



# XI IAHN CONGRESS

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**HISTORY OF NEPHROLOGY**

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Under the auspices:

Hellenic Society  
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The International Hippocratic  
Foundation of Kos (IHFK)



Society for the Dissemination  
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PLENARY  
LECTURES



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## **01. NEPHROLOGY IN AN ALEXANDRIAN MANUSCRIPT OF LATE ANTIQUITY.**

### **Marselos Marios**

*Professor Emeritus of Pharmacology, Medical Faculty, University of Ioannina, Greece*

A medical manuscript with the title “Dynameron” is kept in the Marciana National Library of Venice (Cod. gr. Z. 295) and originates from a text initially written in Greek by a physician named Aelius Promotus, who lived and worked in Alexandria (2nd century AD). This manuscript should not be confused with the enormous “Mega Dynameron” of Nicolaos Myrepsos, containing 2667 recipes, which was written in the 13<sup>th</sup> century. “Dynameron” contains 130 chapters dealing with different diseases and their treatment. The recipes related to Nephrology are various mixtures of about 80 herbs. In addition, there are nine ingredients of animal origin and two minerals. The large number of ingredients used in each recipe implies that Aelius Promotus was a follower of the so called “empiric school”, although in his work are easily recognizable also influences from other medical sects. Many of the herbal ingredients proposed by the author are known for their diuretic, spasmolytic, analgesic and antiseptic properties. Hence, they are suitable for treating nephrolithiasis, stranguria, dysuria, hematuria, as well as inflammations of the kidneys and the urinary bladder. Some of the recipes refer to ingredients that cannot be granted any apparent therapeutic reasoning. Additionally, there are a few examples of treatments, which seem more like superstitious rituals. However, when “Dynameron” is evaluated as a whole, the conclusion is that Aelius Promotus was a competent practicing physician with great expertise, typical of the famous medical tradition of Alexandria during the late Roman era. There is evidence that “Dynameron” was highly estimated and was copied several times thereafter, in order to serve as a therapeutic index for the common ailments a physician might encounter in his everyday practice. We elaborate on the treatise’s origin, its popularity and on the validity of the substances proposed for treatment of renal ailments.

## **02. LEONARD GEORGE ROWNTREE (1883- 1959): A NOW ALMOST FORGOTTEN FOUNDER OF 20<sup>TH</sup> CENTURY NORTH AMERICAN NEPHROLOGY**

### **Cameron, J Stewart**

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Most historians of medicine would name major figures in the founding of 20th Century North American Nephrology in the 1920s and 1930s as Henry Christian, Donald van Slyke, Maurice Fishberg, Thomas Addis, and of course Homer W Smith. Leonard Rowntree has some claim to be added to this list.

Today, Rowntree is known almost exclusively for his role in the performance of the first continuous in vivo haemodialysis of blood at Johns Hopkins, to which he was recruited by Sir William Osler. In this, understandably Rowntree’s contribution has been overshadowed by the work of the leader of the team which performed this feat, pharmacologist John Jacob Abel (1857-1938) (Later in the 1920s at the Mayo clinic, Rowntree also did important work on clotting within extracorporeal circuits). At Hopkins, working in Abel’s lab with J Geraghty, Rowntree had already introduced a test for overall renal excretion, based on the excretion of phenolsulphthalein (PSP), which was still in wide use into the 1960s. This was the standard test until creatinine excretion and GFR approximations took over. He then worked with Norman Keith (1885-1976), still in Baltimore, and described a widely-used dilution method for blood volume, and together wrote a book on the subject. After a period in service in WWI studying aviation physiology, he returned to the Mayo Clinic as joint chief of medicine: whilst at the Hopkins he was a member of teams led by others, now he took charge, remaining in the Mayo for 13 1/2 years until 1932, and publishing over 100 papers, a number on the now nascent nephrology. Apart from the clotting studies already mentioned, he described in 1923 the use of sodium iodide as a means of visualizing the urinary tract, leading to the IVU which remained the standard for some 40 years. He attracted Keith to move to the Mayo, resulting in a seminal description of lupus nephritis, especially its histology, in 1922. Finally, with AW Adson he investigated the use of lumbar sympathectomy for severe hypertension in 1925. He had established amongst other divisions a renal service headed by Keith. Of his many other studies in general medicine perhaps the most notable was the use of adrenal extracts for adrenal failure, after his return East in 1931 to Philadelphia where he published a further 47 papers. He spent WWII working in the administrative side of the armed forces, then retired. He lived to see clinical dialysis and transplantation, and the emergence of Nephrology. In 1958 a year before he died he published a rambling part- autobiography and part-history of American medicine in the 1920s and 1930s, Amid masters of twentieth century medicine.

### **03. EXPLORING THE STRUCTURE OF THE KIDNEY IN ANTIQUITY**

#### **Touwaide Alain**

*PhD, UCLA, and Institute for the Preservation of Medical Traditions, USA*

Medico-historical research on the function of the kidneys in Antiquity has increased over the past decades. However productive this renewed activity might have been, it has not explored thus far the research made in Antiquity to explore the structure of the kidneys. This presentation will attempt to determine what ancient physicians from Hippocrates in the 5th century BCE to Galen in the 2<sup>nd</sup>/early 3<sup>rd</sup> century CE knew of the anatomical structure of the kidneys (if anything) and how they did so. Since no anatomical illustration have been preserved (assuming that they existed), this presentation will rely on the only available material, that is, the treatises by the Hippocratic physicians and Galen, together with all the other from the 5th century BCE to the 3<sup>rd</sup> CE, and it will rely on a systematic screening of the full text of these works in the original language to possibly trace relevant passages and reconstruct the ancient knowledge of kidneys, in a dynamic way, including the time and places where major or basic discoveries took place. The research leading to this presentation is expected to bring to light an anatomical research activity remained unnoticed thus far.

### **04. REFERENCES TO URINARY TRACT DISEASES IN MIHI COMPETIT BY THOMAS OF WROCLAW (1297-1378)**

#### **Ostrowski Janusz<sup>1</sup>, Źmudzki Paweł<sup>2</sup>**

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Contrary to the opinions about the weakness of mediaeval medicine, there is a lot of data against such views. These include the emergence of Europe's first universities educating doctors such as Arnaldo De Villanova in France and others. The next generation of outstanding doctors includes Thomas of Wroclaw born in this Silesian town in 1297. At the age of 16 he started education at the university in Montpellier, France where he met his renowned teachers: Peter Abano, Henry de Mondeville, or Bernard de Gordon. After completing his studies in Montpellier, he continued his scientific trip to Toledo (Spain), Salerno, Padua, Bologna and Rome (Italy) and to Oxford (England).

Having earned a pan-European reputation, despite numerous job offers from universities, he returned to his homeland to become a court doctor for John of Bohemia and Charles IV, king of Bohemia and the Holy Roman Emperor. He died in Wroclaw in 1378 and was buried at the nearby St.Vincent Abbey. Thomas is known to have written a few works, yet *Mihi Competit*, completed at the age of 63, must be the most prominent. It comprises 4 parts: *Practica Sanitatis*, *Aggregatum*, *Antidotarium* and *Practica Medicinalis*. Modern nephrologists might find the last one the most interesting as its chapters no. 81-87 of part 112 refer to urinary tract diseases. The titles of the subsequent parts are: *De debilitate et dolore renum* (On Renal Disease and Pain), *De apostemate renum* (On Renal Abscess), *De ulceribus renum et vesice* (On Kidney and Bladder Ulcers), *De lapide renum et vesice* (On Kidney and Bladder Stone), *De difficultate mingendi* (On Problems with Urination), *De diampne* (On Urinary Incontinence) and *De diabete* (On Diabetes Insipidus).

There are no known translations of the Latin-written *Michi Competit* into modern languages. Finding some of the views depicted in the work historically interesting, the authors undertook to translate it aiming to present it to a wider audience.



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## **05. LUPUS NEPHRITIS: A HISTORICAL APPRAISAL.**

**Eknoyan Garabed**

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It all started as a nondescript skin disease. First defined by Hippocrates as 'herpes esthiomenos' for any destructive skin lesion that spread like a crawling snake. The term 'lupus', derived from Latin for wolf, entered the medical lexicon in the 10th century, after deforestations brought wolves in close contact with farmers and the similarity of wolf bites to the still nonspecific ulcerative and necrotic skin lesions noted. It was the differentiation of selected erythematous butterfly rashes from the necrotic skin lesions of cancer and tuberculosis in 1828 that led to their characterization as 'lupus erythematosus' in 1850, a nomenclature still in use. The systemic manifestation of this new entity were noted in 1872 leading to their being termed "disseminated lupus erythematosus", and shortly thereafter by the preferred "systemic lupus erythematosus" that prevails to this day. Albuminuria and renal abnormalities were noted in cases of systemic lupus erythematosus early on but were not characterized as 'lupus nephritis' until 1902, based on post-mortem studies. Refinements in the description of lupus nephritis were made after the introduction of needle kidney biopsies in 1951, and its varied renal morphologic features elucidated by electron microscopic and immunofluorescent studies thereafter. These were then classified in 1975, expanded in 2013 and continue to be refined.

## **06. NEPHROLOGY A DISCIPLINE EVOLVING INTO COMPLEXITY: BETWEEN COMPLEX SYSTEMS AND PHILOSOPHY**

**De Santo Natale Gaspare**

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In the last quarter of the past century a growing opposition to specialization occurred in the course of a quest for unity of culture. To address the problem of fragmentation that plagues specialization, a new complex method of interdisciplinary teaching not based on disciplines, but crossing specialties was adopted. The method flourished thanks to (i) the foundation in 1984 of the Santa Fe Institute in New Mexico, inspired by Murray Gellman and (ii) the publication in 1994 of the Charter of Transdisciplinarity signed by Lima de Freitas, Edgar Morin and Basarab Nicolescu. Complexity emerged from 3 main streams: cybernetics, general systems theory and dynamical system theory. Now it is seen as an indispensable tool to advance science without losing the role of specialties that are of paramount importance for solving practical problems.

Disciplines play a great role in disseminating and furthering knowledge. They are born - without aiming to eternity - in order to warrant the originality of the scientists who existed, exist and will exist in the future. In the quest for originality, a vital priority in the world scientific enterprise they are forced to scrape smaller and smaller niches where they can protect themselves and their contributions. Disciplines however are like fractals their boundary regions are zones where exchanges are wider than those occurring in their own internal zones.

"Nephrology is one of the flowers of medical biology and medical pharmacology, a flower permeated by genetic and molecular biology"(Richet). Nephrology, born in the fifties of last century, is now charged with the responsibility to answer the health demands of more than 12% of the world population. It holds all the characteristics of a discipline born in the fertile world of complexity and continuously expanding its boundaries into that of other disciplines. Nephrology is characterized by the "the exponential information overload being generated. The pattern began in the 1960s that has continued and is magnified by the increasing number of specialty journals that have appeared since then" (Eknoyan). It is characterized by a unique exponential growth of information generated and by the capability of matching the challenges of big data algorithms and omics platforms. The most successful contributions of nephrology were driven by 2 main ideas: (i) The identification of CKD by the impact of the KDOQI (Kidney Disease Outcomes Quality Initiative) guidelines that defined CKD based on estimated glomerular filtration rate (Eknoyan) and (ii) the identification of uremia as a fatal systemic disease (Zoccali).



# ORAL PRESENTATIONS



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## 01. RICHARD BRIGHT - A REMINDER FROM A FAMILY LINK

### Phillips Malcolm

#### *Charing Cross Hospital, London*

Richard Bright was born in Bristol in 1789. He studied medicine at Edinburgh and Guys Hospital. He developed a keen interest in Pathology, studying organs carefully at post-mortems and often using his artistic skills to record appearances. In 1811 he drew "a granular kidney". He graduated in 1813.

He became interested in the condition known as "dropsy"- gross fluid retention, believing it was related to kidney malfunction. The patient whose granular kidneys he had sketched had died from dropsy. A Parisian doctor-Pierre Rayer-agreed with his views and coined the phrase "Maladie de Bright".

In 1824 he became Physician and Lecturer at Guys. His teaching was criticised. He actually undressed patients to examine them; he used "the suspect method of percussion"; and used "that foolish toy-the stethoscope"! He remained fascinated by dropsy and published 23 cases, mostly with renal failure of whom 17 died. Autopsies showed "nephritis". In 1832, at the College of Physicians, he described high blood urea levels and albuminuria in relation to dropsy. His clinical description of his disease, as he found it, in Guys Hospital Reports, 1836, is still widely quoted, verbatim, in medical texts.

In 1851 he found he had aortic stenosis but continued to see patients from all walks of life. Among them was Isambard Kingdom Brunel, the famed engineer, who had developed oedema. Bright diagnosed renal failure which gradually worsened. Bright attended him regularly but in 1859 (after Bright's death) Brunel died from a stroke and renal failure.

Bright had died somewhat unexpectedly in December of the previous year. Details are very limited. The Lancet recorded "he contributed more than, perhaps, any other to form the medical opinion of his day".

What prompted this "Reminder of Bright"?

Before my retirement I saw a 94 year old lady patient in clinic. She was a great, great niece of the famous nephrologist. She had mild renal impairment. Subsequently she showed me a book that she had written- "The Inner Circle. A view of war from the top". This was an account of her work when based in the underground Cabinet War Rooms, where Churchill spent much time. She was in charge of the information centre which communicated with allied military leaders in the field. She organised written records of war events worldwide for commanders to review when in London. She also administered domestic matters when Churchill and others travelled for conferences with leaders such as Roosevelt and Stalin.

A truly remarkable lady from a remarkable family. She died aged 97; her renal function had not deteriorated.



