterns and risk of dementia

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Key words: Patterns, Biomarkers, Dementia, Prospective Cohort

Abstract: **Objective:** Nutrition may contribute to prevent Alzheimer's disease (AD); yet previous research on individual nutrients and dementia may have inadequately reflected the complexity of diet-brain relationships. We sought to characterize nutrient biomarker patterns (which provide a more holistic approach of dietary exposure and bioavailability) associated with long-term risk of dementia in a large cohort of older persons, the Three-City (3C) study.

Methods: We included 666 participants from the 3C study not demented and with blood measurements of 22 fat-soluble nutrients (12 fatty acids, 6 carotenoids, vitamin D, 2 forms of vitamin E, and vitamin A) at baseline, who were followed for up to 12 years for incidence of dementia/AD. Nutrient patterns associated with dementia risk were characterized using Partial Least Square regression for Cox models (PLS-Cox).

Results: A "deleterious" nutrient biomarker pattern combining lower blood vitamin D, carotenoids and polyunsaturated fats and higher blood saturated fats, was strongly associated with a higher risk of dementia. After adjustment for a large set of potential confounders, compared to individuals in the first quintile of PLS-Cox score, participants in the highest quintile of score had a four-fold increased risk of dementia (HR=4.20, 95% CI 1.86-9.42, P for trend < 0.001); this association appeared stronger than associations found with any individual nutrient biomarker.

Conclusion: A blood nutrient pattern reflecting deficiencies in vitamin D, carotenoids and polyunsaturated fats in non-demented older persons appeared strongly associated with a greater risk of dementia over the decade following biomarker assessment in this large cohort of older persons.

SESSION 4 - FAT SOLUBLE VITAMINS - ORAL COMMUNICATION**Marielle Margier - Abstract n° FSV4**

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Title of abstract: Impact of pulses on fat-soluble vitamins bioavailability

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Key words: pulses, fat-soluble vitamins, bioavailability

Abstract: Fat-soluble vitamins play a key role in the prevention of eye, bone, neurodegenerative and cardiovascular diseases. However, their beneficial properties depend on their bioavailability, which can be modified by interactions with other meal components. Pulse consumption is encouraged as a protein source with low environmental impact and their capabilities to decrease the circulating levels of cholesterol and triglycerides. Such capabilities suggested that pulses could also impact on fat-soluble vitamin digestion-absorption. The aim of our study was to assess the impact of pulses (lentils, white beans, kidney beans, flageolets and chickpeas) and their preparation modes (home cooking vs. canning) on the bioavailability of vitamin A (and its precursor: beta-carotene), D, E and K.

In vitro digestion models were used to compare fat-soluble vitamin bioaccessibility when ingested in a test meal containing either potatoes (control) or pulses. Mixed micelles from the in vitro digestions were then delivered to human intestinal Caco-2 TC7 cells in order to assess cell ability to absorb fat-soluble vitamins. Pearson's correlations between tannins, phytates, saponins, fibre contents and bioavailability of vitamins and beta-carotene were calculated.

Fat-soluble vitamins and β -carotene bioaccessibility decreased in meals containing pulses (from -11% to -70%) compared to the meal control ($p < 0.05$). Interestingly, canning could significantly improve fat-soluble vitamin bioaccessibility compared to home cooking: β -carotene and cholecalciferol bioaccessibility was higher for canned rather than boiled chickpeas (respectively +52% and +18%, $p < 0.05$). Furthermore, the absorption of vitamins D, E and K by Caco-2 cells significantly decreased when vitamins were in micelles from digested meals containing pulses (from -22% to -66%) as compared to micelles from the digested control meal ($p < 0.05$). Canning could also improve fat-soluble vitamins absorption in some conditions, i.e. the absorption of vitamin K from the meals containing canned white beans and canned lentils increased of 35.5% and 76.3% compared to home cooked pulses ($p < 0.05$). Correlations between bioaccessibility and bioavailability was positive for all vitamins ($p < 0.05$) except for vitamin A and β -carotene. Furthermore, tannins, phytates, saponins and fibre contents were negatively correlated to both bioaccessibility and bioavailability of vitamins ($p < 0.05$), except vitamin A and β -carotene.

Altogether, these results showed that the presence of pulses in meals reduces both bioaccessibility and uptake by intestinal cells of fat-soluble vitamins, and that the mode of pulse preparation is a significant parameter. Identifying the compounds responsible for these effects should enable to propose appropriate solutions for the development of pulse-based products that will preserve the nutritional quality of meals. These results may also be used as a basis for dietary recommendations regarding vegetarian diets

SESSION 4 - FAT SOLUBLE VITAMINS - ORAL COMMUNICATION

Irene Pusceddu - Abstract n° FSV5

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Title of abstract: The role of B and D vitamins in telomere length: results from the LURIC study and the Sud-Tyrolean study

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Key words: telomere length, vitamin D, homocysteine,

Abstract: Background: Telomeres are essential for the maintenance of genomic integrity. Telomere length declines with age and telomere shortening/dysfunction has been proposed as a biomarker for age-related diseases. B and D vitamins are essential cofactors for numerous cellular processes including the synthesis of purines and nucleotides, DNA methylation, cell differentiation, proliferation and apoptosis. B and D vitamin deficiencies are risk factors for the development of age-related diseases. The aim of this study was to evaluate the effects of B and D vitamin on telomere biology. Methods: We analyzed the LURIC study (3316 cardiovascular patients) and the Sud-Tyrolean study (STVS 350 healthy subjects). Relative telomere length (RTL) and telomerase activity were performed using a qPCR-based assay. Vitamin B6, B9, B12, homocysteine (HCY), 25OH vitamin D, 1,25(OH)₂ vitamin D, parathormone (PTH), advanced glycation end-products (AGEs), Klotho and FGF-23 were analyzed. Results: In the STVS, RTL correlated negatively with age, PTH and HCY, and positively with vitamin B12 in men and 25OH vitamin D in subjects with vitamin D deficiency. Telomerase activity was higher in subjects with higher vitamin B12 concentrations and telomerase activity correlated positively with 1,25(OH)₂ vitamin D. In subjects with RTL below the median, AGEs correlated positively with telomerase activity, HCY and negatively with folic acid, vitamin B12 and 25-OH vitamin D. The multivariate analyses revealed age, HCY and PTH as negative independent predictors of RTL. In the LURIC study, RTL correlated negatively with age, HCY and 1,25(OH)₂ vitamin D and positively with 25OH vitamin D. In subjects with vitamin D deficiency, RTL correlated negatively with FGF-23 and positively with Klotho. The multivariate analyses revealed age, HCY and 1,25(OH)₂ vitamin D as negative independent predictors of RTL and folic acid as a positive independent predictor of RTL. Conclusions: The results from the two studies provide evidence for an association between vitamin B and D status and telomere length. However, further statistical analyses are needed to confirm these results.

