Objectives: By studying the metabolic changes that impact on the response to MSU crystals in a murine model of gout, we hope to identify the dietary effect on metabolites that are associated with the inflammatory response to MSU crystals.

Methods: Male mice (C57BL/6) were fed either a normal diet (ND) or high fat diet HFD (DIO D12492) for >6 weeks. During the last 4 weeks of feeding, half the mice in each group were treated with antibiotics (Enrofloxacin 0.25% + co-amoxicillin) to induce a germ-free state. At day 0, mice were injected i-p with 1 mg of MSU crystals. Mice were sacrificed 6h after i-p injection. Serum, plasma and peritoneal exudate samples were collected at sacrifice and plasma obtained 3 weeks before sacrifice. Untargeted and targeted liquid chromatography – mass spectrometry based-metabolomics approach was performed on serum and plasma samples. IL1 and IL6 were measured in serum and peritoneal exudates by ELISA. Animal experimental authorization was obtained for these experiments.

Results: Mice fed a HFD had a greater serum and peritoneal IL6 response to MSU. In an untargeted analysis, multiple metabolic alterations were observed related to diet. Targeted analyses of sphingolipids were performed. Both diet and inflammation (MSU injection) altered plasma sphingolipid levels. No effect of antibiotics was observed. MSU injection induced marked changes in the sphingolipid profile (38.2% of explained variance), while diet had a lesser effect (16.2% of explained variance). Mice fed an HFD had significantly higher serum IL6 before and peritoneal IL6 levels after MSU injection than mice fed a ND. DhCer C16:0 and Cer C16:0 levels decreased significantly after MSU injection. Pre-MSU levels of DhCer C16:0 and Cer C16:0 showed significantly negative correlations with IL6p levels after i-p injection in HFD animals.

Conclusion: The sphingolipid profile was significantly changed by diet and inflammation. In mice given a HFD, the levels of particular ceramides were significantly correlated with subsequent inflammatory response as assessed by IL6 secretion, suggesting that they may play a role in modulating the inflammatory response to MSU. These same ceramides and their derivatives have been linked to susceptibility to diabetes and cardiovascular diseases^{1,2}. Further investigation of these sphingolipids in gout in man is warranted.

REFERENCES:

- [1] Wigger L, et al. Cell Rep. 2017 Feb 28;18(9):2269-2279. doi: 10.1016/j.celrep.2017.02.019
- [2] Summers SA. Cell Metab. 2018 Feb 6;27(2):276-280. doi: 10.1016/j.cmet.2017.12.003

Disclosure of Interests: Alexander So Consultant for: SOBI, Grunenthal, Speakers bureau: Grunenthal, Florence Mehl: None declared, Nicola Harris: None declared, Veronique Chobaz: None declared, Hector Gallart-Ayala: None declared

DOI: 10.1136/annrheumdis-2019-eular.6681

OP0054 OCCUPATIONAL EXPOSURE TO INORGANIC DUST – A NOVEL RISK FACTOR FOR INCIDENT GOUT?

Valgerdur Sigurdardottir^{1,2}, Anna Svärd¹, Lennart T.H. Jacobsson², Linus Schiöler³, Kjell Torén³, Mats Dehlin². ¹Uppsala University, Center for Clinical Research Dalarna, Falun, Sweden; ²Sahlgrenska Academy, University of Gothenburg, Department of Rheumatology and Inflammation Research, Gothenburg, Sweden; ³Sahlgrenska Academy, University of Gothenburg, Section of Occupational and Environmental Medicine, Gothenburg, Sweden

Background: Hyperuricemia and factors contributing to it are strong risk factors for gout but it is still unexplained why only some individuals with hyperuricemia develop gout. Additional risk factors for gout could be genetic or related to comorbidity, lifestyle or occupation. Occupational exposure to inorganic dust has previously been linked to an increased occurrence of inflammatory rheumatic diseases such as rheumatoid arthritis and could possibly increase the risk of gout.

Objectives: To evaluate if occupational exposure to inorganic dust increases the risk of incident gout.

Methods: Gout was defined as having at least one ICD-10 code for gout (M10 or M14.0) in the population based health care database of the Western Swedish Health Care Region (VEGA), during the years 2006-2012, without any gout diagnosis during at least 6 years previously. Individuals with gout that were employed in the 5-year period prior to first diagnosis were included for analysis. Population controls without gout were identified in the census register by Statistics Sweden, matching up to 5 controls per case on the basis of age, sex and place of residence, excluding controls that were not employed during the predictor period. Data on occupation (coded by the ISCO-88 standard) for the 5 years prior to inclusion were collected from official registries and were used to assign exposure status using a job exposure matrix for inorganic dust previously developed.^[1] Data on predefined comorbidities (psoriasis, renal disease, alcohol abuse, obesity and diuretic treatment) considered to be possibly relevant confounders for the analyses were collected from VEGA, defined by ICD-10 codes. Alcohol abuse and obesity were found to be related both to gout and exposure to inorganic dusts and

were therefore adjusted for in multivariate analyses. The effect of exposure to inorganic dust on risk of gout was described with odds ratios, calculated using conditional logistic regression, for the whole population and stratified by sex.