## **02. THE HAEMOLYTIC - URAEMIC SYNDROME:**

### **A case occurred in Thessaloniki in 1918**

**George Charles**

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Conrad Gasser and his colleagues from Bern in Switzerland usually receive credit for discovering the haemolytic-uraemic syndrome because of their paper published under that title in 1955. Two (at least) other observers, J. Bamforth and W. Hensley, had however previously reported similar, but now rarely acknowledged, cases. The present communication will review the clinical reports of the latter that appeared in 1923 and 1952 respectively, and will discuss some philosophical implications suggested by this situation.

Bamforth's patient was a soldier admitted to a British Army Hospital in Thessaloniki in Greece in 1918 with fever and profound diarrhoea. He became anuric after eight days and died after ten days. An autopsy identified renal cortical necrosis with an intra-renal micro-vascular insult as the probable mechanism. Hensley's patient was an 8-month old infant who was hospitalized in Sydney with severe diarrhoea, haemolytic anaemia, thrombocytopenia, and uraemia. He died after eight days: an autopsy showed acute necrosis both of his glomeruli and of his renal tubules. Gasser et alia reported on five children who developed haemolytic anaemia, uraemia, poikilocytosis, and sometimes thrombocytopenia, with renal cortical necrosis. The evocative name that they proposed for the condition promptly attracted international attention. Investigations later identified Shiga toxin as a sometimes-causal infectious agent; whereas complement abnormalities, often genetically-based, predisposed to other cases. The importance of the Swiss report, therefore, was not that it provided the first documentation of the haemolytic-uraemic syndrome, but that it proposed a distinctive name for it. This became a symbolic index item that enlightened many people about it, and that stimulated others to explore its mechanisms and ramifications. I suggest that this situation — in which the trumpet-call proposal of a distinctive name coalesces previous observations and insights into a recognisable concept to gain greater credit for the trumpeter than for the original observers — occurs quite often in the semiotics of science and medicine, but remains singularly under-recognised.

## **03. THE EMPEROR'S NEW CLOTHES IN NEPHROLOGY: PAST AND PRESENT**

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In, the philosophy of science (and medicine) a hypothesis should have verifiability being empirically verifiable thus meaningful. It should also be falsifiable, that is honestly rejected if it is contradicted by a basic observation. The question arises who will voice the contradiction. In the tale "The Emperor's new clothes" (H.C. Andersen 1835) the emperor and courtiers were silent because they feared being revealed as stupid or incompetent. Scientists often do not challenge data with which they might not agree, or conclusions that are perhaps overblown or overstated for these and other reasons. Nephrology offers us similar examples from the past and the present.

Past: Galen (129-216 AD) described Diabetes as a disease specific to the kidneys because of a weakness in their retentive faculties. A theory challenged only in the 19th century. Aristotle (384-322 BC) incorrectly observed the absence of the kidney in fish and birds and deduced that it was not essential for the existence of a living organism. This proved wrong in the last century. He also wrongly deduced from examination of dead cows, where each kidney was located on each side of the spinal column, that this was the case also for the living animal. A hypothesis rejected only last year.

Present: Highly costly treatments still persist based mainly only on experimental and observational studies but not robust randomized controlled trials: The use of phosphate binders for phosphate lowering in advanced kidney disease. The use of statins for cholesterol lowering in dialysis patients. Meanwhile simpler and cheaper treatments are not actively promoted.

In Anderson's story the child who cried out "But he isn't wearing anything at all" opened the eyes of the whole town. In the current scientific milieu, although the lack of evidence is testified, a person out crying the obvious risks to face harassment from the modern tailors (Journals, Sponsors, Academia) who produce the clothes of our kings.



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## 04. CHLORIDE ANION AND ARTERIAL HYPERTENSION: A HISTORICAL REVIEW

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In 1929 Robert Berghoff and Angelo Geraci published the results of a primitive experiment upon fifty persons, seven of whom were hypertensive. They substituted sodium chloride in their diet by sodium bicarbonate and observed a considerable decrease in their blood pressure. It was the first experimental observation that chloride anion may be responsible for blood pressure elevation produced by increased salt consumption.

In 1939 Walter Kempner at Duke University in Durham, North Carolina, introduced the "rice diet" with a rigid restriction of sodium (0,15 gm/day) and chloride (0,2 gr/day) which proved efficacious in treating hypertension.

In 1971 Floyd Kregenow showed experimentally that duck's erythrocytes, placed in a hypertonic environment, after an initial shrinkage, restore their volume to normal values by inwardly moving of potassium and chloride ions.

One year later in 1972 Arthur Guyton and colleagues introduced the conception of infinite blood volume regulation by the kidney as the etiology of essential hypertension based upon the "pressure natriuresis" phenomenon and turned the lights of investigation toward the sodium as the principal ion related to hypertension.

In 1978 Theodore Kotchen et al. showed experimentally that chloride anion inhibits plasma rennin activity in sodium deprived rats.

In 1981 Rainer Greger and Eberhard Schlatter discovered the sodium potassium 2 chloride co-transporter (NKCC2) in the thick ascending limb (TAL) of Henle's loop of rabbit kidney.

In 1993 and 1994 Geraldo Gamba et al cloned and purified the thiazide sensitive sodium chloride co-transporter (NCC) in distal convoluted tubule (DCT) and bumetanide sensitive sodium potassium 2 chloride co-transporter (NKCC2) in the thick ascending limb of Henle's loop (TAL).

In 1996 David Simon et al showed that mutations in the genes encoding NCC and NKCC2 are responsible for Gitelman and Bartter syndromes.

In 2001 Frederic Wilson et al described two mutations in genes encoding WNK1 and WNK4, as the cause of Gordon's syndrome which mirrors the phenotype of Bartter and Gitelman syndromes.

In 2014 Alexander Piala et al showed experimentally that WNK1 acts as an intracellular chloride sensor and is capable to regulate its own phosphorylation or dephosphorylation, and hence activation or deactivation, according to intracellular chloride concentration.

Parallel to the above mentioned work, in 2011 and 2013, Dominique Eladari and his team showed, in intercalated cells of mice, the presence of thiazide sensitive sodium driven chloride bicarbonate exchanger (NDCBE). The exchanger operates in parallel with the sodium independent chloride/bicarbonate exchanger pendrin and the net result of the coupled function of NDCBE/pendrin is the absorption of sodium chloride with resultant increase of extracellular volume and blood pressure.

**Conclusion:** After almost one century of vigorous research efforts we know now that although sodium is the principal extra cellular cation which determines the magnitude of extracellular volume and hence the magnitude of blood pressure its reabsorption from the kidney and movement to the extracellular space is principally depended upon chloride anion. After that may it is time to talk about "chloride sensitive" and not sodium sensitive hypertension.

## 05. HERBAL PRESCRIPTIONS FOR THE TREATMENT OF KIDNEY DISEASES IN THE BYZANTINE ERA

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**Introduction:** This article focuses on nephrology diseases and illnesses as well as on the treatment of herbal formulations that were used in the late Byzantine era and are recorded in medical texts. The medical Texts which have been investigated refer to the Byzantine period from the 4th to the 15th century. In this period Texts were written which contributed to the evolution of medical science to both the West and East. In Particular the text which were referred excluding to Urine, were studied from doctors. Those books are separated in two categories: Books focused in the observation of the Urine (Uroscopy) with a diagnosis of the kidney diseases, and Books of the treatment of kidneys diseases.

**Materials and Methods:** Our primary source material was the medical collections by Oribasius, Aetius, Alexandros of Tralleis, Paul of Aegina, Symeon Sith, Nikolaos Myrepsos and Ioannis Actuarius, who report nephrological diseases and herbs that face them.

**Results:** These studies have confirmed the ongoing search and methodological approach to urine testing. Also, in herbal medicines, herbal combinations are recommended for the treatment of dysuria, strangury, lithiasis and nephropathy. The plants belong to various families of which the most frequent: Apiaceae, Lamiaceae, Asteraceae, Fabaceae and Rosaceae.

**Conclusions:** This research leads us to the conclusion that the content of this books gives us a detailed view of the urology and properties of the herbs that were able to effectively deal with kidney diseases and the level of knowledge that existed during the Byzantine era.

## 06. CYSTIC LITHIASIS TREATMENT IN “MEGA DYNAMERON”

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Nikolaos Myrepsos from Alexandria was a well-known doctor, botanologist and pharmacologist of late Byzantine period (13<sup>th</sup> century), who coded and summarized the knowledge in Pharmacy until his era. His book “Mega Dynameron” includes more than 2500 pharmaceutical recipes and has been the reference drug book in Europe for about three centuries after its publication. Our study aimed to focus on recipes for nephrolithiasis, especially cystic lithiasis.

For the purpose of this study we used the Latin translation of “Mega Dynameron” published by Leonhart Fuchs (1549, Basel), available at the Biblioteca Digital Dioscórides of Universidad Complutense of Madrid, as well as the Greek encoded text by Ilias Valiakos (2014).

Dynameron includes 24 sections, following the 24 letters of the Greek alphabet. Myrepsos refers to renal diseases in a substantial number of recipes in his work. Most of them are intended for use in non-renal pathologies as well, and only a part of them are specific for renal and cystic lithiasis. “Antidotarium” in section “alpha” includes eight recipes referring specifically in cystic stones dissolving. Two of them are exclusive to cystic lithiasis (ν/LI and νβ/LIII), while μδ/XLII and ρζα/CXCIII are used both for renal and cystic stones. The rest four (β/II, λθ/XL, πη/XC and τιδ/CCCXX) are indicated for other diseases as well. Recipes include a rich variety of herbs, plants, vegetables and fruits, insects (cicada) and animal products (goat’s blood), with detailed preparation instructions. Ingredients are mixed with honey, sugar, water, wine or chamomile, and are administered in specific doses and duration of treatment. More recipes about renal inflammation, lithiasis and colics in Dynameron are found in sections for ointments, patches, enemas, cathartics and others, with a couple of specific cystic stones recipes referred in index pilularum (“περί Κοκκίων”) and index lexyretorum (“περί Ληξοπυρέτων”).

Nikolaos Myrepsos with his reference drug book “Mega Dynameron” disseminated invaluable knowledge for lithiasis treatment throughout the centuries, highlighting the recognition of importance of kidney function and uropathies.



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## 07. RESEARCH ON THE KIDNEY AND HAIR LOSS BASED ON ANCIENT CHINESE MEDICINE LITERATURE

Li Haiying

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*Huang Di Nei Jing* (《黄帝内经》 *Inner Canon of the Yellow Emperor*) embodies the distinctive view of human body in Chinese medicine system. Its important concepts include the interpretation of the life cycle and the theory of visceral manifestations. In *Su Wen* (《素问》 *Plain Questions*), it pointed out that the kidney governs storage and stores the essence, and its bloom manifests in the hair. It also interpreted the close relationship between the production, growth, whitening and loss of the hair and the state of kidney qi. The records from *Ling Shu* (《灵枢》 *Miraculous Pivot*) and *Jin Gui Yao Lue* (《金匱要略》 *Synopsis of Prescriptions of the Golden Chamber*) also reflected view of doctors in early stage on etiology and pathogenesis of hair loss from the perspectives of kidney deficiency, seminal emission, and qi-blood deficiency.

Located on the surface of human body, hair refers to an important appendant organ of the skin. In Chinese medicine, it is believed that interior conditions will manifest in the exterior, and external changes of human body are caused by changes of internal organs, qi and blood. Hair loss not only affects patients' appearance, but also refers to the morbid manifestation of latent existence of predisposing factors in the body and dysfunction of qi and blood, with complex pathogenic factors.

In *Huang Di Nei Jing* (《黄帝内经》 *Inner Canon of the Yellow Emperor*), it records that over intake of food in sweet taste will lead to bone pain and hair loss and if kidney qi is sufficient, the hair and permanent teeth will grow. If kidney qi is debilitating, it will cause hair loss and withered teeth, pointing out that excessive sweet food will damage bones and hair, and that insufficient kidney essential qi and blood failing to nourish the body are the important causes of hair loss. Reviewing on the relevant literatures of Chinese medicine in the past dynasties, it shows that Chinese medicine is very rich in the contents of etiology, pathogenesis, and formulas of hair loss. There are also many methods for nourishing the hair, of important academic values.

## 08. THE REFRAMING OF THE NEPHROLOGY VIDEO LEGACY PROJECT 30 YEARS ON

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Thirty years ago, we both were attracted by the idea of recording video interviews of individuals who had played a key role in the founding and early expansion of Nephrology as a speciality, most of whom were alive. Sadly, a number of individuals in this category had already been lost, principally Homer Smith (USA), Jean Hamburger (France), John Merrill (USA) and Nils Alwall (Sweden). Occasionally however we were lucky in such finds as a film recording of John Jacob Abel talking in 1929. The result of this endeavour was recordings of about 50 giants of Nephrology by 2007. A major feature was not to impose a standard format but allow subjects to talk in a manner and for as long they wanted. These recordings were made on VHS tapes, but it became obvious that digitisation of the material was essential, and this also was undertaken as the 21<sup>st</sup> century began. Some of these recordings transferred to CD format were available in the early years of the century through the ISN who had helped sponsor the project, but in reorganisation of the ISN website they were deleted and vanished from view. Now they re available in an expanded series of recordings which continues to grow in collaboration with Pierre Ronco and Giordina Piccoli of the ERA, Italian Society and Francophone Society and their colleagues at [https://www.youtube.com/playlist?list=PLS1ZP4out6bM\\_\\_j9\\_rxTgy4V\\_aoTNPFpu](https://www.youtube.com/playlist?list=PLS1ZP4out6bM__j9_rxTgy4V_aoTNPFpu)

We believe that today's participants and trainees in Nephrology need to be reminded of the inconsistency of a rolling present through understanding of how present hypotheses, concepts and treatment recommendations came about. Despite a strong movement amongst professional historians to downgrade the role of "great men" in the progress of ideas, these ideas in sum came from an endless series of talented individuals. Hearing directly on video from this series of such men and women, almost all of whom have now passed away, not only gives a vivid idea of their characters but also an insight into how their minds worked. During the IAHHN meeting delegates will be free to watch all or parts of some 50 early interviews from the Video Legacy series.