SESSION 4 - FAT SOLUBLE VITAMINS - ORAL COMMUNICATION

Damien Prévéraud - Abstract n° FSV6

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Title of abstract: Cholecalciferol (vitamin D₃) and retinyl palmitate (vitamin A) display different solubilization capacities in mixed micelle solutions: effect of interactions with mixed micelle components and of cholecalciferol to self-associating properties

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Key words: digestion, bioaccessibility, surface tension, lipid monolayers

Abstract: Scope: Cholecalciferol (D₃) and retinyl palmitate (RP) are the two main fat-soluble vitamins found in foods from animal origin. It is assumed that they are solubilized in mixed micelles prior to their uptake by intestinal cells but only scarce data are available on the relative efficiency of this process and on the physicochemical parameters that govern it.

Methods: The solubility of D₃ and RP in synthetic mixed micelles composed of bile lipids, sodium taurocholate (NaTC) and lipid digestion products was measured by HPLC. Surface tension and surface pressure-surface area measurements of vitamin and mixed micelle monolayers, alone or in combination, were performed to analyze the interactions between these components.

Results: Mixture of lipids and NaTC allowed formation of micelles with higher molecular order at lower concentrations than pure NaTC molecules. D₃ solubilization in mixed micelle solutions was several times higher than that of RP. NaTC and mixed lipids interacted better with a D₃ monolayer than with a RP one. Furthermore, D₃ showed some self-association properties in aqueous solution.

Conclusions: Solubilization efficiency of D₃ in an aqueous phase rich in mixed micelles is several times higher than that of RP because D₃ is incorporated into NaTC and lipid domains much more efficiently than RP, and because it is able to self-aggregate in soluble micelle-like structures.

SESSION 4 - FAT SOLUBLE VITAMINS - KEY NOTE

Adrian Franke - Abstract n° FSV7

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Title of abstract: Technology and methodology improvement of analytical approaches for FSV determination in biological samples

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Key words: fat-soluble, vitamins, carotenoids, HPLC

Abstract: Epidemiological and clinical studies commonly require accurate, fast, and affordable analyses that provide multiple biomarkers using minimal volume from a single blood specimen. Essential circulating fat soluble vitamins (FSV) and other lipophilic antioxidants play important roles in health maintenance and disease prevention and can, therefore, serve as useful risk markers. We developed simple, fast, affordable, robust, and accurate HPLC assays with diode array detection (DAD) that can simultaneously measure circulating vitamin D metabolites (25-hydroxy vitamin D₂ and D₃), vitamin A (retinol), vitamin E (α -, β -, γ -, and δ -tocopherol), all major carotenoids including their isomers, and coenzyme Q10 compounds (ubiquinol-10 and ubiquinone-10) from small blood volumes ($\leq 100 \mu\text{L}$) in a single chromatographic run. Method 1 uses a C18 column alone that separates all major analytes but with insufficient resolution for the vitamin D metabolites and lycopene isomers and co-elution of lutein with zeaxanthin and β - with γ -tocopherol. Method 2 uses a C30 column alone that successfully separates the carotenoid isomers and β - from γ -tocopherol but fails to resolve carotenoids from Q10 compounds. Method 3 connects a C18 to a C30 column with a 6-port valve between the columns and a DAD after the columns; this 2-dimensional approach results in all analytes and isomers of interest to be separated with no interferences or back pressure. The run times of these methods varies from 45 minutes (method 3) for all analytes and isomers to 25-30 minutes (methods 1 and 2) for fewer analytes

Our isocratic 2-D methods are able to analyze all FSV and lipophilic antioxidants of interest in a single run and can be modified to meet the needs of individual projects depending on analyte requirements. These methods have been previously applied to study coenzyme Q10 stability in serum and plasma (Franke et al, *Free Radic Biol Med* 2010: 48, 1610), to investigate vitamin D status in multiethnic populations (Halm, et al *J Am Coll Nutr* 2013: 32, 215), to measure FSV in umbilical cord plasma from multiethnic mothers (Franke, et al *Free Radic Res* 2013: 47, 757), to examine changes in FSV in young children after receiving X-irradiation via medically indicated computed tomography (Halm, et al *Arch Biochem Biophys* 2014: 547, 37), and to study the relationships in diet, lifestyle and medical history (Kolonel et al *J Epidemiology*, 2000: 151, 346). Current applications include studies in multiethnic populations investigating FSV associations with total and regional adiposity (Exposome Project), mortality (Multiethnic Cohort Study) and relationships between macular pigment optical density (carotenoid levels in the macula) and cognitive function. Preliminary results on these and other studies will be presented.

