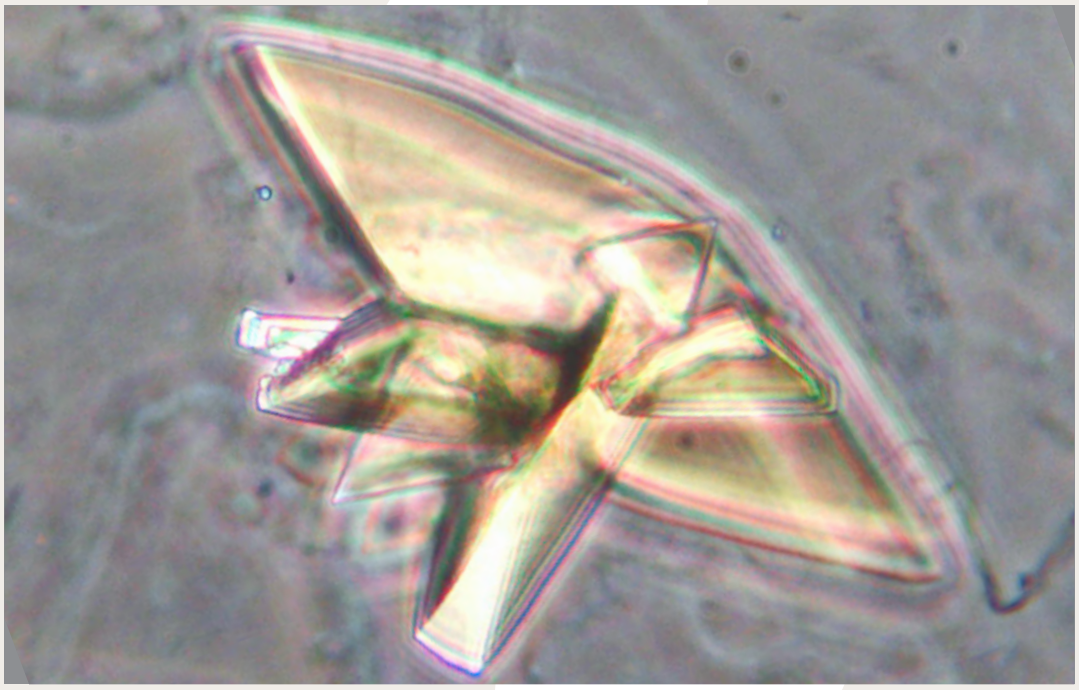
SWISS NATIONAL CENTRE OF COMPETENCE IN RESEARCH

KIDNEY
CONTROL OF HOMEOSTASIS

NEWSLETTER ::: NO. 7 ::: DEZEMBER 2013

SWISS KIDNEY STONE COHORT



Urine crystal, photo: Prof. G.B. Fogazzi

Kidney stones are widespread in industrialized countries and cause extreme pain. Although kidney-stone episodes are normally not life-threatening they require costly treatment and are often associated with complications such as pain and chronic urinary-tract infections.

HIGH HEALTH- AND ECONOMIC BURDENS

An estimated 6–15% of the population develop kidney stones (nephrolithiasis) at least once in their lifetime, with incidence rates currently increasing. Statistically, men develop kidney stones approximately two to three times more frequently than women. Many patients have recurrent kidney-stone episodes and, therefore, a high individual health burden. Renal colic is usually very painful and sufferers are often sent to hospital immediately. For this reason, many emergency departments treat one or more patients with acute renal colic daily.

Economically, kidney stones are associated with high costs for absence from work, diagnosis, and treatment. The cost of kidney-stone illnesses in the US alone is estimated to be 2.1 billion USD per year based on data from 2000. Despite the complexity of the disease, diagnosis, therapy, and prevention are not fully standardized and a detailed work-up for diagnosis and prevention of future episodes is often required.

DIFFERENT TYPES OF STONES

Kidney stones are made of inorganic and organic components, and can be classified into four main types:

- **Calcium stones** – approximately 90% of kidney stones are so-called calcium stones. They occur either as calcium oxalate or calcium phosphate stones. The vast majority (70–80%) of all kidney stones are composed of calcium and oxalate.