## **09. DIMITRIS OREOPOULOS, MY FATHER**

### Oreopoulos Antigone

Dimitrios Oreopoulos is best known for his innovations and contributions to field of peritoneal dialysis. As his daughter, however, I have a different perspective on my father's greatest legacy, which I believe is love, faith, fearlessness and passion.

I have created a video that shares my experience of our father - daughter relationship, his role as a teacher and colleague to many around the world in the nephrology community, his belief in the necessity of compassion and connection during the delivery of medical care and his views on Christianity.

My father was my friend, mentor, and the greatest humanitarian I have ever known. My childhood is filled with good memories of foreign trainees at our home for Christmas and Thanksgiving dinners so they would not be alone for the holidays. I often witnessed my father give money to individuals in need, charities, and the Church. He maintained a corporate account that was used to help patients pay for medication or rent when they could not afford it.

My father taught me that words and ideas can change the world; he wrote letters to the Prime Minister, Steve Jobs of Apple, and Members of Canadian Parliament when he had a concern or a commendation, and was unafraid of failure or large problems that needed to be solved. He was able to create the first Greek School for children and the first Greek nursing home in Toronto, Canada, wrote a children's book and founded a medical journal that promoted the restoration of humane medicine. Always modest about his impressive accomplishments, he never strived to impress others.

One of the qualities I admired most about my father was that he could have a meaningful conversation with anyone no matter the race, age, religion or cultural background. He always found something to connect with people on. He made others feel loved and respected through being genuinely interested in their story, without passing judgment. My father's efforts in his own spiritual journey and his faith in the belief that there is always good to be found in any situation were also a part of his legacy that had a lasting impact on me.

## **10. GREEK GIANTS OF NEPHROLOGY**

### Mountokalakis Theodore

#### *Medical School, National and Kapodistrian University, Athens, Greece*

Rufus of Ephesus and Aretaeus of Cappadocia (1<sup>st</sup> – 2<sup>nd</sup> century CE) can be considered as the first Greek "giants" of Nephrology since they are the first exponents of Hippocratic medicine who recognized the specific function of the kidney and described renal diseases. In the modern era, several Greek doctors contributed to the establishment and advance of Nephrology in Greece. I will refer only to those who are no longer alive. I will also refrain from mentioning the great contribution of Dimitris Oreopoulos since a special tribute to his legacy has been arranged to be paid in this meeting. Hippocrates Yatzides (1923-2013), a principal mentor to Oreopoulos and one of the founders of EDTA in 1964, is deemed as a pioneer of hemodialysis for the reason that, in 1965, he used activated uncoated carbon hemoperfusion to treat barbiturate poisoning. Yatzidis's early attempts to establish a national Society of Nephrology, in 1966, were fruitless. Three years later, Sotiris Papastamatis (1912-1979), associate professor of Medicine in the University of Athens and his close friend Dimitrios Valtis (1917-1973), professor of Medicine in the University of Thessaloniki, collaborated in the foundation of the Hellenic Society of Nephrology (HSN). Other departed colleagues noteworthy for their contribution to the advance of the study of renal diseases and the introduction of chronic hemodialysis in our country are Panayotis Metaxas (1929-2007) (Valtis's disciple, member of the 1<sup>st</sup> HSN Council, president of the 8th International Congress of Nephrology held in Athens in 1981), Antonis Billis (1932-2013) (Papastamatis's disciple, vice-president of the 2<sup>nd</sup> HSN Council, president of the 3<sup>rd</sup> HSN Council and of the 1<sup>st</sup> National Congress of Nephrology), and Gregory Vosnides (1943-1996) (Billis's disciple, secretary of the 32nd EDTA-ERA Congress held in Athens in 1995, co-organizer with Spyros Marketos of the 1st International Congress of the History of Nephrology held in Cos in 1996). Further to breaking new ground in the development of Nephrology in our country, these colleagues continue to serve as role models to younger Greek nephrologists. And this attribute should be viewed as one of their most important accomplishments.



# XI IAHN CONGRESS

## 11. 300 YEARS OF NEPHROLOGY IN SCOTLAND

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For over 200 years from the early 1700s, medical education was a dominant activity of Scotland's universities. Scotland's graduates reached just about every corner of the world. They practised the scientific approach to improving medical care that they had learned there, and established hospitals and medical schools as they travelled. Nephrology came late to this, but made up for it. Dr Cullen wrote famously, but gloomily, in one of his consultations by correspondence in 1784, on the dropsy suffered by Samuel Johnson. Its cause was unknown, and management symptomatic.

Richard Bright, inventor of Nephrology, studied in Edinburgh 1808-10. His examination in 1813 including scrutiny (in Latin) of his thesis on erysipelas, but his 1827 'Reports of Medical Cases' reverberated around the world. Suddenly everyone wanted to test for proteinuria.

Amongst those taking Bright's work further were Robert Christison, professor of Medicine in Edinburgh, and Pierre Rayer (Paris), whose classic works followed in 1837 and 1839. Despite some striking insights, Christison's work has been relatively neglected. His campaign to prevent the graduation of women may have contributed to that.

Soon after Bright's publication, Thomas Latta demonstrated in Leith in 1832 that patients who were moribund from Asian cholera could be revived by infusing saline into a vein. This was a discovery of much more immediate importance than Bright's, but was neglected for the next 50 years.

Thomas Graham meanwhile described the phenomenon of dialysis, and distinguished colloids and crystalloids, in work initially largely done in Glasgow and published 1830-61. The 1861 paper described its application to urea in urine, laying the ground for the first attempts at therapeutic dialysis.

Dialysis reached Scotland's academic centres in 1959. The first kidney transplant in the UK was undertaken between identical twins in Edinburgh in 1960. A period of intense interest in immunology and immunopathology followed. The second use of Azathioprine in transplantation was in Edinburgh in 1962.

In 1969-70, the world's worst dialysis-associated Hepatitis B was experienced in Edinburgh. A remarkable ensuing project created the recombinant vaccine Engerix B, marketed in 1986, the income from which was fed back into basic research.

## 12. THE URINARY DISEASES IN THE MOROCCAN TRADITIONAL PHARMACOPOEIA: ETHNOLOGY AND HISTORICAL EPISTEMOLOGY

Bammi Jamal

*Botanist, Anthropologist, Director of the Center for Studies and Research on the History of Sciences in Islamic Civilization, Rabita Mohammedia of the Ulemas, (RABAT), Member of the Heritage Committee, Faculty of Medicine of Fez*

This work, based mainly on ethnobotany, is a contribution to the knowledge of the Moroccan pharmacopoeia concerning the treatment of diseases of the urinary system.

My approach is both synchronic and diachronic, as it seeks to elucidate the historical anchoring of current traditional medical practices through a comparative study of the Moroccan traditional pharmacopoeia recipes of related to urinary diseases and of some Arabic medical texts: i.e. Razes's "Treatise on stones in kidneys and bladder"; Avenzoar's "Tayssir", Ibn Al-Jazzar's "Viaticum" and Ibn Al-Baytar's "comprehensive of medicinal and alimentary simples".

I will try to show the persistence of historical medical knowledge in traditional medical practices, thereby questioning the relevance of the presumed epistemological break between traditional medical knowledge and scholarly discourse.

Key-words: Urinary Diseases, Ethnobotany, Moroccan Pharmacopoeia, Historical Medical Knowledge.

### **13. UROLITHIASIS AND HYPERTENSION: THE APPARENT AND THE HIDDEN IN ANCIENT GREEK AND THE ORIENTAL MEDICAL TRADITIONS**

**Grivas Constantinos**

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Urolithiasis symptoms like renal colic, dysuria and hematuria were easily observed and associated with the urinary system, in any of the long-standing medical traditions of antiquity. On the contrary, a modern symptom like hypertension could not be readily identified with a specific pathology. Investigation and comparison between the Ancient Greek Medicine, Ayurveda, Chinese and Tibetan medical systems on the theoretical causes behind these diseases, their diagnosis and treatment were based on the classical texts and the long tradition of practice. For example for the Hippocratic physicians hypertension could be categorized as *plethora* or abundance of blood, while their Chinese colleagues would classify it as "wind in blood" and "blood stasis" syndromes. The suggested treatments covered the whole medical arsenal of antiquity, from surgical operations, like perineal lithotomy for cystolithiasis, mentioned both in Corpus Hippocraticum and Sushruta Samhita, to bloodletting and especially the use of leeches (hirudotherapy), a rational way to relieve blood abundance, or to the herbal remedies which played a crucial role in the treatment of both urolithiasis and hypertension, and are still used by a considerable number of patients in Greece, India and China. The careful examination of these data can direct us to the better understanding of medical thought in distant civilizations, focusing in their similarities and differences. Last, but not least, they can reveal a possible and plausible materia medica for the modern application.

### **14. PETRUS LEO: A HISTORY OF MEDICINE, ASTROLOGY AND MURDER**

**Colucci Marco<sup>1,2</sup>, Torreggiani Massimo<sup>1</sup>, Confalonieri Carlo Enrico<sup>1</sup>, Esposito Ciro<sup>1,2</sup>**

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Petrus Leo (also known as Pierleone Leoni or Piero Leoni) was born in Spoleto, Italy, around 1445 and studied medicine in Rome. He was an eminent physician and during his life he was professor of medicine in Pisa and Padua. However, most of his fame was due to the fact that he was the personal doctor of Lorenzo de' Medici ("the Magnificent"). He practiced medicine according to the school of Galenus, criticizing Avicenna's unsystematic theories and improving his teaching applying the new systematic approach inspired by Ramon Llull. However, Leo was a man of his time and his interests covered also astrology and philosophy, being part of the neoplatonic circle along with Marsilius Ficinus and Giovanni Pico della Mirandola who were close friends of him. In 1478 he wrote a treatise entitled "De urinis" which was later published by a venetian editor in 1514 in appendix to Gilles de Corbeille's "De urinis et pulsibus" which was widely diffused in academic environments. Petrus' manuscript was nothing unknown but its main innovation resided in listing all the possible urine appearances in color and thickness, expanding the canonical medieval uroscopy wheel from 20 to 42 colors and applying the lullian "ars combinatoria" to combine all the different features to reach a final diagnosis. Moreover, he detailed a standard methodology for uroscopy. His rich and wealthy life tragically ended on April 9<sup>th</sup>, 1492, a day after the Magnificent's death. Piero de' Medici accused Petrus for the death of his brother "the Magnificent" and Leo's body was found in a well not far from the medicean country mansion. Later, history attributed Lorenzo's death to an inferior limb gangrene due to gout but Petrus' name was associated to the most beloved Florentine statesman passing for a long time due to its cabalistic interests and the rumors diffused by the Medici family.



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## 15. A JOURNEY THROUGH THE HISTORY OF DIALYSIS IN SUB-SAHARAN AFRICA

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Sub-Saharan Africa (SSA) is a heterogeneous region with 47 countries, almost one billion people, and a gross domestic product of 1.7 trillion in 2017. The development of dialysis in Africa reflects the local socio-political circumstances. Up to seventies, Africa was recovering from long years of colonization and political turmoil, so limited countries were able to establish dialysis centres.

### **Era before seventies:**

- South Africa was the first country in SSA which started dialysis in 1957, by a general practitioner in Krugersdorp hospital, to dialyse 2 patients with acute kidney injury (AKI).
- In Kenya, acute haemodialysis (HD) started in 1961 by Professor *L.S. Otieno*, followed by peritoneal dialysis (PD) two years later.
- In Nigeria, limited acute dialysis has been available in Lagos since 1965 and acute PD in Ibadan since 1967. Regular HD was firstly established at Lagos Teaching Hospital in 1981 by Professor *T.A. Odotola*.
- In Sudan, the first dialysis centre was a home dialysis unit, established in 1968 supervised by Mr. *Osman Awadalla*.

### **Era after seventies:**

- In Côte d'Ivoire, the first acute PD was performed in 1974 in Abidjan by Professor *Alain Bondurand* to treat black fever patient with AKI.
- In Zimbabwe, Drs. *John Forbes* and *Janet Seggie* placed a dialysis machine in Harare Central Hospital in the early 1970s; yet the machine was occasionally used for the treatment of AKI until 1980.
- In Ethiopia, PD dialysis and less often HD were started in 1980 as reported by Dr. *Berhanu Habte* to treat AKI at Addis-Ababa University Hospital.
- In Tanzania, Dr. *J.P. Miabaji* reported that two dialysis machines were available at Dar-El-Salam University Hospital in the early 1980, to treat AKI or important patients with plans of transplantation abroad.
- In Ghana, Dr. *T.C. Ankrab* provided acute PD and sporadic HD for AKI in 1980.

Other SSA countries started to establish dialysis units afterwards. However, dialysis services are still sparse in most countries due to the high costs and shortage of skilled personnel.





## 16. HISTORY OF RENAL TRANSPLANTATION IN ARAB WORLD

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History of renal transplantation from 17 Arab countries will be highlighted.

In Egypt, Mansoura led transplant program by performing the first two transplants, 1976, Egyptian experience exceeded 19000 in 39 centers. Cairo University performed first unrelated donor in 1983 and deceased donor transplant in 1980. First two transplants in Algeria were in 1986, 1987, total transplants 220 live donors (LD) and 4 deceased donors (DD).

Sudan, first case was in 1972 and overall experience 1600. Iraq performed first case in 1985, the same year where Morocco experience started. They performed 56 transplants in 2015.

Saudi Arabia started transplantation in 1979 with 6939 LD, 2038 DD. First case in Yemen was in 1998 with overall transplants exceeded 400 cases. Syrian first transplant was in 1979. Tunis performed LD and DD in 1986 and 1988. Jordan started transplantation by DD case in 1972 with 4500 transplants.