SESSION 4 - FAT SOLUBLE VITAMINS - POSTER

Adrian Franke - Abstract n° FSV8

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Title of abstract: Simultaneous analysis of circulating 25-hydroxy-vitamin D₃, 25-hydroxy-vitamin D₂, carotenoids, retinoids, tocopherols, and oxidized and reduced coenzyme Q10 by HPLC with photo diode-array detection using C18 and C30 columns alone or in combination

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Key words: HPLC circulating carotenoids, tocopherols coenzyme Q10

Abstract: Modern epidemiological and clinical studies commonly require high-throughput analyses that provide multiple biomarkers from a small volume, single blood specimen. Essential circulating lipid-soluble compounds play important roles in health and disease prevention and can, therefore, serve as useful biomarkers. We sought to develop a simple, fast, affordable, and highly accurate HPLC assay with diode array detection (DAD) that simultaneously measured all circulating lipid-soluble compounds.

In our study, 25-hydroxy vitamin D₂ and D₃, retinol, alpha-, beta-, gamma-, and delta-tocopherol, all major carotenoids including their isomers, and ubiquinol-10 and ubiquinone-10 were accurately quantitated in a single chromatographic run using 1) a C18 column alone; 2) a C30 column alone; or 3) C18 and C30 columns connected in series. After several modifications, we refined our methods to resolve all analytes within 45-90 minutes or fewer analytes within 10 minutes.

The C18 alone excellently separated all major analytes but insufficiently resolved the vitamin D metabolites, lycopene isomers, and resulted in co-elution of lutein with zeaxanthin and beta- with gamma-tocopherol. The C30 alone was superior at separating the carotenoid isomers and beta- from gamma-tocopherol, but failed to resolve carotenoids from Q10 compounds. Connecting C18 and C30 in series with a DAD between and after the columns resulted in accurate quantitation of all analytes, however, was unacceptably long (90 minutes) due to the very low flow rate requirement imposed by back pressure limitations. Connecting C18 and C30 in series with only one DAD after the C30 column also resulted in carotenoid- Q10 interferences, but was remedied by adding a 6-port valve between the columns, which permitted resolution of all analytes in 45 minutes with a possible shortening of 15-20 minutes depending on the analytes included. In summary, our proposed methods can be custom designed to meet the needs of individual projects depending on analyte requirements. Associations of these analytes with colorectal and breast cancer risk from ongoing epidemiologic studies will be presented.

SESSION 5 - CAROTENOIDS - KEY NOTE**Torsten Bohn - Abstract n° C1**

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Institution: Luxembourg Institute of Health

Speciality: Phytochemicals, micronutrients, diet, health, inflammation, digestion

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Title of abstract: Carotenoids - from Occurrence to Bioavailability to Biactivity.**Authors and addresses:** Bohn, Torsten. Luxembourg Institute of Health, Strassen Luxembourg**Key words:** apocarotenoids, health, bioaccessibility, novel aspects

Abstract: Carotenoid dietary intake and plasma levels have been associated with a reduced risk of a number of chronic diseases, including diabetes mellitus type 2, the metabolic syndrome, cardiovascular disease, and several types of cancer. However, their predominant ways of action remain controversial, and it often is not apparent whether the effects are due to native carotenoids, their metabolites, or both. Recent studies have highlighted that their beneficial health effects may be due to influences on cellular signalling pathways, interacting with transcription factors such as NF- κ B and Nrf2, altering gene expression. There are also indications that several of the beta-carotene oxygenase (1/2) metabolites, or more polar breakdown products, may be better activators of such signal transduction cascades than their native precursors, due to their better cytosolic solubility and higher electrophilic properties. Similarly, certain lycopeneoids have been suggested to interact with RAR/RXR receptors, showing vitamin A-like properties. Such metabolites have also been proposed to alter adipocyte differentiation. Nevertheless, it also remains unclear whether clear doses-response relations exist, or whether these may follow e.g. a U-shaped curve, as negative health outcomes have been reported upon supplementation of individual carotenoids at high doses.

In addition, carotenoid absorption from the diet is typically low, depending on a variety of dietary and host factors. For example, while a diet rich in lipids may foster micellization and absorption, dietary fiber such as pectins and divalent minerals may have the opposite effects, perturbing the transition from lipid droplets to mixed micelles, reducing bioavailability. However, such factors do also interact with host related factors such as a variety of single nucleotide polymorphisms (SNPs) of genes related to digestive enzymes, carotenoid cellular uptake transporters and cleavage enzymes. Such host related factors are also likely to explain the large inter-individual responses in terms of carotenoid bioavailability, and possibly also observed health effects. Finally, while native carotenoids such as lutein, lycopene, and beta-carotene have been investigated for some time, very little is known on the effects of apocarotenoids present in plants such as bixin, crocin, or abscisic acid, some of which appear well bioavailable, and also bioactive. Such «novel» carotenoid derived compounds warrant further investigation.

Within this overview presentation, it is strived to highlight several selected recently discovered and discussed aspects around carotenoids and their metabolites, as well as their bioavailability and bioactivity, which appear important regarding their associated health benefits.

SESSION 5 - CAROTENOIDS - ORAL COMMUNICATION**Judith Hempel - Abstract n° C2**

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Title of abstract: Food sources of macular pigments: studies into the bioaccessibility and physical deposition form of carotenoids from goji berries (*Lycium barbarum* L.)