KIDNEY
CONTROL OF HOMEOSTASIS
SWISS NATIONAL CENTRE
OF COMPETENCE IN RESEARCH

University of Zurich[UZH]

FNSNF
Swiss National Science Foundation

EDITORIAL

Reto Krapf
is director of the Dept. of Medicine at Klinik St. Anna, Luzerne, and professor for medicine at the University of Basel. He leads the Clinical Study Group at Kidney.CH and is a member of the steering committee.

The Swiss Kidney Stone Cohort is the first initiative which takes place within the Clinical Study Group of the NCCR Kidney Control of Homeostasis. Together with Carsten Wagner, I have the pleasure and privilege of leading the cohort's steering committee. All five of the university centres of nephrology and urology which participate in the Kidney.CH network will also participate in the cohort which has now received the approval of all relevant ethical boards. I am delighted to observe that all these centres have bundled their ideas, expertise, and resources to make the founding of such a cohort possible.

I am very confident that the investigators working on this project will contribute significantly to the understanding of the patho-mechanisms leading to kidney-stone formation, and to their detection, treatment, and prevention.

The initiative was made possible by the collaborative spirit of all of the participants and for this I owe them a great deal of thanks. I would also like to thank Matthias Meier for providing the administrative lead and support and Julia Dober, our clinical study manager, for her diligent work in preparing the cohort and assuring the high quality enrolment of kidney-stone patients.

Reto Krapf

- **Uric-acid stones** — Uric-acid stones are the second most commonly occurring type of stone (approximately 5–10% of all stones). They are formed when urine becomes saturated with uric acid.
- **Struvite stones** account for 1–2% of all kidney stones. They are composed of mixtures of magnesium, ammonium, phosphate, and calcium carbonate phosphate crystals. Recurrent or chronic urinary tract infections are seen as the main reason these stones develop.
- **Cystine stones** account for only 1% of all kidney stones.

MECHANISMS LEADING TO STONE FORMATION REMAIN POORLY UNDERSTOOD

Kidney-stone diseases have multifactorial causes. They have a strong genetic predisposition, but are also influenced by environmental factors, lifestyle, and dietary components, which complicates the analysis of the underlying basis of the disease. Consequently, the identification of genetic, dietary and other factors requires the collection of highly standardized data and samples in large cohorts of patients to reach the power necessary for detection. Only very few such cohorts exist worldwide, mostly in the US and the UK. To the best of our knowledge, no such cohort — with a national coverage of patients — exists in continental Europe.

SWISS KIDNEY STONE COHORT (SKSC)

The main aims of this cohort are to foster clinical studies and to offer access to human material (e.g. DNA or urine) to enable research into disorders of mineral and pH homeostasis in a well-defined patient population. The SKSC will include a large number of patients from all regions of Switzerland covering various lifestyles, and different genetic predispositions, nutritional habits, and environments. The cohort will therefore enable research into this patient-population by collecting standardized data on activity, environment, and nutrition. This will be done by collecting urine and blood samples for later comprehensive analysis of metabolic factors, and by collecting DNA for genetic testing of single-risk genes and testing for genome-wide associations. A major strength of the cohort will be the long-term follow-up of patients to correlate

ORGANIZATION OF THE SKSC

NCCR KIDNEY.CH STEERING COMMITTEE

CLINICAL STUDY GROUP KIDNEY.CH

Lead: Reto Krapf
Clinical study manager: Julia Dober

SWISS KIDNEY STONE COHORT (SKSC)

Managment: Reto Krapf (lead)
Carsten Wagner (co-lead)
Julia Dober (manager)

Investigators from the 5 core centres:

Nilufar Mohebbi (ZH)
Olivier Bonny (LAU)
Thomas Ernandez (GE)
Catherine Stoermann (GE)
Min-Jeong Kim (BS)
Andreas Pasch (BE)

Urologist: tba.

SCIENTIFIC ADVISORY BOARD
External experts from science & industry

OUR MAIN INVESTIGATORS FROM THE FIVE PARTICIPATING SWISS UNIVERSITY HOSPITALS:

Nilufar Mohebbi, MD
Zurich
I'm working as a nephrologist at the Division of Nephrology at the University Hospital of Zurich. In addition to kidney stones I am very much interested in different acid-base and electrolyte disorders.

Olivier Bonny, MD, Assist. Prof.
Lausanne
The keywords characterizing my work are: kidney stone and mineral metabolism, renal uric acid handling and inherited kidney disorders.