United Arab of Emirates performed 160 LD and 2 DD transplants. Libya launched transplant program in 1989 and resumed activity in 2004. Lebanon had national organ donation in 1999. Oman performed 60 transplants till 1998. Kuwait program started in 1979 with total transplants 2500. Bahrain entered transplantation field in 1995 (LD) and 2001 (DD), with total 100 LD, 25 DD transplants till end of 2017. Lastly Qatar performed LD transplant in 1986 and DD in 1996.

I hope that in near future Arab transplant should be established to supervise organ distribution, set up regional database, raising funds to less privileged centers and support research.

## 17. WHAT DID AL-RĀZĪ (RHAZES) QUOTE FROM PHILAGRIUS OF EPIRUS ON KIDNEY DISEASES IN *KITĀB AL-HĀWĪ FĪ AL-ṬĪBB (LIBER CONTINENS)*?

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*Kitāb al-Hāwī fī al-Ṭībb (Liber Continens)* of Rhazes (865-925) is a significant work on account of its valuable quotations from the works of Greek, Indian and Arabic authors. These quotations make Rhazes's work important in terms of history of medicine because it provides us with information about the works of the authors which have not survived until today. Philagrius of Epirus, flourished in Thessaloniki in the second half of the fourth century, is one of those writers in Rhazes's work. The purpose of this study is to present the quotations from Philagrius related to kidney diseases in *Liber Continens* and to bring them to the literature in English. The 10<sup>th</sup> book of *Kitāb al-Hāwī fī al-Ṭībb* entitled as "fī amrād al-kulā was majāri al-bawl was ghayrihā/de dispositionibus renum et vesice et aliqua lter veretri tractans continet tractatus tres" is about the diseases of the kidneys, urinary tract and others. The quotations from Philagrius were found out in this book of *Kitāb al-Hāwī*'s both in Arabic and Latin texts (*Liber Continens*), and then these fragments were compared to each other, and translated into English. In *Kitāb al-Hāwī fī al-Ṭībb /Liber Continens*, the quotations from Philagrius are related to kidney pain and its symptoms and signs, kidney stones, and diabetes. Fragments from Philagrius recorded in *Kitāb al-Hāwī fī al-Ṭībb /Liber Continens* on diseases of the kidneys, are discussed and brought to the literature in English.



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## 18. A STUDY ON CHAPTERS RELATED TO NEPHROLOGY IN *QIṬĀ'ĀTU NEQĀVE Fİ TERCEMETİ KELİMĀTİ BOERHĀVE* BY SUBHĪ-ZĀDE 'ABD AL-'AZİZ EFENDİ IN THE 18TH CENTURY

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Chief-Physician Subhī-zāde 'Abd al-'Aziz Efendi (1735-1783) translated the famous Dutch Physician Hermann Boerhaave's (1668-1738) aphorisms named as *Aphorismi de cognoscendis et curandis morbis in usum doctrinae domesticae digesti* into Turkish as *Qıṭā'ātu neqāve fī tercemeti kelimāti Boerhāve* (1769). It has been found important by the Turkish medical historians because this is one of the "first complete translations of European medicine" into Ottoman medicine. We aimed to determine and evaluate the topics related to nephrology in *Qıṭā'ātu neqāve fī tercemeti kelimāti Boerhāve*. In this study, manuscripts of this work registered in Süleymaniye Manuscripts Library, Esad Efendi Collection, nr. 2462 and Beyazıt State Library, Veliyüddin Efendi Collection, nr. 2484 were examined. First, the sections of the mentioned work regarding nephrological diseases were determined, and then Turkish texts written in Arabic letters were transliterated to the contemporary Turkish alphabet. *Boerhaave's Aphorisms: Concerning the Knowledge and Cure of Diseases* was used for comparison. The subjects related to nephrology in the work are examined under the headings of "kidney pain" and "urolithiasis". The section of "kidney pain" or "nephritis" consists of 14 aphorisms (993-1006), explaining the causes, signs and symptoms, and treatment of nephritis. "Urolithiasis" section contains 26 aphorisms (1414-1439), mentioning the causes, signs and symptoms, treatments and some interventional methods, such as lithotomy, of kidney and bladder stones. We may conclude that *Qıṭā'ātu neqāve fī tercemeti kelimāti Boerhāve* explaining the approach of European medicine to nephrological diseases has been transferred to the Ottoman medical literature, with a little delay. In this book, Latin medical terms such as nephritis, pelvis, ureter, and the surgical intervention called as lithotomy by Europeans are probably used for the first time in the Ottoman medical literature.

## 19. SHA'BĀN SHIFĀ'Ī OF AYASH AND HIS SUGGESTIONS ON NEPHROLOGICAL PROBLEMS IN CHILDREN

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The work named as *Tadbīr al-Mawlūd* (1701), written by Sha'bān Shifā'ī of Ayash (d.1705), is considered as the first book written extensively on child health and diseases in the Classical Period of Ottoman Medicine. In the present study, it has been aimed to determine and evaluate the topics related to nephrological problems in children.

For the study, the copy of manuscript *Tadbīr al-Mawlūd*, from his own handwriting of Sha'bān Shifā'ī of Ayash's found in İstanbul Süleymaniye Manuscript Library, Mihrīşah Sultan Collection, nr. 344 have been reviewed. Firstly, the nephrological sections of the document were determined, and then these Turkish texts written in Arabic letters were transliterated into the contemporary Turkish alphabet.

The subjects related to nephrology in the *Tadbīr al-Mawlūd* have been discussed under the main heading of "Diseases of kidneys and bladder", together with three subheadings; "Urinary tract stones in children", "Urinary retention in children" and "Bed-wetting". The causes and treatment options of kidney and bladder stones, urinary retention and voiding difficulties, and finally the causes and treatment of enuresis in children have been discussed. It has been noticed that Sha'bān Shifā'ī of Ayash benefited from the works of Ibn Sina and Ibn al-Nafis, valuable physicians in the Middle Ages. It is understood that the principles of humoral paradigm, which is an accepted medical understanding of that period, was valid in explaining the etiology of nephrological diseases and its treatment. These documents are important in terms of being the first written work about the approach to pediatric diseases and urological problems in children in the Ottoman period.

## **20. A BOTANICAL SCIENTIST IN THE 13TH CENTURY AND HIS SUGGESTIONS ON URINARY TRACT PROBLEMS; IBN AL-BAITAR**

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Ibn Al-Baitar was born in Malaga, Andalusia in the last quarter of the 12<sup>th</sup> century. He took botanical lessons in Andalusia and worked on plants until 20 year-old. He traveled to north Africa to increase his knowledge and experience between 1220-1223, and came to Anatolia in 1223. Later, he traveled to the northern Mediterranean coast and Greece islands and moved to Alexandria. He became the chief botanist and pharmacist of the Ayyubid sultanate in Egypt and made a lot of researches in botanics in the Middle East, and educated many students in Cairo and Damascus.

He collected many drugs, vegetables, animal products, and firstly introduced many plants and drugs to the medical world. He was recognized as the greatest botanical scientist and pharmacist of his time.

'Kitab Al-jami li-mufradat al-adwiya wa al-aghdiyya' is Ibn al-Baitar's best-known work, and accepted as the largest plant and drug book of the Middle Ages. It contains detailed description of several medicinal plants, foods, and drugs together with their therapeutic values. This book was used in Europe until the 19th century. In 1875, it has been published in Arabic language, and translated into Latin, German, and French languages.

Recently, it has been published in Turkish by the Department of Medical History and Ethics in Health Sciences University (2017), and its original copy is protected in Library of Hagia Sophia (written in 1573).

We searched the drugs effective on urinary tract (UT) in this book. Almost 175 drugs were effective on UT and 150 of them were herbals. In this study, we will summarise Ibn Al Baitar's suggestions on UT problems.



## 21. MISCONCEPTIONS IN HYPERTENSION - PATHOGENESIS AND TREATMENT

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Our cells live in an extracellular salty environment, which is maintained stable by the functions of the circulatory system and the kidneys. The Egyptian physician Imhotep (3000 B.C.) observed that the pulse is the index of the heart. Chinese records (2600 B.C.) hold mention of a hard pulse in individuals consuming large quantities of salt. The ancient physician Galen first proposed the existence of blood in human body and William Harvey in 17c AD presented convincing proof of the circulatory system. Blood pressure (BP) was first measured in a horse in 1733, when Reverent Stephen Hales inserted a glass tube into an artery. In 1828 Poiseulle devised the mercury manometer and in 1897 Riva Rocci designed the first clinically acceptable sphygmomanometer. Korotkoff heard the sounds made by the constriction of the brachial artery in 1905, a method that has been widely used until today. In the 1960s, the first ambulatory blood pressure recording devices were developed. These have since been improved, and allowed the recognition of masked and white-coat hypertension, the determination of patient as «dipper» or «non-dipper» and the better assessment of the response to treatment.

Over the past century elegant experiments have proved that the kidney is the principle organ ultimately regulating blood pressure levels, and transplantation experiments showed that “hypertension travels along with the kidney”. In 1934 Goldblatt developed clamps for constriction of renal arteries in dogs and observed a temporary elevation of blood pressure, which returned to normal when the clamp was removed. In the 1950s Guyton became most famous for his experiments regarding renal-pressure natriuresis and long-term BP regulation by the kidney. In 1970’s Dr. Laragh demonstrated the central role of an overactive renin angiotensin system for causing most hypertension. Following discovery of molecular biology many genetic studies identified certain gene regions linked with BP control.

For centuries hypertension and apoplexy have been treated by leeching, phlebotomy and acupuncture. The discoveries that revolutionized modern therapy of BP have included: the use of the first thiazide diuretic (1958); the discovery of propranolol (1964) and nifedipine (1972); the development of captopril by Gushman and Ondetti (1975); the approval of losartan in 1995; and the approval of the direct renin antagonist aliskiren (2007). Single pill combinations of two or three drugs are generally recommended by current guidelines to improve compliance and reduce cost.

Over the past 50 years various misconceptions regarding the threshold of hypertension and the goal of treatment have been clarified by randomized trials. These misconceptions have included:

1. Hypertension cannot be prevented. Modifications in life style that have been proven capable to prevent or delay hypertension, included weight reduction by a combination of healthy eating and regular exercise, reduction of fat, sugar, and salt intake, moderate alcohol consumption and smoke cessation.
2. The common variety of hypertension, the so called essential hypertension is a benign condition and should not be treated. Since 1967 when the first randomized VA study was released it became obvious that antihypertensive treatment effectively reduce cardiovascular complications and death.
3. There is no benefit in treating mild hypertension in younger individuals. In 1985, MRC trial of treatment of mild hypertension in 17,354 men and women 35-64 years old, randomized to bendrofluzide or propranolol vs placebo showed reduction in stroke, but not in coronary events or mortality from all cause.
4. There is no benefit in treating elderly patients with isolated systolic hypertension. In 1991 the SHEP Program included 4736 patients >60 years with systolic BP >160 mmHg, diastolic BP <90 mmHg randomized to active treatment vs placebo. After an average follow-up of 4.5 years active treatment decreased the risk for stroke by 36%, for MI by 23%, for CVD by 22% and for deaths from all cause by 13%.
5. In diabetic patients is more important to lower blood sugar than treating hypertension. In 1998 UKPDS, a randomized study in DMT2 patients concluded that tight blood pressure control offered very significant benefits in various categories much more so than tight blood sugar control. It reduced microvascular complications by 24%, deaths related to diabetes by 32% and strokes by 44%.
6. There is no benefit in treating very elderly patients. In 2008 HYVET, a randomized placebo control trial, in patients > 80 years with systolic blood pressure > 160 mmHg on indapamide with or without perindopril (n=1933) vs placebo (n=1912) showed a 30% reduction in stroke, 39% reduction in death from stroke and 21% reduction in death from any causes, 23% reduction in the rate of death from cardiovascular causes and 64% reduction in the rate of heart failure.

7. By lowering thresholds to define hypertension than previous guidelines, the prevalence of patients with hypertension is expected to significantly increase, but the clinical benefit will be insignificant. In 2018 Vaduganathan et al. found that patients with hypertension based on prior guidelines compared with those newly identified with hypertension based on the new guidelines had similar risk of the primary endpoint, and therefore, the lower thresholds can identify greater numbers of patients who will ultimately experience adverse cardiovascular events and deserve aggressive treatment.
8. The SGLT2 inhibitors that block the reabsorption of glucose and sodium in the proximal tubules of the kidney and enhance their urinary excretion may reduce arterial blood pressure and lower the blood glucose levels, but on the other hand could damage the kidney due to chronic glycosuria. Recent randomized trials and meta analysis showed favorable effects of SGLT2 inhibition in diabetic patients, such as restoration of tubuloglomerular feedback and reduction of the intraglomerular pressure and hyperfiltration, reduction of albuminuria and proteinuria and cardioprotection and renoprotection on top of RAS inhibition.

In conclusion, major breakthrough trials in hypertension over the twentieth century have helped to resolve many misconceptions and permitted a more successful treatment of hypertension.

## **22. VITAMINS DISCOVERY AND CHRONIC KIDNEY DISEASE - CASIMIR FUNK STORY**

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Wide discrepancies exist in the use of vitamins in kidney disease, and evidence-based recommendations are sparse. Water-soluble vitamin levels may be inadequate in patients not receiving supplements and this may be associated with increased mortality, which deserves further attention to increase strength of evidence. Supplements should be administered cautiously as renal mechanisms to prevent hypervitaminosis are no longer functional. In dialyzed patients importance of supplementation vitamins rises many questions. Research on the vitamins that are related to major deficiency syndromes began when the germ theory of disease was dominant and dogma held that only four nutritional factors were essential. Clinicians soon recognized scurvy, beriberi, rickets, pellagra, and xerophthalmia as specific vitamin deficiencies, rather than diseases due to infections or toxins. Everything would not be possible without previous achievements. The discovery of the vitamins was a major scientific achievement in our understanding of health and disease. One among other scientists who worked in this area was Casimir Funk, a biochemist born in Poland but trained in several European countries. He moved to London in 1910. In the following year, he reported that he had isolated the active factor, pyrimidine-related concentrate from rice polishings that was curative for polyneuritis in pigeons. He then went on to suggest that this material belonged to the chemical class of "amines", therefore he coined the term "vitamine" for these "vital amines." When it was realized a few years later that others in the class were not "amines," but a word was still needed, it was shortened to "vitamin". The vitamins Casimir discovered are now called B1 (thiamine), B2 (riboflavin), C (ascorbic acid) and D (cholecalciferol). He died in 1967 in the USA.