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Key words: zeaxanthin; lutein; bioavailability; chromoplast ultrastructure

Abstract: Lutein and zeaxanthin, two naturally occurring oxygenated carotenoids, have recently gained increasing scientific and economic interest. Particularly, these lipophilic micronutrients are specifically accumulated in the human eye and neural tissues, suggesting their biological importance. For instance, their frequent dietary intake has been related with delaying the onset or even preventing age-related macular degeneration, cataract and retinitis pigmentosa¹. The second age-related eye disease study (AREDS2)² proposed a ratio of lutein to zeaxanthin of 5:1 for supplements treating age-related macular degeneration. Considerable amounts of lutein are present in numerous popular vegetables and fruits, e.g. in green leafy vegetables and bell peppers. In contrast, relevant levels of zeaxanthin are rarely found in foods, except for the unique goji (*Lycium barbarum* L.) berries containing exceptionally high amounts of zeaxanthin (36 mg/100 g FW). For comparison, zeaxanthin-rich egg yolks from corn-fed hens were shown to contain 0.64 mg/100 g FW³. Prior to exerting any health beneficial functions in the human body, carotenoids need to be released from the food matrix, micellized in the small intestine, and absorbed to the human body. In the present study, the detailed profile of carotenoids and carotenoid esters as well as their liberation and micellization (bioaccessibility) during a simulated in vitro-digestion were determined. Bioaccessibility of zeaxanthin from goji berries was unexpectedly high, particularly, when compared to that of lutein from spinach. Due to its previously reported importance for the bioaccessibility from plant foods⁴, the physical deposition form of carotenoids in goji berries was investigated by light and transmission electron microscopy, revealing a presumably liquid-crystalline form within tubular chromoplasts. In contrast, carotenoids in spinach were earlier shown to be deposited in poorly accessible protein-pigment complexes within chloroplasts. Thus, we hypothesize that the observed differences in bioaccessibility might be related to the substantial difference in their natural deposition form within the food matrix. Irrespective of the causal explanation, goji berries might represent a potent food source of highly bioaccessible zeaxanthin.

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SESSION 5 - CAROTENOIDS - ORAL COMMUNICATION

Emmanuelle Reboul - Abstract n°C3

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Speciality: Nutrition

Title of abstract: Canned spinach matrix does not significantly affect lutein bioavailability

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Key words: Lutein, mixed micelles, digestion, intestinal absorption

Abstract: Lutein is a xanthophyll involved in the prevention of age-related macular degeneration. Its health effects obviously depend on its bioavailability, which can be modulated by the food matrix. Indeed, the matrix can either hold back its embedded micronutrients, or protect them from a possible degradation in the upper gastrointestinal tract. Thus, the purpose of this study was to determine the impact of the matrix of canned spinach on lutein bioavailability.

In vitro digestions were first used to compare lutein bioaccessibility (percentage level of lutein released from the matrix to mixed micelles) when lutein was added to the test meal either as a pure molecule or in canned spinach. Then, mixed micelles isolated from these in vitro digestions were delivered to human intestinal Caco-2 TC7 cells to assess lutein uptake and efflux. To strengthen these results, an experiment was performed in piglets to verify in vivo the impact of the canned spinach matrix on lutein bioavailability, which was evaluated by comparison of the postprandial plasma lutein responses (0-12 h area under the curve of the plasma lutein concentrations) after test meals that contained either pure lutein or lutein in canned spinach.

Our results showed that lutein bioaccessibility was significantly higher when lutein was digested in spinach as compared to in vitro digestion of the pure form (+35%, $p < 0.05$). However, lutein uptake by Caco-2 cells was less effective when lutein was given in micelles containing its pure form compared to micelles isolated from spinach digestion (-55%, $p < 0.05$). This second step contributed to decrease the favorable effect of spinach observed during in vitro digestions. These data were confirmed by the postprandial study in piglets where no significant difference was observed between postprandial lutein responses to the two test meals.

Overall, our results reveal that lutein bioavailability does not significantly change whether it is ingested as a purified molecule or within its usual vegetable matrix. However, it is important to remind that spinach consumption remains interesting since it brings both large quantities of lutein as well as other micronutrients that likely display additional health effects besides lutein properties.

SESSION 5 - CAROTENOIDS - ORAL COMMUNICATION**Ilya Vasilyev - Abstract n° C4**

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Title of abstract: First identification of C₅₀ carotenoids biosynthesis gene cluster in nematode-associated bacterium *Agreia bicolorata* strain VKM AC-1804 and its abundance in coryneform actinobacteria group

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Key words: C₅₀ carotenoids, whole-genome sequencing, coryneform bacteria, actinobacteria

Abstract: *Agreia* spp. are high-%GC aerobic coryneform bacteria found in different psychrotolerant environments such as soils, permafrost ices, air etc. Most of coryneform bacteria produce yellow or pale pigments while *Agreia bicolorata* strain VKM AC-1804 synthesizes orange and red compounds, probably isoprenoids. The strain AC-1804 was originally isolated from narrow reed grass (*Calamagrostis neglecta*) infected by the plant-parasitic nematode (*Heteroanguina graminophila*) in Moscow region, Russia (1). We have performed the de novo whole-genome sequencing of the strain VKM AC-1804 in order to reconstruct the possible pathway of the pigment biosynthesis (2). The processed genome sequence contained predicted genes involved in MEP/DOXP pathway of isoprenoid biosynthesis. We also found a gene cluster encoded certain enzymes of carotenoid biosynthesis: a phytoene synthase (*crtB*), phytoene desaturase (*crtI*), C₅₀ carotenoid epsilon cyclase (*crtYe/f*), lycopene elongase (*crtEb*). The metabolic role of these predicted proteins are related to biosynthesis of probably C₄₀ and C₅₀ carotenoids – acyclic lycopene, flavuxanthin and epsilon-cyclic decaprenoxanthin. The structure of the found gene cluster is considered to be common within coryneform bacteria group since discovered in *Corynebacterium glutamicum* (3). The phylogenetic analysis of the gene cluster has revealed the close affiliation between the strain VKM AC-1804 and *Rathayibacter toxicus*, an infective agent causing mass neurological disease of livestock known as annual ryegrass toxicity (ARGT). *A. bicolorata* VKM AC-1804 and *R. toxicus* have similar cultural properties and are vectored by *Anguina*-form nematode (4). Moreover, homologous gene clusters were found in a variety of known and possible human or plant pathogens such as *Kocuria rhizophila*, *Micrococcus luteus*, *Corynebacterium atypicum*, *Clavibacter michiganensis* subsp. *michiganensis*, and in completely free-living bacteria as well.