Results: 6120 gout cases and 25074 controls were included. Frequencies of exposures (n (%)) and odds ratios (OR (95% conf. int.)) for association of risk factors with incident gout are shown in the table below.

		Exposed to inorganic dust	Alcohol abuse	Obesity
Whole population	Gout cases, n=6120	1836 (30)	299 (5)	671 (11)
	Controls, n=25074	7074 (28)	538 (2)	821 (3)
	OR univariable	1.10 (1.04 to 1.17)	2.37 (2.04 to 2.76)	3.81 (3.42 to 4.26)
	OR multivariable*	1.07 (0.99 to 1.14)	2.26 (1.94 to 2.62)	3.75 (3.36 to 4.19)
Men	Gout cases, n=4751	1615 (34)	267 (6)	489 (10)
	Population controls, n=19339	6343 (33)	471 (2)	576 (3)
	OR univariable	1.07 (1.00 to 1.15)	2.42 (2.07 to 2.82)	3.93 (3.45 to 4.48)
	OR multivariable*	1.03 (0.97 to 1.11)	2.29 (1.95 to 2.69)	3.85 (3.38 to 4.39)
Women	Gout cases, n=1369	221 (16)	32 (2)	182 (13)
	Population controls, n=5735	731 (13)	67 (1)	245 (4)
	OR univariable	1.33 (1.12 to 1.57)	2.02 (1.31 to 3.11)	3.53 (2.87 to 4.34)
	OR multivariable*	1.27 (1.07 to 1.51)	2.03 (1.31 to 3.14)	3.50 (2.85 to 4.31)

*includes inorganic dust, alcohol abuse and obesity as covariates.

Conclusion: As expected, previously known risk factors for gout such as obesity and alcoholism were strongly associated with incident gout. In univariate analyses, exposure to inorganic dust was also associated with gout. After adjusting for alcohol abuse and obesity, the relationship was attenuated in men but remained in women, providing evidence that occupational exposure to inorganic dust might be a previously unknown risk factor for gout.

REFERENCE:

- [1] Lillienberg L, et al. Occupational exposure and new-onset asthma in a population-based study in Northern Europe (RHINE). Ann Occup Hyg. 2013;57:482-92.

Disclosure of Interests: Valgerdur Sigurdardottir: None declared, Anna Svärd: None declared, Lennart T.H. Jacobsson Consultant for: LJ has received lecture and consulting fees from Pfizer, Abbvie, Novartis, Eli-Lilly and Janssen, Linus Schiöler: None declared, Kjell Torén: None declared, Mats Dehlin: None declared
DOI: 10.1136/annrheumdis-2019-eular.804

WEDNESDAY, 12 JUNE 2019

JIA: From new horizons of treatment to perspectives of current ones

OP0055 EFFICACY OF CANAKINUMAB, ON A REDUCED DOSE OR A PROLONGED DOSE INTERVAL WITHOUT CONCOMITANT CORTICOSTEROIDS AND METHOTREXATE, IN PATIENTS WITH SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS

Pierre Quartier¹, Ekaterina Alexeeva², Carine Wouters³, Inmaculada Calvo⁴, Tilmann Kallinich⁵, Nico Wulffraat⁶, Xiaoling Wei⁷, Alan Slade⁸, Ken Abrams⁹, Alberto Martini⁹. ¹Necker-Enfants Malades Hospital, Paris, France; ²National Medical Research Center of Children's Health and I.M. Sechenov First Moscow State Medical University, Moscow, Russian Federation; ³Gasthuisberg University Hospital, Leuven, Belgium; ⁴Hospital Universitario La Fe, Valencia, Spain; ⁵Charité Berlin Campus Virchow, Berlin, Germany; ⁶University Medical Center Utrecht, Utrecht, Sweden; ⁷China Novartis Institutes for Biomedical Research Co., Ltd, Beijing, China; ⁸Novartis Pharmaceuticals Corporation, East Hanover, United States of America; ⁹Università di Genova Pediatria II, Genoa, Italy

Background: Canakinumab (CAN), a selective, human anti-IL-1β mAb, has shown sustained therapeutic effect along with corticosteroid (CS) dose reduction/discontinuation in patients (pts) with systemic juvenile idiopathic arthritis (SJIA), in a long-term extension study (NCT00891046).¹

Objectives: To evaluate the efficacy and safety of 2 different CAN tapering regimens in SJIA pts who were in clinical remission (NCT02296424).