## **23. HISTORY OF PAROXYSMAL NOCTURNAL HEMOGLOBINURIA: FROM THE ORIGINS TO THE FUTURE DIRECTION OF THE COMPLEMENT INHIBITION THERAPY**

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Paroxysmal nocturnal hemoglobinuria (PNH) is a rare hematological disorder that affects about 1 to 5 cases per million individuals, characterized by hemolysis, peripheral blood cytopenias, bone marrow dysfunction, and thrombosis.

The origin of PNH is the mutation of the phosphatidylinositol glycan class A (PIG-A) gene. This condition leads to a deficiency of surface proteins that protect the cells against damage caused by the complement system.

The first case of PNH was probably described in 1793 by Dr Charles Stewart, in the medical commentaries "Account of a singular periodical discharge of blood from the urethra". In the next decades several cases have been reported by the most eminent physicians and scientists of the time. Dressier, in 1854, published a report of an "Intermittent Albuminuria and Chromaturia", describing urine contained brown amorphous pigments without blood corpuscles.

The first detailed account has been described only in 1866, when Sir William Gull reported a case of a young "anemic looking" tanner with several episodes of dark urine, calling this condition "intermittent hematuria". In 1882 Strübing identified paroxysmal nocturnal hemoglobinuria as a disease entity, indicating that these patients could have an intravascular hemolysis with a defect of red blood cells.

Hijmans van den Bergh in 1911 confirmed that the hemolytic process was due to a defective red cell and related to complement dysregulation. The same year, the Italian scientist Ettore Marchiafava scrupulously described the pathogenesis of the affection and several year later further elaborations has been performed by Ferdinando Micheli: thanks to their contributions this disease has been also named Marchiafava-Micheli Syndrome. In the 1925 Enneking coined the name "paroxysmal nocturnal hemoglobinuria", which has since become the universally approved definition. In 1938 Thomas Hale Ham and John Vivian Dacie found more evidence about the connection between the lysis of blood cells and the complement activation.

Despite the increased knowledge of this syndrome, therapies for PNH were still only experimental and symptomatic, with the use of antimicrobial agents, corticosteroids and blood transfusions.

The natural history of PNH changed drastically only in the 2007 with the introduction of Eculizumab complement blockade agent. It is a monoclonal antibody complement inhibitor, actually the only licensed therapy for PNH. The development of second generation of terminal complement inhibitors, with the potential use of their progenitor, the Ravulizumab, represents a promising instrument for the future approaches against PNH.

## 24. ERYTHROPOIETIN, FIRST INTUITION OF RENAL SECRETION

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The paper aims to highlight an underestimated intuition of Giustiniano Nicolucci on a possible respiratory function of the kidneys, which anticipates of more than hundred years the actual extraction of the erythropoietin molecule from the urine of a patient with aplastic anemia made by Takaji Miyake in 1977.

In 1846 a young Nicolucci published in the Neapolitan periodical *Filiatre Sebezio* an article titled «Sull'Intima struttura dei reni con alcune considerazioni sulla loro funzioni e malattie». He assumes that the aforementioned respiratory function of the kidneys can be accomplished through the formation and multiplication of red blood cells, as recently observed in the liver of a human embryo by Koelliker. The paper compares Nicolucci's intuition with contemporary knowledges, particularly with the observations by Jacobson (1821) on the renal portal system in fishes, birds and reptiles, and the abovementioned research by Koelliker. Nicolucci had not found in the human kidney the anatomical formation of a so-called "portal vein", existing in fishes, birds and reptiles.

Because of this reason, he stated that in mammals the respiratory function should also have occurred through humoral action, which could not be limited to the multiplication and growth of red blood cells, but it should also have affected the formation of new vessels.

Only about 50 years after this Nicolucci' hypothesis, it was noticed that the bone marrow was capable of producing a greater quantity of red blood cells. The existence of a hormone able to regulate the production of erythrocytes by the bone marrow was hypothesized in 1906 by Paul Carnot and his assistant Camille Deflandre. The substance was called haemopoietin.

In the forties of the twentieth century, Bonsdorff and Jalavisto gave this substance the name of erythropoietin. A few years later, Kurt Reismann showed that the kidney was the main production site of this substance, but only in 1977 was Takaji Miyake able to extract the molecule from the urine of a patient.



## 25. ANOTHER CASE OF ORGAN BLINDNESS IN THE HISTORY OF COMBINED EYE AND KIDNEY DISORDERS: PSEUDOSCLEROSIS OR WILSON'S DISEASE

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Wilson's disease, or hepatolenticular degeneration, is a rare, genetic disorder of copper metabolism. The disease leads to the accumulation of copper into the brain, the liver, the eyes, and the kidney. The dominant triad of the syndrome is nodular liver cirrhosis, Kayser - Fleischer ring in the corneas, lesions of the cortex and basal ganglia. In addition, a defect in proximal tubule reabsorption has been noted. The syndrome involving the basal ganglia degeneration and the liver damage has been named after Samuel Alexander Kinnier Wilson (1878-1937). The syndrome was initially a pure brain disease described by Frerichs in 1861, in a 9-year old boy with invasive neurological symptoms and cirrhosis at autopsy. In 1883 Carl Westphal in Germany described two cases with neurological aspects similar to the "multiple sclerosis", but without white matter degeneration at autopsy; he named the disease as "pseudosclerosis", without noticing the liver involvement. Adolph Strümpell in Germany in 1898 described other cases of Westphal's pseudosclerosis, and in one case also the presence of liver cirrhosis. These and other reports led finally Wilson in the UK to propose the existence of the new clinical entity with degeneration of the brain lenticular nucleus and of the liver in 1912. Only later the "pseudosclerosis" and "Wilson's disease" were found to be the same disease. In 1913 Rumpel introduced the study of copper in the liver in a case of pseudosclerosis, which was confirmed by Malory in 1925; copper accumulation in the kidney was described by Wintrobe in 1954. The renal dysfunction included the discovery of aminoaciduria, glycosuria, increased urate excretion reduced renal plasma flow (RPF) and glomerular filtration rate (GFR), and specific histological lesions. Stein et al and Bickel et al characterized aminoaciduria and found a loss of glycine, histidine, threonine, cysteine, serine, alanine, glutamine, tyrosine, lysine, glutamic acid, leucine, phenylalanine. Their findings definitely excluded that Wilson's syndrome was an inborn error of metabolism. A complete physiological study of the kidney was then presented in 1957 by Bearn and Gutman, who confirmed the reduced RPF and reduced GFR, and reduced secretory and reabsorptive tubular function. The ocular findings in Wilson's disease have been identified in 1902 by Bernhard Kayser and Bruno Fleischer in Germany who first described the typical ring in the cornea that still brings their names. In conclusion, the history of renal and eye involvement in Wilson's disease appears as another case of organ blindness that is the attention of predominant symptom leads to neglecting involvement of other organs in multisystemic diseases. The sequence of discoveries and hypotheses reflects the technical advancement of each specific historical period.



## **26. URINE COLOR VARIATION IN INTERNAL DISEASES ACCORDING TO ENRICO CAUCHI**

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In the ancient times urine was considered an important element not only for religious tradition but also for diagnostic procedures. Pithagoras and Hippocrates were the first to show the variation of urine color in gonorrhea and tuberculosis. Over time several researchers reported on how urine variation may help diagnosis different diseases. Enrico Cauchi, member of the Medical Council of Malta, in 1933 collected all comprehensively organized info in his book "Fisiologia e Patologia dell'urina" edited by A. Wasserman, Milano, Italy. Enrico Cauchi following the suggestions of "Urological Curves" by Augusto Murri reported all the variable evidences at that time about urine color variation. Moritz and Weisz reported gold yellow and canary yellow color of urine were typical of tuberculosis whereas Comas and Martinez observed urine precipitate of blue and green color. Greenish and orange yellow or intense green urine were reported in abdominal typhus by Russo and Wiener whereas Petzetakis and De Silvestri reported gold yellow and brown urine color. Cammidge showed urine containing needles like crystal in golden yellow color that was dissolved with a 33 % sulfuric acid solution in pancreas diseases. Brown color urine of barium sulfate precipitate and light yellow brownish color in malignant tumor were reported by Davis. Ehrlich reported urine variation color from pink to red in heart diseases and Bruno observed blue and ruby red urine color in appendicitis. Aradas reported green color of urine in flu and Jefnoso observed grey and black color of urine in worms disease. Roch observed violet cloud in urine during liver diseases. Russo reported light green color of urine in smallpox. Becker evidenced urine color variations in kidney diseases. The previously knowledges were considered before 1931 by various medical doctors who used the urine color examination in their daily clinical activity.

## **27. KNOWLEDGE ON KIDNEY DISEASES DURING AMERICAN CIVIL WAR**

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American Civil War changed many aspects of life in America including understanding of the diseases. This presentation will critically examine the definition, understanding, and management of kidney diseases during the period of the War (1861-1865). Data are extracted from "Medical and Surgical History of the War of Rebellion" (MSHWR) published between 1870-1888. This treatise represents one of the most extensive data collection efforts in the history of wartime medicine. MSHWR contains approximately 3000 pages, comprise of medical (vol I, part I-III) and surgical (vol II, part I-III) aspects of the Civil War. Part II of the medical volume provides statistics of the medical reports, detailed case studies and discussion of symptoms of diseases and therapy. Interesting data on Bright's disease are presented. This disease was diagnosed during the 5 years of the War in 1403 White soldiers with 114 deaths. Average strengths of the White troops per year was 437, 237 soldiers giving the incidence of Bright's disease 0.07% per year. Between Colored troops, Bright's disease was diagnosed in 404 soldiers with 68 deaths. Average strengths of the Colored troops per year were 60,854 soldiers giving incidence of the disease 0.22% per year. These data are suggesting three times higher incidence of Bright's disease in Colored troops than in White troops. There was no difference in incidence of diabetes between White or Colored troops. Thirteen cases of kidney diseases are presented in MSHWR and discussed in details. No kidney biopsy findings were reported. Whole chapter (12 pages) in part II, vol. II is devoted to wounds of the kidney and suprarenal capsules. Many basic lithographs of injured kidneys accompany the text.

Data on other diagnosis pertinent to kidney and urinary organs are also presented and discussed. Many cases of acute kidney dysfunction were observed in soldiers with typhoid fever. The understanding of the kidney diseases presented by MSHWR where in line with good academic knowledge of the 1860thies. In many aspects, such as data collection and statistical presentation MSHWR brought innovation and progress in the field of nephrology.



# XI IAHN CONGRESS

## **28. THE ROLE OF THE MICROSCOPE IN RENAL DISEASE AS DESCRIBED BY GIULIO BIZZAZERO: HANDBOOK OF CLINICAL MICROSCOPY - 1879**

**Bellinghieri Guido<sup>1</sup>, Gembillo Guido<sup>1</sup>, Antonino Salvo<sup>1</sup>, Domenico Santoro<sup>1</sup>, Vincenzo Savica<sup>2</sup>**

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Giulio Bizzazero (20 March 1846 - 8 April 1901) was an eminent Italian pathologist, who first described the platelets as the third morphological element of the blood and identified their role in the coagulation. Among his original discoveries there are the hematopoietic function of the bone marrow, the studies on the phagocytosis, the histological structure of the epidermis, and many others important findings. Since the beginning he has been extremely productive and for his valuable research works, at the age of 26, Giulio Bizzazero was appointed full Professor of General Pathology at the University of Turin, Italy. Here he emphasized the use of microscopy against the outdated vision of old academics and promulgated the experimental methods, in competition with the vitalistic philosophy of the time. Bizzazero's revolutionary vision of medicine had the purpose to permit every scientist to reach new discoveries in their field, previously the privilege of elite, being a model of a doctor as a humanist.

The advancement of his studies and the development of the art of microscopy led to the publishing of his masterpiece in 1879 "Manuale di Microscopia Clinica" (Handbook of Clinical Microscopy). Here he underlined how the microscopic examination of the urine gave to the physicians of the time indicative criteria of alteration of the kidney, often essential for diagnosis. The author operated a detailed analysis of the methods of the time, laying the foundations for modern microscopy. During his career, he was also elected president of many medical societies and member of several public health commissions.

The contribution of this esteemed scientist has been significant in both the growing of knowledge in scientific community and in promoting public understanding of the benefits of medicine.

## **29. NEPHRO-UROLOGY IN GREEK-ROMAN MEDICINE. AN UNPARALLELED INSTRUMENT FROM THE LISBON NATIONAL MUSEUM OF ARCHAEOLOGY**

**Barroso Maria do Sameiro**

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Galen of Pergamon (130-210 A.D.) correctly summed up the knowledge on the anatomy and physiology of the urinary tract from the Hippocratic physicians (fifth-fourth century B.C.) until his time, reviewing the clinical symptoms and nephrology and urology conditions and treatment. Caius Cornelius Celsus (25 B.C.-50 A.D.), in his work "On Medicine", described a large number of surgical operations performed in Western medicine for the first time. Surgical management of urinary obstruction and bladder stone lithotomy is amongst them, featured as the last attempt when medical treatments failed. The existence of instruments specifically devised for the procedure, such as special knives, hooks and hollow S-shaped catheters, adapted to men's urethra, is documented since Erasistratus (304-250 B.C.). Celsus advises an ear scoop to remove stones. A long thin solid tube of copper alloy, ending in a small scoop, was found in a rectangular salting basin (saltery 22) from the fish salting factory of Tróia, a Roman archaeological site in the Peninsula of Setúbal, near Lisbon. This paper presents the finding in its archaeological context and discusses its similarity with the published catheters of Roman time.