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SESSION 6 - VITAMIN A - KEY NOTE**Patrick Sauvant - Abstract n° A1**

City: Bordeaux Country: France
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Title of abstract: Seeing through the dark: vitamin A from deficiency in developing countries to retinoic acid as a powerful and promising drug.

Authors and addresses: Patrick Sauvant 1,2

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Abstract: Close to the centennial of the discovery of vitamin A by Mc Collum for its role in normal embryonic development and growth, retinol metabolism and functions have been largely described but our understanding of the functions of this major micronutrient is still evolving. Vitamin A can be provided from the cleavage of provitamin A carotenoids (of vegetal origin) in the small intestine or by consumption of preformed vitamin A (retinyl palmitate) in food of animal origin. In humans, another non-negligible and increasingly frequent source of vitamin A over the last 20 years has been food supplements and/or enriched food in industrialized countries. A subtle balance in terms of quantity and quality of vitamin A intake should be respected in order to avoid health problems and the nutritional management of this vitamin by governmental organizations is difficult.

In developing countries, manifestations of vitamin A deficiency (VAD) are obvious during pregnancy and in the early postpartum period, with infants born from VAD mothers becoming xerophthalmic, experiencing night blindness and even death. Prevention programs have been developed mainly by the WHO (World Health Organization), which established the eradication of VAD as a global health priority before the end of the 20th century. Despite the beneficial effects of vitamin A supplementation (VAS) on mortality has been proved to be effective against the mortality and morbidity of children, VAD is still observed in the 21st century in more than 100 countries, with the highest prevalence in Africa and South-East Asia where almost 50% of preschool children are affected. Why, to date, maternal and neonatal VAS policies have led to conflicting results regarding maternal and newborn mortality outcomes?

In contrast, VAD due to inadequate nutritional intakes is more than scarce in industrialized countries where highly absorbed vitamin A is largely present in food as preformed vitamin A or in food supplement for people who had correct vitamin A status. Much of researches in this part of the globe are focused on the potential use of Retinoic Acid (RA), an active metabolite of vitamin A, which exhibit powerful and promising effects as drug for treatment of diseases like type I diabetes, pancreatic diseases or coronary artery diseases.

Finally, vitamin A from deficiency in mothers or infants to toxicity or sub-toxicity in industrialized people or patients cause a puzzling dilemma to governmental organizations who had to manage vitamin A intake and utilization.

SESSION 6 - VITAMIN A - ORAL COMMUNICATION

Consuelo Macias-Matos - Abstract n° A2

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Title of abstract: CUBA-UNICEF: 18 years working together against vitamin A deficiency

Authors and addresses: C Macías-Matos*, O Rodríguez-Martínez**, G Pita-Rodríguez*, B Basabe-Tuero*, D Herrera-Javier*.
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Key words: vitamin A deficiency, micronutrient, UNICEF, Cuba

Abstract: In Cuba, an action plan was launched in 1993 in order to maintain and improve the nutritional status of vitamin A. It consisted of universal supplementation with a preparation containing 2500IU of vitamin A, promotion of breastfeeding, supply of 1L of daily milk at a subsidized price to children up to 7y old and food diversification promotion that leads to an increase in the consumption of fruits and vegetables sustained by the development of urban agriculture.

Since 1998, several projects has been working with the support of UNICEF:

1998. Supplementation with high doses of vitamin A for preschoolers and schoolchildren up to 18 years of age in boarding school throughout the island. More than 80% of students were supplemented in two phases of the year. 1999-2000. Diagnosis of nutritional status of vitamin A in children 6 to 24 months old. 2371 children were evaluated nationally and a prevalence of subclinical deficiency of 3.6% was found that according to WHO was not a health problem. 2002-2004. Diagnosis of the nutritional status of vitamin A in schoolchildren aged 6 to 12 years. 1191 schoolchildren were evaluated at the national level. In the eastern provinces, 2% of subclinical deficiency and 19% of suboptimal values were found and in the central and western provinces 0.3% and 3.8% were found respectively. In the eastern provinces measures were implemented to improve the status of vitamin A. 2010-2013. Re-evaluation of vitamin A in children 6-59 months of age. 2710 children were evaluated and the prevalence of subclinical deficiency at national level was 8.5%, which corresponds to a mild health problem. Three provinces presented subclinical deficiency, 3 provinces as moderate and 2 provinces as severe. 2014-2018. Nutritional intervention to improve vitamin A status in Cuban pre-school children. This intervention has been addressed to the 5 most affected provinces according to the «global thinking, local action» model. The project is intersectoral, health, agriculture, education authorities and the media work together. In a first stage the training of these authorities was carried out in each province and its municipalities and in a second one each province and municipality developed community promotional activities for healthy eating with focus on the consumption of fruits and vegetables. An emphasis is also placed on breastfeeding and consumption of vitamin supplements. Learned lessons. The implementation of these projects at a national level has been successfully carried out thanks to the National Public Health System that has a network of Provincial Centers of Hygiene and Epidemiology with nutritionists in the provinces and in their municipalities and also a strong primary care model with its base in family doctors and nurses. Working together different sectors allowed a greater scope of intervention, focusing in food production, training of stakeholders and health promotion.

SESSION 6 - VITAMIN A - ORAL COMMUNICATION

Georg Lietz - Abstract n° A3

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Speciality: Nutrition

Title of abstract: Influence of nutritional and physiological factors on total body vitamin A stores using the isotope dilution technique

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Key words: Total body stores of vitamin A, Gender, Provitamin A carotenoids, random forest

Abstract: Retinol isotope dilution (RID) is used to determine vitamin A total body stores (TBS) after an oral dose of a vitamin A stable isotope. Since the RID technique is dependent on absorption, distribution, mixing, and disposal of a labeled VA dose, we evaluated the influence of various physiological and nutritional factors to evaluate the importance of these factors on total body stores of vitamin A in 111 healthy individuals. The Random forest algorithm was applied to the data using the “randomForest” package (Liaw & Wiener 2002) in the R programme (R Core Team 2016). We used the random forests program to identify the “importance” of variables using the increase in node purity as a measure of importance.