Thomas Ernandez, MD
Geneva
My research field is focused on physiological regulation of sodium and water homeostasis. Specifically, I am studying how mechanical forces as well as the primary cilium is involved in the regulation of sodium reabsorption in the collecting duct.

Min-Jeong Kim, MD
Basel
I am working as attending nephrologist at the University Hospital Basel. I am in charge of general nephrology outpatient clinic and inhospital consultations. My key research interest is glomerulonephritis, especially the pathogenesis and treatment of IgA nephropathy.

Andreas Pasch, MD
Berne
My primary research interest is to better understand the mechanisms leading to pathological calcifications (e.g. vascular calcification) and to search for new diagnostic and therapeutic measures. This also applies for kidney stone disease, which represents a special form of pathological calcifications.

Catherine Stoermann, MD
Geneva
She studied medicine at the University of Geneva and is today senior consultant at University Hospital of Geneva (HUG), Service of Nephrology.

changes in nutrition, environment, and other factors with disease frequency and severity.
The initial start phase of the SKSC is being financed by the NCCR Kidney.CH. To expand the initiative and guarantee its continuing existence, additional financing is being sought.

BIOBANKING

Structural collection of human specimens and associated data has gained more and more importance in medical research during recent decades. Furthermore, worldwide initiatives emphasise the need for collaboration between different biobanks and the importance of a high quality and quantity of biospecimens.

Within the SKSC, a biobank containing blood, urine, and DNA samples will be established. While the blood samples for DNA extraction will be processed and stored in Geneva (Dr. Georg B. Ehret, University Hospital Geneva), all the other biospecimens will be stored locally at the participating centres.
Centralized coordination of the biospecimens will allow unambiguous assignment of the samples to associated data such as patient questionnaires, medical histories, and other laboratory parameters. A 2-D barcode system, including an alphanumeric code, will assure pseudonymic data-storage, traceability, and — furthermore — a well-structured, readily analysable data format.

Julia Dober
is the clinical study manager for the NCCR Kidney.CH and responsible for the coordination of the SKSC.
She holds a Master's degree in biology and economics, and has several years of experience in clinical research within the medical industry. In March 2013 she joined the NCCR Kidney.CH.

Carsten Wagner
is professor at the Institute of Physiology at University of Zurich. He leads the Kidney.CH research module Acid & Minerals and is a member of the steering committee. He co-leads the initiative of the Swiss Kidney Stone Cohort.

CLINICAL STUDY GROUP

To foster translational research the NCCR Kidney.CH created this clinical study group, headed by Prof. Reto Krapf, in 2012. The main goals of the group are to:

1. foster, coordinate, and organise joint clinical kidney research projects in Switzerland
2. establish a clinical study team with data management and statistical support
3. foster multicentre research and translational transfers in the fields of the main Kidney.CH research topics
4. help educate young, independent clinical researchers in the field

PORTRAIT

WHERE ENGINEERING, MEDICINE, AND BIOLOGY MEET

Interview with Assist. Prof. Vartan Kurtcuoglu

You are originally Armenian and were born in Turkey. How did you end up in Switzerland?
As Christians facing discrimination, my parents decided to emigrate when I was still in kindergarten. While they worked hard to establish a new life for our family in Switzerland, my sister and I immersed ourselves in Swiss culture through school and friends. I eventually became a Swiss citizen, did my military service here, and also received my primary as well as most of my secondary education in Switzerland, with the exception of my senior year of high school (secondary school) spent in California. That's where I met my wife, and that encounter had an important influence on my career choice.

How so?
In high school I was aiming to study medicine. Given the length of medical studies and my desire to make the long-distance aspect of my relationship with my future wife as short as possible, I opted for a field of study with a more compact schedule — mechanical engineering.

But you didn't stay in mechanical engineering. Why was that?
My initial interest in medicine eventually caught up with me when I decided to do my PhD in biomedical engineering. I was fascinated by the computational hemodynamics research of Prof. Dimos Poulikakos at ETH Zurich. He offered me a PhD student position to expand his investigations into the cerebrospinal fluid space, and I immediately accepted. That was at a time when I didn't even know that there was such a thing as cerebrospinal fluid. I was just fascinated by the idea of doing research between engineering and medicine.