Keywords: Roman surgical instruments; bladder stones; History of Nephrology; History of Urology

### **Short CV**

Maria do Sameiro Barroso is Medicine Doctor, Family Medicine Specialist, poet, translator, essayist, and medical historian. She is Director of the Department of History of Medicine of the Portuguese Medical Association, invited lecturer of History of Medicine at the Faculty of Medicine, University of Lisbon, researcher of the Centre for History, Faculty of Letters, University of Lisbon and of the CIAS (Research Centre for Anthropology and Health), Faculty of Science, University of Coimbra. She was Vice-President of the 46<sup>th</sup> ISHM Congress.



# POSTER PRESENTATIONS



# XI IAHN CONGRESS

## 01. HISTORY OF NEPHROLOGY IN ARAB WORLD

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Nephrology was first recognized as a specialty in 1960, hemodialysis (HD) used in clinical ground in 1960- 1965 and peritoneal dialysis (PD) in 1978. Egypt started dialysis in 1958 with first of dialysis department in 1979, currently approaching 61 thousands hemodialysis patients. Algeria performed PD, HD for acute cases in 1962, 1971 respectively. In Sudan there are 60 dialysis centers treating 6000 patients out of them 122 are on PD. First hemodialysis in Iraq was in 1964. Morocco started HD in 1978. Saudi Arabia entered HD field in 1972 and currently there are 184 dialysis units, while PD started on 1980. Yemen dialysis began on 1980. Syria national dialysis program was working in 1986. Tunisia used PD for acute cases in 1962 with first artificial kidney in 1963, nowadays there are 13dialysis units. Jordan performed first dialysis in 1968; today there are 84 HD centers. United Arab Emirates initiated PD in 1976 and HD in 1977. First two dialysis units in Libya were 1971, 1979. Lebanon used PD for acute cases in late fifties and in 1994 started PD; currently there are 61 HD centers. Nephrology service started in Oman in 1981 and first PD patient was treated on 1983. Dialysis started in Kuwait in 1976 and currently there are 9 centers. Qatar introduced PD in 1976 and HD in 1981. Lastly Bahrain started HD in 1972. At the end highlighting this history shaded the light on Arab experiences aiming for achievement in future.

## 02. CROSS DONOR CIRCULATION – REVISITING AN OLD TECHNIQUE FOR INNOVATION POTENTIAL IN TRANSPLANTATION

Duni Anila<sup>1,2</sup>, Harrisis Haris<sup>2</sup>, Rapsomanikis Karolos<sup>1</sup>, Pappas Charalampos<sup>1,2</sup>, Mitsis Michalis<sup>2</sup>, Dounousi Evangelia<sup>1,2</sup>

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**Introduction:** Historically, the term 'cross-circulation' or 'donor circulation' refers to the perfusion of one individual by another. Subsequently when organs of one of the individuals in reciprocal blood transfer are not working efficiently, their functions can be taken over by the other individual through connection of circulations. The methods applied for reciprocal blood transfer are, *parabiosis* which requires the union of the two individuals by a tissue bridge, *cross circulation* which implies blood transfer between the individuals by using the arteries and *cross transfusion* where the venous side of the circulation is used as a source of blood. According to past medical cases reported in the literature, the application of cross-circulation was easy to apply, safe from a mechanical point of view and effective, causing relatively minor side effects in the donor.

**Methods:** A comprehensive search of the literature for related publications to cross donor circulation was performed, with first reports dating back to 1926.

**Results:** One of the principal fields where this technique was applied is cardiovascular surgery, as an inexpensive mean of instituting cardiopulmonary bypass in humans. As an alternative to kidney transplantation in conditions of renal failure. There have been studies conducted in animal models utilizing the kidneys of healthy animals such as rabbits as hemoperfusion units for other uremic animals. The procedure of homohemodialysis involves the circulation of anticoagulated blood from the uremic animal to the normal one and then back to the uremic animal through the femoral vessels using a tube system. Other fields of application were, extracorporeal liver perfusions bridging patients with fulminant liver failure to recovery or transplantation and extracorporeal utilization of xenospleens as means of detoxification in sepsis or burns.

**Conclusion:** In the setting of specific clinical indications it might be proper to restore our attention to this old therapeutic modality in order to readjust its applications in challenging clinical scenarios of modern medicine such as renal transplantation.

### **03. HYPOXIA - INDUCIBLE FACTOR STABILIZERS FOR ANEMIA OF CHRONIC KIDNEY DISEASE: A NEW CLASS OF DRUGS WITH ALMOST ONE CENTURY OF HISTORY**

**Eleftheriadis Theodoros, Pissas Georgios, Nikolaou Eudokia, Filippidis Georgios, Golfopoulos Spyridon, Zafirouli Vassiliki, Sarianni Aristeia Ioanna, Stefanidis Ioannis**

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Hypoxia-inducible factor (HIF) stabilizers are a new class of drugs, which are tested in phase III clinical trials for the treatment of anemia of chronic kidney disease (CKD). HIF stabilizers prevent HIF1 $\alpha$  and HIF2 $\alpha$  degradation increasing the transcription of erythropoietin encoding gene. However, another compound, the cobalt chloride (CoCl<sub>2</sub>), was used in the past, before the discovery of HIF, for treating anemia of CKD. Cobalt increases erythropoietin production by stabilizing HIF.

We searched the literature, mainly but not exclusively the PubMed database, to find out the origins of CoCl<sub>2</sub> use for the treatment of anemia of CKD and the reasons that led to its abandonment.

It was 1929 when Klara and Karl Waltner showed that cobalt administration induces polycythemia in rats. Thereafter, studies confirmed the above in other species. Clinical trials on the use of cobalt as an anti-anemic agent were performed from the late 1940s to the late 1970s. Usually, cobalt was administered as tablets of CoCl<sub>2</sub> at daily doses 25-300 mg. Gardner published in 1953 the first clinical study showing that CoCl<sub>2</sub> stimulates erythropoiesis in CKD patients within one month. From 1953 to 1978, seven more clinical studies confirmed the efficacy of CoCl<sub>2</sub> in the treatment of anemia of CKD. However, in one study published in 1976, a patient died due to cardiomyopathy, and myocardial cobalt was found to be 25-80 times higher than in the control samples. Accumulated evidence showed that cobalt might induce gastrointestinal upset, reversible hypothyroidism, cardiomyopathy, reversible hearing loss, and optic nerve atrophy. As a consequence, CoCl<sub>2</sub> for the treatment of anemia of CKD was abandoned.

The above data indicate that in the past, empirical observations led to trials with compounds that act in ways similar to those currently investigated for the discovery of modern drugs. The safety of the new HIF stabilizers remains to be confirmed.

### **04. THE PAST AND THE FUTURE HISTORY OF NEPHROLOGY. FROM KIDNEY ORGAN TO KIDNEY ORGANOID.**

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Medical science was always in accordance with philosophical aspects of its era. Initially the astonished “newborn” man was standing in front of unexplained nature miracles dividing and giving them a “magical/theological” background (polytheism). Gradually as philosophy started to emerge it became faintly seen that logic and reason could explain the former unexplained issues and the labor of science began. Science (including medicine) started to cancel, explain and unify many of the former theological models searching the beginning of all in order to answer the fundamental arising question/statement: Which is the origin of everything? The one is the origin of everything (monotheism). Today as many of principal questions concerning human nature have been answered there is the same trend to unify knowledge under the one the origin of all: the human pluripotent stem cell (hPSCs).

Recognition of the importance of the kidney itself is a relatively recent event, and ancient depictions of this organ are scarce. Now days due to increasing incidence of chronic kidney disease (CKD) and augmented demand for renal replacement therapy, new therapeutic options are urgently needed. Growing clusters of kidney cells in the lab (regenerative medicine), is a potentially attractive therapeutic option for CKD. One day, so-called kidney organoids – grown from human stem cells – may help repair damaged kidneys, test drugs, model genetic kidney disease, act as a source of specific kidney cell types and generate functional bioengineered kidney tissues.

Despite the many obstacles to overcome for their clinical use (safety and rogue cells) kidney organoids appear to have great potential and may be a promising therapeutic option. Maybe in the future the statement “prevent and cure” the disease in vivo will be replaced by a modern one “model and cure the disease in vitro”. But for such promising future there is a need of strongly justified present and past. As this challenging future is still under birth the past and present history of Nephrology remaining the definitive one for its progress.



# XI IAHN CONGRESS

## **05. THE SELDINGER PROCEDURE - THE METHOD OF VASCULAR ACCESS IN ALL CLINICAL SETTINGS, INCLUDING NEPHROLOGY**

**Kurkus Jan**

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Sven-Ivar Seldinger (1921-1998) came from the small town of Mora, north of Stockholm, Sweden. He completed his medical studies at the Karolinska Institute in Stockholm, and started his career at the Radiology Department of Karolinska Hospital in 1950. He was especially interested in angiography. Several members of Seldinger's family worked in watch-making and fine mechanics, which certainly influenced his interest in medical technology. At that time, the intravascular administration of contrast media involved catheterization of the vessel after surgical incision of the skin/vessel or the introduction of a small polyethylene catheter via the lumen of a needle, or direct puncture of the vessel with the needle. In many cases, the contrast medium could not be injected sufficiently rapidly, and complications were common. In April 1952, Seldinger had "an attack of common sense". He realized that the sequence in the procedure of catheter introduction to the vessel should be: needle in – guide-wire in – needle out – catheter in over the guide-wire – guide-wire out. His brainwave instantly revolutionized the procedure (*Acta Radiol.* 1953;39:368-376). The Seldinger procedure became widely used in interventional radiology in Scandinavia, and gradually spread to other clinical settings worldwide.

Vascular access had been the "Achilles heel" of hemodialysis treatment since its introduction in the 1940s, and the need for dialysis was continuously increasing. The employment of the Quinton–Scribner shunt in 1960 (and later the Cimino–Brescia arteriovenous fistula in 1966) was the most important steps in improvement of hemodialysis treatment but still the method of vascular access for acute need of therapy or investigation was missing. The Seldinger procedure solved this problem and was unrivaled due to its simplicity, rapidity, and low risk of complication. Stanley Shaldon introduced this procedure in dialysis in 1961 (*Lancet* ii, 857-859). Since then, it has been used for all extracorporeal procedures in dialysis department when no other vascular access is attainable. Seldinger applied this procedure also for catheterization of the renal artery (1955) and selective renal angiography (1964), and many other pioneering interventions. He returned to Mora in 1966 and worked at the local hospital until his retirement in 1986.

## **06. ELECTRONIC HEALTH SERVICES IN END-STAGE RENAL DISEASE: TRANSITION FROM THE TRADITIONAL WAY OF ARCHIVING TO ONLINE HEALTH APPLICATIONS. THE GREEK EXPERIENCE**

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Chronic kidney disease is a serious public health issue. According to international data, one out of ten individuals suffers from some degree of chronic kidney injury. Unfortunately, there is no official data in Greece, which is particularly worrying. It is, therefore of paramount importance to move from the traditional way of archiving to the use of electronic health records and online applications.

According to data, in 2016, 24.7% patients in Greece were undergoing hemodialysis via a tunneled central venous catheter. However, there is lack of important information such as who placed the catheter, the catheter's tip location, its lifetime, its complications, or the morbidity and mortality rates of these patients. This results in a lack of public health strategy regarding this sensitive group of patients.

The Nephrology Department in our hospital in collaboration with the Information Technologies Institute of Center for Research and Technology-Hellas and with the support of Hellenic Society of Nephrology, developed the first national online application of patients dialyzed via a tunneled central venous catheter. In December 2018 the application was made known and available to all dialysis units in order for them to register their data and at the same time to collect all necessary information for the management of the disease.

This will benefit the doctors, the patients and the national health care system. The application provides (promote) an electronic collaborative environment with direct exchange of information among physicians, interconnection with patients and ultimately more efficient management of the health system resources.

In conclusion, in chronic kidney disease, the focus should be placed on electronic health actions and information systems while at the same time personalizing the health services provided and the patients should be actively involved in the management of their disease through the electronic health network.



# XI IAHN CONGRESS

## 07. HISTORICAL MISCONCEPTIONS IN PERITONEAL DIALYSIS

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We aimed to address certain misconceptions that occurred in the history of Peritoneal Dialysis (PD) and their understanding changed the course of the method.

When PD was firstly presented as a therapeutic alternative for end-stage renal disease (ESRD), it was prescribed as intermittent (IPD) intensive 48h sessions with catheter removal and reinsertion. In 1959, the New England Journal of Medicine rejected the paper by Ruben et al., who successfully treated a young ESRD woman without removing the catheter.

In 1975, the American Society for Artificial Internal Organs (ASAIO) rejected an abstract by Popovich and Moncrief describing the continuous ambulatory peritoneal dialysis (CAPD) method. Later, in 1978, their results were published in the Annals of Internal Medicine.

In 1980, Buoncristiani et al., proposed the Y-set technique reducing peritonitis rate from one episode every 12 to one every 36 months. However, it took 5 years for PD centers in Canada and USA to adopt this development, because the results were suspected not to be true.

In 1996, the results published by the randomized, multicenter CANUSA (Canada-USA Peritoneal Dialysis Study Group) study, supported a close association between the level of peritoneal clearance and survival in CAPD patients. However, in 2001, in a re-evaluation of the CANUSA study, Bargman et al. showed that the favorable results in those patients were mainly due to their residual renal function (RRF).