The largest contributing factors to TBS were provitamin A carotenoids as well as preformed vitamin A intake in our volunteers, followed by body fat and BMI. There was very little influence of gender on total TBS determination.

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SESSION 6 - VITAMIN A - ORAL COMMUNICATION

Maria Vaiou - Abstract n° A4

City: Larissa Country: GREECE
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Title of abstract: Comparative effects of Retinoic Acid and cytostatic drugs on arterial smooth muscle cell proliferation.

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Key words: Retinoic acid, vitamin A, smooth muscle cells, proliferation

Abstract: Purpose: One of the characteristics of coronary artery disease (CAD), a leading cause of death in many developed countries, is stenosis i.e. narrowing of arteries due to plaque formation. Treatments for stenosis include the use of combination medical devices such as endovascular drug eluting balloons and drug eluting stents for re-opening the arteries with simultaneous local application of anti-proliferative drugs for preventing restenosis. The drugs currently in use on these devices are cytotoxic or cytostatic drugs such as paclitaxel and rapamycin and its analogues. Retinoic acid (RA), a vitamin A derivative, is known to have effects on cell proliferation. Aim of the current study was to investigate the use of RA as a new candidate drug for medical devices by testing the effect of RA on the proliferation of human coronary arterial smooth muscle cells (HCASMCs) in culture.

Materials & Methods: In order to examine the influence of RA on HCASMCs growth, the tested agents were added to proliferative HCASMCs cultures for 10 and 60 min respectively. Two final concentrations of 1.46 $\mu\text{mol/l}$ ("low concentration") or 14.6 $\mu\text{mol/l}$ ("high concentration") in the incubation solution were tested. Single dose applications were performed and cell proliferation was determined after 0, 3, 6, 9 and 12 days by cell counting. The degree and duration of proliferation inhibition was also compared to existing cytostatic drugs (paclitaxel and everolimus), that have already been shown to be effective and safe in commercially available drug eluting vascular devices.

Results: RA alone reduces proliferation of HCASMCs but the effect of this drug is lower in the "low" dose compared to paclitaxel and everolimus. However the "high" dose of RA produces a reduction in the proliferation comparable to that of everolimus but still lower in the long term (9-12 days) of that of paclitaxel. It is noteworthy that the action of retinoic acid remains even at 12 days, while the action of everolimus seems to be diminished after day 9.

Conclusions: Our data suggest for the first time a role of the RA in regulating the proliferation of HCASMC in culture. Further studies are needed to confirm its role as a novel promising approach for applications in drug eluting stents or balloons.

SESSION 6 - VITAMIN A - ORAL COMMUNICATION

Simone Frey - Abstract n° A5

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Speciality: Vitamin A Metabolism

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Title of abstract: Quantification of Vitamin A in Palm Oil Using a Fast and Simple Portable Device: Method Validation and Comparison to High-Performance Liquid Chromatography.

Authors and addresses: Fabian Rohner, Simone Frey, Florian J. Schweigert

Key words: Vitamin A, edible oil fortification, rapid test kit

Abstract: Vitamin A deficiency continues to be a global public health problem. Fortification of oil with vitamin A is considered a cost-effective, feasible strategy to prevent this problem but quality control poses a challenge to program implementation. To overcome this, we have validated a newly developed device that quantitatively measures the content of retinyl palmitate in refined palm oil, is simple to use, and yields immediate results. Linearity of analysis ranged from 2.5 – 30 mg retinol equivalents (RE)/ kg of palm oil, with 2.5 mg RE/ kg being the determination limit; inter- and intra-assay precision ranged from 1.4 – 7.1 %. Comparison with a high-performance liquid chromatography method showed high agreement between the methods ($R^2 = 0.92$; Limits of Agreement: -1.24 mg to 2.53 mg RE/kg), and further comparisons illustrate that the new device is useful in low-resource settings. This device offers a field- and user-friendly solution to quantifying the vitamin A content in refined palm oil.

SESSION 6 - VITAMIN A - FLASH POSTER

Imar Djibrine Soudy - Abstract n° A6

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Title of abstract: Vitamin A status in non-pregnant women eating traditionally spirulina (Dihé) in Chad

Authors and addresses: Imar Djibrine Soudy¹, Regine Minet-Quinard², Alhadj Djidda Mahamat¹, Hadjé Fatimé Ngoua⁴, Abdelaziz Arada⁶, Abdelsalam Tidjani⁶, Elisabeth Ngo Bum⁵, Jehan-François Desjeux³ and Vincent Sapin²

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Abstract: Background: Chad is a country with high prevalence of vitamin A deficiency (VAD). Spirulina, known under the name of "Dihé", is an important source of β -carotene, a precursor of vitamin A. This algae is produced around Chad Lake (region of Lac and region of Kanem). Objective: The aim of the study is to assess if non pregnant women (n=35) living near Chad Lake and consume spirulina have a repleted vitamin A status compared to those (n=35) living in the same region but do not eat spirulina. Design: Retinol and β -carotene concentrations in serum were determined by HPLC. To achieve nutritional assessment, plasma proteins (Retinol Binding Protein (RBP), Transthyretin (TTR), Albumin, Alpha 1- Glycoprotein Acid (Orosomucoide) and C-Reactive Protein (CRP)) concentrations were also measured by immune-nephelometric method (Vista System).

Results: The results shown that retinol serum concentration is significantly different (P value = 0.018) between the two groups of these population with an average of 1.26 $\mu\text{mol/L}$ (± 0.43) in non pregnant women living near Chad Lake consuming spirulina and of 1.03 $\mu\text{mol/L}$ (± 0.32) to those living in the same region but do not eat spirulina. Serum β -carotene concentration of non pregnant women living near Chad Lake consuming spirulina is higher than that of non pregnant women living in the same region but do not eat spirulina with average of 0.59 $\mu\text{mol/L}$ (± 0.38) and 0.46 $\mu\text{mol/L}$ (± 0.36), respectively but statistically similar.