How did you end up at the NCCR Kidney.CH?
This was a process that started even before Kidney.CH's inception. I had temporarily joined Prof. Peter Libby's group at Harvard to learn more about biology, but came back to Zurich with much more than I had expected: I'd realized that I wanted to position my research at the point at which engineering, biology, and medicine meet. And when my current position at Kidney.CH was advertised, it felt like it was made for me. I didn't hesitate to apply for it and was overjoyed when I was given the opportunity to join the NCCR.

What are your goals at the NCCR?
My goal is to bring in computational modelling based on 3-D imaging as a powerful tool that will complement the experimental methods used so far at the NCCR. My group is currently working on the calculation of renal-tissue oxygen distribution based on micro-computed tomography data within the context of the NCCR's Oxygen module. We have several other modelling projects in store. Stay tuned.

Fig. Volume rendering of a mouse's renal vascular corrosion cast acquired using micro-computed tomography (collaboration with Prof. Bert Müller, University of Basel). Voxel size: 1.5 µm.

E-LEARNING MODULE 2 STARTED

After last year's success of the first e-learning module in basics in nephrology, a new module was created, in collaboration with the Health Science eTraining Foundation (HSeT), and added this year. Whereas the first module focussed on salt & water handling, the second module focuses on acid-base handling of the kidney, and on associated diseases when this balance is disturbed.

The kick off for this new module took place in October 2013 and included presentations on "Acid-base homeostasis: a view on transporters, metabolic pathways, and sensors" (by Carsten Wagner from the University of Zurich) and "Clinical evaluation of acid-base disorders" (by Nilufar Mohebbi from the University Hospital of Zurich).

Participants will first individually study the six annotated online articles. Then, groups of four to six participants will be assembled, and individual articles will be allocated to each group. Each group will then work in greater depth on its article. On 27 March 2014 the groups will meet to present and discuss their work in front of our panel of Kidney.CH experts.

Progress will be self-assessed during the course.

The goal of the e-learning programme is to offer a range of comprehensive modules enabling a better understanding of the basics of kidney physiology and pathophysiology. We also plan to develop additional modules to build a comprehensive education programme in basics in nephrology, which shall be validated and, in the future, be offered as an official CAS- and MAS-certified course or courses.

IMPRESSIONS FROM THE 3RD INTERNATIONAL KIDNEY.CH SYMPOSIUM

The 3rd Kidney.CH Symposium was held on June 20 at University Hospital Zurich. This year's topic was the role of the kidney in mineral homeostasis. We would like to take this opportunity to warmly thank all the speakers and those who participated at this excellent event. (Fotos: Heinz Sonderegger)

Speakers: Olivier Bonny, Carsten Wagner, Markus Bleich
Kenneth E. White, Murielle Bochud, Martin Konrad
Pascal Houillier, Orson Moe, Diana Graus-Porta

Kidney – Control of Homeostasis is a Swiss research initiative, headquartered at University of Zurich, bringing together leading specialists in experimental and clinical nephrology and physiology from the Universities of Basel, Berne, Fribourg, Geneva, Lausanne and Zurich, and corresponding University Hospitals.

EVENTS

4TH NCCR KIDNEY.CH RETREAT
February 6–8, 2014,
Morat, Switzerland

93RD ANNUAL MEETING OF THE DEUTSCHE PHYSIOLOGISCHE GESELLSCHAFT (DPG)
March 13–15, 2014,
Mainz, Germany

E-LEARNING FINAL MEETING MODULE 2
March 27, 2014,
Bern, Switzerland

38. NEPHROLOGISCHES SEMINAR
April 3–5, 2014,
Heidelberg, Germany

51ST ERA-EDTA CONGRESS
May 31 – June 3, 2014,
Amsterdam, Netherlands

4TH INTERNATIONAL NCCR KIDNEY.CH SYMPOSIUM
June 20, 2014,
Lausanne, Switzerland

Imprint
Editor: Matthias Meier
Design: bigfish.ch
Print: SuterKeller Druck AG

NCCR-Kidney.CH
Institute of Physiology
University of Zurich
Winterthurerstrasse 190
8057 Zurich | Switzerland
Tel: +41 44 635 5216
Fax: +41 44 635 6814
www.nccr-kidney.ch
info@nccr-kidney.ch