Contrary to what expected, the large prospective ADEMEX (Adequacy of Peritoneal Dialysis in Mexico) study showed that increased dose of peritoneal small molecule clearance delivered by PD was not associated with patient survival or better quality of life.

In the short history of PD, there were several breakthroughs that changed the application and future of the method, highlighting that medical knowledge is continuously evolving.

## 08. THE HISTORY OF HEMODIALYSIS IN TURKEY

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Our first encounter with the concept of hemodialysis was based on the fact when a plane crashed at Ankara Ulus Square in 1963. The lack of dialysis was then understood and the term “acute renal failure” first appeared on the agenda. There was not yet a chapter in Nephrology and kidney diseases were treated within Internal Medicine. Media paid a great deal of attention to dialysis due to the accident and The World Health Organization donated three hemodialysis (HD) machines for the treatment of those who were injured in the accident.

Research shows that at the end of year 1961, a tank type HD machine was imported and first used in the treatment of a patient in Ankara University Faculty of Medicine in June 1962. There were no places, no professional staff allocated to conduct applications of dialysis at that time. Later applications in Turkey were made in Istanbul University Cerrahpaşa Faculty of Medicine (1965), Faculty of Çapa (1969), Faculty of Gülhane (1972), Hacettepe University Faculty of Medicine Pediatrics (1974), Atatürk University, where I myself established, and Uludağ University (1975).

Today, there are about 882 HD centers in Turkey two-thirds of which are private and one-third are public. The fees of these patients are covered by the government and no extra payment is required. These centers are spread all over Turkey and there is no patient who has died due to lack of HD treatment. Patients are taken from and to their homes free and meals are provided by HD centers.

Procedures and regulations related to HD are thoroughly arranged. All centers are supervised twice a year regularly. A certificate program has been implemented since 2000 and authorized staff has been trained and given their certificates for a period of five years.

Recent data reveals that the number of patients in Turkey is about 63,349 and that of devices is 17,322. The rate of annual mortality is 15%. The number of patients who are applied home HD has exceeded 500, which rates Turkey the third in Europe.



## 09. HISTORY OF PERITONEAL DIALYSIS IN TURKEY

San Ayla

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Wegner published his first experimental studies on peritoneal lavage in 1877. George Ganter practiced live peritoneal dialysis (PD) in 1923. The same year Trac Putnam presented PD and dialysis membrane studies on animals. The first stimulus in the treatment of patients with uremia was by Kolff in Holland in 1940 with his artificial kidney application. F.Seligman and Fine put PD into practice in 1946 with peritoneal irrigation.

K. Önen first practiced PD with C. Öker in Istanbul in the early 1950s applying catheter and irrigating with a solution similar to ringer solution. In 1965 Ü. Ülkü and his research team started using PD which is used today.

Acute PD practices were done by N. Koçak in Istanbul University in 1964. In 1965-1966 first domestic commercial PD solutions were produced. Bottle dialysis and Intermittent PD practices started in 1968-1970. Since 1979 it has been used by the patients themselves. The use of modern Continuous Ambulatory PD (CAPD) with imported bags in several university centers was a successful practice in Ankara. CAPD practice started in Ankara University in 1985 with the use of Braun plastic vacuum bags, Tenckhoff type of silastic permanent catheters and intermediate sets in the modern sense.

CAPD was applied to 33 patients with chronic renal failure between 1985 and 1986. The results of the study were sent to the "4<sup>th</sup> Renal Diseases and Transplantation Congress" Hacettepe University, Ankara, in 1987. This study was then published in Ankara Bulletin of Medicine, being the first article on CAPD.

Automatic Peritoneal Dialysis (APD) practices were started by S.Bozfakioğlu in Istanbul University in 1994.

Domestic CAPD bags were produced in Turkey in 1995.

Turkish multicenter peritoneal dialysis study group (TULIP), the introduction of nationwide standards and regulations for the clinical use of peritoneal dialysis had a significant role (1998).

The number of PD including pediatric cases in Turkey is 3346 according to the data of 2017 from Ministry of Health and Association of Turkish Nephrology. The rate of PD patients according to gender was 45% in women and 55% in men.

## 10. SAINT HIEROMARTYR THERAPON BISHOP OF ANCIENT KITON, CYPRUS: HEALER OF KIDNEY PAINS

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Hieromartyr Therapon Bishop of ancient Kition, Cyprus (3-4<sup>th</sup> century AD), was born in the East and lived ascetical life. Later he moved to the island of Cyprus, where he served as a Bishop. He died a martyr's death, probably during the persecution under Diocletian (284-305AD).

The saint's relics, initially kept in Cyprus, were transferred to Constantinople, in order to be preserved from the second Arab invasion (653AD). They were placed in a temple in honor of the Icon of Maria "Eleousa" translated "the Merciful". In 806AD the saint's relics were transferred again into a temple built in his honor. During the relics' transfer myrrh flowed and miracles took place.

From that time and up to date people believe, that the seriously ill are healed through Saint Therapon's prayers. He is considered the protector saint of children suffering from fever and the healer of kidney pains. Miraculous healing of kidney pains happens in a monument in Larnaka, believed to be the grave of the saint. Healing of the patient's kidney pain is accomplished by rubbing the waist upon the monument of the saint.

The role of Therapon in the eastern church, as a healer Saint, is explained by his miracles and also simply by his name – Therapon in greek means server and healer. The belief of him as a healer of kidney pains is mainly practiced on the island of Cyprus. Another recognized patron saint of kidney sufferers is the Saint virgin and martyr Marina of Antiochia in Pisidia (255–270AD).



## 11. THE HARD WAY FROM BENCH TO BEDSIDE: HISTORY LESSONS FROM THE PATHOGENESIS OF IDIOPATHIC MEMBRANOUS NEPHROPATHY (MN)

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MN is the most common cause of adult nephrotic syndrome. Histopathology involves typical subepithelial immunocomplexes, with obvious pathogenetic role. Today, study of pathogenesis, which began in 1959, has proven that MN is an organ-specific autoimmune disease. Our aim was to follow and draw some historical lessons from this 60 year long course of studies on MN.

Heymann nephritis (HN; 1959) is the classical animal model, in which the pathogenetic role of immunocomplexes in MN was first established. HN is induced by injection in rats of tubules brush border (BB) antigens (active HN) or the corresponding antibodies (anti-BB; passive HN). In 1978, lesions of HN forming ex vivo after anti-BB injection in an isolated perfused rat kidney model, i.e. in the absence of circulating BB antigens, proved that immune-complex formation occurs in situ. In 1982, megalin was identified as the epithelial auto-antigen in HN. However, as megalin could not be detected in human podocytes, pathogenesis of human MN still remained unresolved. In 2002, neutral endopeptidase was identified as the podocyte antigen in cases of antenatal allo-immune human MN, clearly implicating the pathogenetic role of podocyte membrane proteins and in situ immune-complex formation. In the next years, phospholipase A2-receptor and Thrombospondin type-1 domain containing 7A were identified as organ-specific auto-antigens associated with MN.

The maxim "scientia facit altus" would precisely describe the evolution of 60 years research on the pathogenesis of MN, which was decisively promoted in 20 years' surges. This pattern may change as we reach the exciting new scientific era.

## 12. ON THE CORRELATION OF THE URINES' SPECIFIC GRAVITY AND THE NATURAL HISTORY OF A RENAL DISEASE ACCORDING TO ANCIENT AND MEDIEVAL GREEK SOURCES

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The urine examination by a naked eye, called uroscopy, was for millennia practically the main laboratory method to reach a diagnosis and prognosis of many diseases and there is an abundant literature on the subject. However, any research concerning its specific gravity, even as an implication could not be traced by us. Thus, the aim of this paper was to try and find out if there was any such implication in the Ancient and Medieval Greek literature and its correlation with the natural history of a renal disease

**Methods:** We read the original relevant works by Hippocrates, Galen, Anonymi Medici Minores, and Stephanos and correlated them with Avicenna's Canon and the 19<sup>th</sup> – 21<sup>st</sup> centuries' literature on the topic.

**Results:** The term "specific gravity" was never mentioned by the ancient and medieval writers. Indirectly, they referred to it by discussing the different location in the matula (urine examining vial) of a semi - solid formation. If it laid at the bottom it was cold "hypostasis" (sediment), if at the middle "enaiorema" (suspension) and if floating at the top "nephelion" (nebulum). All the mentioned medical authors agreed that sediment usually testifies a healthy condition and a floating formation a very severe disease. The suspension could either be a sign of recovery if it followed a nebulum and was thus descending or of deterioration if it followed a sediment and was thus assenting. As its location depended on the difference of weight between the semisolid formation and the liquid part of the urine, indirectly it measured its specific gravity. Very recently the urine specific gravity is considered an accurate mark of renal function equal to creatinine clearance or proteinuria.

**Discussion - Conclusion:** Indirectly the location incorporated in sperm the principle of the hydrometer by which we estimate the difference of weight between any liquid and the particles immersed in it. As the weight of the former frequently depends on its viscosity, the studied ancient and medieval authors correlated in practice proteinuria and/or concentrating ability of the kidneys with the semi-solid's location.

## 13. HIPPOCRATES YATZIDIS: A GREAT AND HUMBLE GREEK PROFESSOR TO REMEMBER

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Professor Hippocrates Yatzidis was born on September 22, 1923 in Athens and died on August 27, 2013. He finished his medical study at the Medical School of Athens in 1950.

After the graduation he continued his studies at Paris at Claude Bernard Center in metabolic disorders from 1955 to 1959. He has been the director of many research units in Greece as well as in other countries and took over the management of Geneva Medical Center for a while. One of his dreams was to create a high profile Nephrology Department in Greece, this is the reason why he encouraged his colleagues to reeducate themselves in other countries and come back to Greece with new ideas and great knowledge.

In 1963 he demonstrated charcoal's binding capacity for toxic substances of endogenous or exogenous origin and used it for hemoperfusion systems. His team designed equipment named "the Carbon Kidney" and connected it to the patient's artery and vein in order to remove barbiturates from two patients, a process that successfully saved their lives. This method is known until nowadays literature as "Yatzidis charcoal artificial kidney". Professor Yatzidis has been more than a mentor for professor Dimitrios Oreopoulos and together worked on various articles. He was the one who suggested in the 1970s that sodium thiosulfate solution might prevent the vascular calcification that led to acral gangrene in dialysis patients and may be useful as a treatment for recurrent calcium nephrolithiasis. In the early 70s he founded the Nephrology Department of Areteion Hospital of Athens.

His publishing activity was manifested in many scientific papers, most of them in international journals, and a lot of citations. In the last period of his life, he continued his research at the laboratory of experimental surgery at the Medical School of Athens. He was known for his kindness and generosity to his associates.



## 14. MIRACULOUS RENAL HEALING IN THE CHURCH OF THE LIFE-GIVING SPRING IN CONSTANTINOPLE: COMPENDIUM (1812) FROM THE ORIGINAL BY NIKIPHOROS KALLISTOS XANTHOPOULOS (1256-1335)

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Nikiphoros Kallistos Xanthopoulos (1256-1335) was a priest in Hagia Sofia and a scholar considered as the last greek ecclesiastical historian. Apart from "Ecclesiasticae Historiae", dedicated to the emperor Andronikos-II Palaeologos (1282-1328), he wrote poems, liturgical hymns and "synaxaria" of the Orthodox Church. His book of the miracles in the church of the life-giving spring in Constantinople was published in a compendium translation in vulgar Greek (1812). Initiated by the ex-Bishop of Stages (Meteara) Paisios (1784-1808), this translation aimed to offer the contemporary greeks a book more comprehensible and thus more beneficial than the original. Our aim was to analyse from this compendium the forms of miraculous healing applied and the renal ailments healed.

Miraculous healings (54 among 63 miracles) included prayers, visions and the spring-water. Drinking was applied in 43, washes in 11 and mud compresses in 8 cases. Renal ailments were present in 11 cases: bladder stones with dysuria, hematuria, and pyuria or urine retention in 9 and hydrops in 2. Emperor Ioustinian (527-565) was healed from an obstructive bladder stone. Help was sought after doctors' treatments failed. In two cases water drinking was applied despite medical advice and side effects of drug-therapy were healed in two other.

In the compendium edition of the book of Nikiphoros Kallistos Xanthopoulos on the miracles of the life-giving spring in Constantinople healing of renal disorders was very often (20%). This publication implicates the narrow relationship of greek scholars, during hellenic Enlightenment (1750-1821), to the Palaeologian Byzantine Humanism.

## 15. PROFESSOR MIROSLAV MYDLÍK, MD, DSC. (1932–2018), A SCIENTIST

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**Aim of the study** was to describe the impact of one the most important pioneers in the field of nephrology in Central Europe in the second half of the 20th century.

**Methods:** I described the life and activities of Miroslav Mydlík.

**Results:** He was born on 7/21/1932 in Kosice (Czechoslovakia) where he died on 9/6/2018. He studied at the Medical Faculty of Charles University (MFCU), in Prague, where he graduated (1957). Thereafter he worked at the Department for Infectious Diseases and from 1959 at the 1st Internal Clinic (IC), (later renamed IVth) of L.Pasteur's University Hospital and Medical Faculty of P.J.Šafárik University (UPJŠ). After specializing in internal medicine and in nephrology (1973), (the first in Slovakia), he was assistant professor. He became "Doctor of Medical Sciences" at the MFCU (1984) and in 1992 was appointed a full Professor of Internal Medicine. His lifelong scientific activity was focused on nephrology, to which he was directed by Professor Pór (his boss) and Professor Brod during his stay in Prague, 1963. He performed the first percutaneous renal biopsy (1963); he was a founder of a dialysis centre at the 1st IC (1966); he carried out the first hemoperfusion (HP) through active charcoal in the former Czechoslovakia (1977). His publishing activity includes over 450 scientific papers. Most of them were on a biochemical basis. His topics were vitamin B6, oxalic acid as uremic toxin and HP in vivo and in vitro. He was the head of IV<sup>th</sup> IC, Nephrological Clinic; Prorector of the UPJŠ and Main advisor for nephrology of the Ministry of Health. He was introduced into the «Hall of Glory of Slovak Medicine» (2015). His hobbies were history and world literature. He was a member (1998–2018) and councillor (2010-2015) of IAHN. His lifelong literary interest was Franz Kafka's works. He created Kafka's monument in High Tatras, where Kafka was treated for lung tuberculosis (1920-1921) and published book *Lung tuberculosis of Franz Kafka. The impact of the disease on his literary work*, (2017).