Conclusions: These results should be explain by the fact that the β -carotene brought in large quantity is more converted in vitamin A, which is a biomarker more stable than the β -carotene which is not right to stay under its shape because it is a precursor.

SESSION 6 - VITAMIN A - FLASH POSTER

Ronald Corbee - Abstract n° A7

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Speciality: Veterinary and Comparative Nutrition

Title of abstract: Chronic vitamin A toxicosis in cats

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Key words: Retinol, cholecalciferol, liver, kidney

Abstract: To date, in nutrition research, much focus is on deficiencies, however the occurrence of clinical deficiencies is becoming rare. More focus should be on the effects of excessive supplementation, as currently, much safe upper limits (SUL) are unknown, or based on very old studies, which is the case for vitamin A SUL in cats. Furthermore, interactions between nutrients should be studied more. Both vitamin A and vitamin D influence bone formation and have been linked in hyperostosis found in cats consuming large amounts of beef and/or pork liver. Similar findings were demonstrated in humans consuming large amounts of fatty fish, cod liver oil, or vitamin A and D supplements. The first aim of this study was to determine whether vitamin D supplementation influences the effects of high vitamin A intake on new bone formation in adult cats. The second aim was to determine whether high vitamin A intake in cats causes liver pathology and, if so, whether the current SUL for the dietary intake of vitamin A for healthy adult cats is safe.

Methods - To this end, 24 healthy adult cats were divided into four groups that received a control diet supplemented with peanut oil (control), or peanut oil containing a 100-fold increase in vitamin A (HA), a 100-fold increase in vitamin A and a 5-fold increase in vitamin D (HAMD), or a 100-fold increase in vitamin A and a 65-fold increase in vitamin D (HAHD) for 18 months.

Results - Cats did not show abnormal locomotion or clinical symptoms of liver failure after 18 months of supplementation but did show subtle skeletal changes, as well as kidney and liver pathology, suggesting that current National Research Council (2006) safe upper limit for vitamin A for cats is too high. The addition of vitamin D did not seem to influence bone pathology. In conclusion, current SUL for vitamin A in cats is too high. While moderately elevated dietary vitamin D levels (HAMD) seemed to protect cats against the liver pathology caused by the consumption of large amounts of vitamin A, higher dietary levels of vitamin D (HAHD) seemed not to be protective. Different vitamin D levels also seem to affect the renal pathology in cats.

SESSION 6 - VITAMIN A - FLASH POSTER

Pierre-Jacques Brun - Abstract n° A8

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Speciality: Vitamin A

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Title of abstract: The dual role of retinoic acid signaling in modulating insulin and glucagon secretion

Authors and addresses: Pierre-Jacques Brun, Yousung Kim, Seung-Ah Lee, Hongfeng Jiang, Koichi Shudo, Hiroyuki Kagechika and William S. Blaner

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Key words: Vitamin A, β -cells, Insulin, Glucagon

Abstract: We investigated, using isolated pancreatic islets obtained from age- and gender-matched adult wild type (WT) and cellular retinol-binding protein, type I-deficient (Crbp1^{-/-}) mice, the essential actions of retinoic acid receptor (RAR) signaling on glucagon and insulin secretion from pancreatic α - and β -cells. Using the RAR-specific pan-antagonist, LE 540, and the RAR-specific pan-agonist, CH 55, we studied effects of ablation or stimulation of the RAR signaling pathway on insulin and glucagon secretion when pancreatic islets are stimulated by glucose and/or arginine. We found that inhibiting RAR signaling decreased insulin and glucagon secretion when stimulated by glucose and arginine, respectively. In contrast, the RAR pan-agonist stimulated insulin and glucagon secretion in the basal state. However, surprisingly glucagon secretion was decreased when islets treated with CH 55 were stimulated with arginine. Insulin and glucagon secretion were also assessed in islets isolated from Crbp1^{-/-} mice. Those islets showed decreased responsiveness to glucose- and arginine-stimulated insulin secretion. Most interestingly, glucagon secretion was increased from islets of Crbp1^{-/-} mice in the basal state, but when stimulated with arginine, compared to matched WT islets, those islets have a decreased capacity to secrete glucagon. We were able to measure retinoid concentrations from pancreatic islet isolates alone by liquid chromatography followed by tandem mass spectrometry. For islets isolated from 150 day old WT mice, all-trans-retinol concentrations were approximately 3 pmol all-trans-retinol per μ g of DNA. Islets from age- and gender matched Crbp1^{-/-} mice possess lower concentrations of all-trans-retinol, by approximately 35%, compared to WT controls. Although retinyl esters are readily measured in whole pancreas, none were found in isolated pancreatic islets. These studies were supported by NIH grant R01 DK068437.

INDEX

Ann Anderson Berry - ORAL COMMUNICATION - VITAMIN E - E5	page 25
Omar Benzakour - ORAL COMMUNICATION - VITAMIN K - K1	page 35
Andrius Bleizgys - ORAL COMMUNICATION - VITAMIN D - D2	page 41
Torsten Bohn - KEY NOTE - CAROTENOIDS - C1	page 99
Lauriane Bonnet - ORAL COMMUNICATION - VITAMIN D - D13	page 61
Pierre-Jacques Brun - FLASH POSTER - VITAMIN A - A8	page 121
Marie-Christine Carlier - POSTER - VITAMIN D - D22	page 79
Tarek Chaabouni - POSTER - VITAMIN D - D23	page 81
Ronald Corbee - FLASH POSTER - VITAMIN A - A7	page 119
Charlotte Cuerq - FLASH POSTER - VITAMIN E - E7	page 29
Natalia Davydova - FLASH POSTER - VITAMIN D - D16	page 67
Charles Desmarchelier - ORAL COMMUNICATION - VITAMIN D - D5	page 47
Catherine Desoto - ORAL COMMUNICATION - VITAMIN K - K2	page 37
Imar Djibrine Soudy - FLASH POSTER - VITAMIN A - A6	page 117
Manfred Eggersdorfer - KEY NOTE - VITAMIN E - E1	page 17
Sharif Elham - POSTER - VITAMIN D - D21	page 77
Catherine Féart - FLASH POSTER - D19	page 73
Catherine Feart - KEY NOTE - FAT SOLUBLE VITAMINS - FSV1/FSV2/FSV3	page 83/87
Jan Frank - ORAL COMMUNICATION - VITAMIN E - E4	page 23
Adrian Franke - KEY NOTE & POSTER - FAT SOLUBLE VITAMINS - FSV7 & FSV8	page 95/97
Simone Frey - ORAL COMMUNICATION - VITAMIN A - A5	page 115
Francesco Galli - ORAL COMMUNICATION - VITAMIN E - E2	page 19
Corrine Hanson - ORAL COMMUNICATION - VITAMIN E - E6	page 27
Judith Hempel - ORAL COMMUNICATION - CAROTENOIDS - C2	page 101
Wolfgang Herrmann - ORAL COMMUNICATION - VITAMIN D - D11	page 57

Elina Hypponen - KEY NOTE & POSTER - VITAMIN D - D8 & D9	page 51/53
Ina Jasutiene - FLASH POSTER - VITAMIN D - D15	page 65
Argjira Juniku-Shkololli - FLASH POSTER - VITAMIN D - D18	page 71
Gaspar Kocharyan - FLASH POSTER - VITAMIN E - E8	page 31
Jean-François Landrier - ORAL COMMUNICATION - VITAMIN D - D1	page 39
Charlotte Lauridsen - FLASH POSTER - VITAMIN D - D17	page 69
Georg Lietz - ORAL COMMUNICATION - VITAMIN A - A3	page 111
Augusto Litonjua - ORAL COMMUNICATION - VITAMIN D - D3	page 43
Consuelo Macias-Matos - ORAL COMMUNICATION - VITAMIN A - A2	page 109
Ludmila Macova - FLASH POSTER - VITAMIN D - D20	page 75
Marielle Margier - ORAL COMMUNICATION - FAT SOLUBLE VITAMINS - FSV4	page 89
Anargyros Moulas & Elisabeth Katsianidou - ORAL COMMUNICATION - VITAMIN D - D6/D7	page 49
Damien Prévéraud - ORAL COMMUNICATION - FAT SOLUBLE VITAMINS - FSV6	page 93
Irene Pusceddu - ORAL COMMUNICATION - FAT SOLUBLE VITAMINS - FSV5	page 91
Emmanuelle Reboul - ORAL COMMUNICATION - VITAMIN D - D4	page 45
Emmanuelle Reboul - ORAL COMMUNICATION - CAROTENOID - C3	page 103
Patrick Sauvart - KEY NOTE - VITAMIN A - A1	page 107
Lisa Schmölz - ORAL COMMUNICATION - VITAMIN E - E3	page 21
Poorya Shojai - FLASH POSTER - VITAMIN D - D14	page 63
Kimitaka Takitani - FLASH POSTER - VITAMIN E - E9	page 33
Jeremie Talvas - ORAL COMMUNICATION - VITAMIN D - D12	page 59
Maria Vaiou - ORAL COMMUNICATION - VITAMIN A - A4	page 113
Ilya Vasilyev - ORAL COMMUNICATION - CAROTENOIDS - C4	page 105
Robert Winwood - ORAL COMMUNICATION - VITAMIN D - D10	page 55



Special Issue

Vitamin E

Guest Editor:

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Deadline for manuscript submissions:
31 October 2017

Message from the Guest Editor

The purpose of this Special Issue is to present recent investigations on the role of vitamin E as antioxidant in health promotion or disease prevention, as well as results on non-antioxidant activities of vitamin E. It is also important to show recent developments for vitamin E in structural characterization of bioactive, endogenous metabolites, and the use of vitamin E in industry.

Vitamin E was first described in 1922 as a necessary dietary factor for reproduction in rats. In contrast to most other vitamins showing a cofactor function or a unique molecular role, such a specific vitamin E function, has not yet been shown. Vitamin E is an important lipophilic antioxidant, protecting in cell membranes. In food, there are four tocopherols and four tocotrienols. In contrast, the most important compound in vivo is α -tocopherol. The hepatic α -tocopherol transfer protein is one reason for this discrimination. Another explanation is the preferential metabolism of non- α -tocopherol congeners by ω -hydroxylation and β -oxidation. Recent investigations showed interesting biological activities of long-chain metabolites of vitamin E.

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Special Issue

Carotenoids—Antioxidant Properties

Guest Editors:

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Deadline for manuscript submissions:

30 September 2017

Message from the Guest Editors

Carotenoids are an important group of natural pigment consisting of more than 600 known compounds that are found in a wide range of biological systems. They serve a vital role in biological processes and in aspects of animal and human health where their consumption has been associated with the prevention of certain diseases.

We welcome papers to this Special Issue, which will bring together current research concerning the antioxidant properties and function of carotenoids relating to the following topics:

The reactions of carotenoids with ROS;

The interaction of carotenoids with other antioxidants, such as vitamin E;

Factors that affect the antioxidant or prooxidant behaviour of carotenoids;

The metabolism of dietary carotenoids in humans;

The bioavailability, transport and cellular/tissue deposition of carotenoids;

Carotenoids and heart disease;

The role of carotenoids in the human macula;

Carotenoids and photoprotection;

Novel analytical methodology for carotenoids;

The uses of carotenoids as antioxidants in foods and foodstuffs.

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*Thank you so much for your participation
Edmond Rock - President of the congress*

16th Fat Soluble Vitamins Congress - March 21-23, 2017 - Paris