**Conclusion:** Professor Mydlík's impact on the field of nephrology in Slovakia was multiple.

## **16. REFERENCES ON KIDNEYS IN GREEK BOOKS OF THE PRE - GREEK INDEPENDENCE REVOLUTION PERIOD (BEGINNING OF THE 19<sup>TH</sup> CENTURY)**

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During the pre- Greek Independence Revolution (1821) period the European Medical Knowledge is transmitted into the Greek lands mainly via translated texts. This stands true for many a scientific and literary texts in a movement called later "The Modern Greek Enlightenment). The movement aimed to the cultural, and eventually the political, rising of the Greek people who were usually illiterate under the Ottoman regime for almost for centuries. In some of those translated books we find scattered references to the kidneys and their function. In a book published in Vienna in 1799 there are references to the anatomical location of the kidneys and their texture, the cortical and medullary parts of them and the malpighian bodies. In the 1810 Anastasios Georgiadis, later professor of Medicine at the newly established Athens University used the term *Urinary tract*. In another book of 1802 titled "Chemical Philosophy" the urine's consistency and the then recently discovered elements urea, uric acid, glucose, phosphates are presented. It was emphatically stressed that that the modern studies on the urine characteristics will attribute to the definition of the body status both for a healthy and an ill person. In the same period the term *diuresis* is introduced as reborrowing in to the Greek medical vocabulary.

## **17. PROFESSOR JIŘÍ JIRKA, MD, DSC. – STUDENT AND SUCCESSOR OF PROFESSOR JAN BROD**

**Opatrná Sylvie<sup>1</sup>, Matoušovic Karel<sup>2</sup>, Jirka Tomáš<sup>3</sup>**

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Jiří Jirka was born on March 3, 1927 in Kroměříž, Czechoslovakia, and died on May 6, 2016. Immediately after World War II, in autumn 1946, he started the studies in Charles University Medical School in Prague. Early during his studies he joined Prof. Belobradek and his team in the Institute of Biology and participated in the first post-war experimental study of this Institute. Later during his studies he also worked at the 1<sup>st</sup> Dept of Medicine, Charles University Prague, where he met Professor Brod. After graduation in 1951 he worked in a department of medicine in a district hospital in Most. In 1953 he changed to Prague to the Institute for Cardiovascular Research, the second institute in the field worldwide that time, whose second director became Jan Brod. Under his supervision Dr Jirka started his research as a research fellow with completing his CSc thesis (roughly equivalent of PhD) in 1958. In 1961, he overtook leadership of the Hypertension Research Group after J Brod and changed the focus of studies from hypertension to acute and chronic kidney failure. In 1971, this Institute became a part of a newly established Institute for Clinical and Experimental medicine where Dr Jirka worked as a scientist and leading physician until 1992. He was actively involved in the introduction of hemodialysis, acute peritoneal dialysis and especially kidney transplantation in the former Czechoslovakia as well as in Cuba. His current science citation index is 781, H-index 8. The most frequently cited publication (almost 500 times) is Circulatory changes underlying blood pressure elevation during acute emotional stress in normotensive and hypertensive subjects published in Clin Sci in 1959 together with J Brod, V Fencel and Z Hejl. The textbook Renal Allograft Biopsy. Image, Interpretation, Interventions (Academia Prague 1997) co-authored P Rossmann and K Matoušovic summarized a 25-year collaboration between two nephrologists and one pathologist (PR) in the field of kidney transplantation.



## 18. VINCENZO DIAMARE (1871-1966) AND THE PRIORITY FOR THE DISCOVERY OF THE ENDOCRINE FUNCTION OF THE PANCREAS (1895)

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Paul Langerhans (1847-1868) - German pathologist, physiologist and biologist - in 1869 described in the thesis (*Beiträge zur mikroskopischen Anatomie der bauchspeicheldrüsen*) the pancreatic islet without advancing hypothesis on their function.

Diamare (1871-1966) - a scientist born and died in Naples where he was professor of Histology, General Physiology and Embriology (1923-1944) - was the most innovative and successful in understanding islet function. He performed comparative studies in teolosts (mainly in *Lophius*), reptiles, mammals, amphibia and birds by utilizing the facilities of the Marine Station founded by Anton Dohrn (1840-1909) and those at the Institute of Comparative Anatomy of the University of Naples.

In studies published in the years 1896-1907 (*Boll Soc Natur Napoli* 1898;117-122; *Int Monatschrift für Anatomie und Physiol* 1899; XVI: 140-155 and 155-176) and XXII 1905; *Il Tommasi Giornale di Biologia e Medicina* 1907: 132-137, 152-155) Vincenzo Diamare demonstrate that 1. The cells of Langherans are epithelial structures different from zymogenic cells and may be considered vascular glands, 2. These cells produce a granular substance colored by fuchsine - which is different from that produced zymogenic acinar cells of the pancreas - and is secreted in blood vessel (endocrine function) 3. These cells are constant in man and vertebrates and independent from zymogenic acinar cells of the pancreas cells; 4. The islet of Langerhans have an endocrine function in connection with the metabolism of glucose: hyperglycemia and diabetes are associated with inadequate functioning.

The internal secretion was named insulin by E. Sharpey- Schafer (1916). John James Rickard Macleod - recipient with Frederick Grant Banting of the Nobel Prize for insulin in 1923 - extensively recognized Diamare's priority (1926) as did many authorities including Sauerbeck, Weichselbaum, Rennie, Schafer, Laguesse, Bowie and Minkowski. Laguesse wrote him: "Vous avez donc beaucoup fait preparer la découvert de Banting!"

## **19. LUDWIK HIRSZFELD (1884 - 1954) – PIONEER OF BLOOD TYPE TESTING. SIGNIFICANCE FOR ORGAN TRANSPLANTS**

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Proper selection of the organ to be transplanted requires a series of tests and determines the effectiveness of the treatment. The first condition is the compliance of the blood types between the donor and the recipient. In 1901 Karl Landsteiner discovered that human blood had different properties and distinguished three blood groups: A, B, and C. In 1910-11 Emil von Dungern and Ludwik Hirszfeld discovered Mendelian inheritance of blood types. Their division into four basic groups A, B, AB and O has been used since 1928. The same researchers found subtypes A1 and A2 within the type A.

Ludwik Hirszfeld (1884-1954) was born in Warsaw and studied medicine in Würzburg. In 1907 he received a doctorate at the University of Berlin and moved to the Cancer Research Centre in Heidelberg and, in 1911, to the University of Zurich. Being a volunteer in World War I in Serbia, he fought a typhus epidemic. In 1918-1919, with his wife Hanna, researched and described the uneven distribution of blood type features that reflects the diverse evolutionary adaptations of humans. In the 1920s, he co-founded the National Institute of Hygiene in Warsaw. During World War II, he spent two years in the Warsaw ghetto, where he fought infectious diseases, typhus and tuberculosis. After the war, he headed the Department of Medical Microbiology at Maria Skłodowska-Curie University in Lublin. In 1945 he worked in Wrocław as the Head of the Department of Microbiology. He died in Wrocław.

The importance of Hirszfeld's contribution to our knowledge of the blood type system was confirmed by Karl Landsteiner in his Nobel Address, by choosing Hirszfeld to the Presidency of the Blood Group of the Second International Congress of Blood Transfusion in Paris in 1937 and by naming after him the Institute of Immunology and Experimental Therapy of the Polish Academy of Sciences in Wrocław.

## **20. WAS POLISH KING JAN III SOBIESKI CONQUERED BY CHRONIC KIDNEY DISEASE?**

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Jan Sobieski was born in the Polish noble family in 1629. Before he became King of Poland in 1674 he successfully fought Cossacks, Tartars and others as the Field Crown Hetman. His wife, Mary, daughter of the French marquise D'Arquien, ex-wife of Jan Sobiepan Zamoyski, was a member of one of the richest aristocratic families in Poland. During his rule (1674-1696) Jan III Sobieski defeated the Turkish Kara Mustafa and his army in the battle of Vienna, thus saving Europe from the Ottoman invasion. It is interesting that for years the king suffered from chronic kidney disease with its distinctive symptoms like headaches, swelling dyspnoea, joint pains or skin eczematous changes.

Reference to these appears in his letter to Mary and also in the notes of his personal physician Emanuel de Jona. He was treated with various drugs including mercurial medicaments. Jan III Sobieski died in 1696 in the summer royal residence in Wilanów. Autopsy, supervised by three independent physicians, among other changes, revealed symptoms of kidney damage with a rather big stone in the right kidney. Moreover, his left kidney was reported to be small and damaged. The doctors' report made a strong suggestion that chronic kidney disease was the main cause of King's death. The same was concluded in three subsequent analyses performed later by clinicians, pathologists and historians on the basis of documents.

In 2017, Israel's Isaak Gath performed a retrospective analysis of all known documents and hypotheses of the King's disease and death. He concluded that, for years, Sobieski presented symptoms of stage III syphilis which he had contracted from his wife. In his opinion, the brain, heart or even kidney disorders were secondary to the main disease. He also suggested that previous descriptions intentionally concealed the real cause of Jan III Sobieski's illness and death. Nevertheless, independently of the presented controversies, primary or secondary kidney damage was an irrefutable fact and, in our opinion, played an important role in the fatal end of our King.



# XI IAHN CONGRESS

## **21. PROFESSOR ANDRZEJ BIERNACKI – PRECURSOR OF NEPHROLOGY IN POLAND**

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It was in the mid-20<sup>th</sup> century that nephrology started to emerge as an independent specialty and Witold Osłowski is regarded as its father. His remarkable successor was Andrzej Biernacki (1903-1963). Born in Lublin, Biernacki graduated from the Medical Department of Warsaw University. During university times he worked at the National Hygiene Institute headed by Ludwik Hirszfeld and trained at the Pasteur Institute in Paris. Then he went to a Polish colony in Brazil to study the health conditions there. In the 1930s, he did an internship at the Forlanini Institute in Rome, and later in Davos and Paris. During WW 2 he fought in the resistance and worked in the 2nd Department of Internal Medicine at the University's Secret Medical Department. After the war, he organised the 1st Department of Internal Medicine. As a WHO scholarship holder, he trained in the USA in 1947. Already a professor, in 1958 as the chairman of the Nephrology Development Committee at the Ministry of Health, he brought 2 Alwall's artificial kidneys to Poland. At his clinic in 1959 the team headed by Tadeusz Orłowski performed the first dialysis session in Warsaw. Biernacki's portfolio includes 75 own works and over 400 conceived under his supervision. The issues investigated concerned lung diseases, including pulmonary tuberculosis, and cardiology. However, his work on nephrology deserves special attention. It deals with key problems of division of hypertension, its malignant phase with changes in the kidneys and pharmacological and balneological treatment. He also describes the case of paroxysmal haemoglobinuria, genitourinary tuberculosis. Additionally, his work concerns the symptoms of uraemia in kidney amyloidosis, the problem of the circadian rhythm of urine production depending on the circulatory capacity and later also the possibility of haemodialysis treatment, including the treatment of mercury poisoning. Nephrology-related topics raised by A. Biernacki were continued by his co-workers and students. Andrzej Biernacki had numerous non-medical interests. He was an expert on music and husband to Grażyna Bacewicz, the outstanding Polish composer and violinist.



## **22. THE HIPPOCRATIC SPIRIT AND RENAL PATIENTS' CARE**

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Nephrology is one of the newest medical specialties that developed during the previous century. The earliest scientific approach to clinical nephrology, however, is attributed to Hippocrates granting him the title “father of clinical nephrology”. The principal essence of renal medicine is in fact hidden within the Hippocratic theory of the four humors, as it remarkably resembles the main kidney function which is preservation of fluid and electrolyte homeostasis.

Hippocrates excelled in the art of uroscopy for the diagnosis of nephrological conditions. Uroscopy was considered the cornerstone of medical diagnosis for many centuries. Moreover, within the Hippocratic corpus there are many references to renal problems, such as kidney stones, gout, nephrotic syndrome, hematuria, and acute tubular necrosis. The writer provided a detailed description of their symptoms accompanied with prognostic and therapeutic guidance.

Nowadays renal patients' care has progressed far beyond the Hippocratic writings. Renal replacement therapy, biologic treatments and organ transplantation have altered the natural course of renal disease. The modern nephrologist must face several dilemmas associated with a chronic terminal condition, such as end-of-life treatment, palliative care and support to both patients and their families. At this time, the Hippocratic spirit emerges as an ethical guide and constant reminder of the moral responsibilities linked to medical profession, in the spirit of the Hippocratic saying “benefit or do no harm”.



## 23. DEATHS CAUSED BY CARDIORENAL DISEASE AMONG 264 POPES FROM ST. PETER TO ST. JOHN PAUL II (64-2005 AD)

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Diseases and deaths of the Popes are well reported. However we still lack a systematic study of papal deaths associated with diseases of the heart or of the genitourinary tract that is the goal of the present work. The study shows that:

- 14 Popes died of gout and its complications: Sisinnius; Honorius IV, Boniface VIII, Pius I, Sixtus IV, Pius III, Julius II, Julius III, Clement VIII, Clement X, Innocent XI, Clement XI, Benedict XIV, Pius VIII.
- 8 Popes died of kidney and bladder stones: Boniface IX, Gregory XIV, Clement IX, Innocent XII, Innocent XIII, Pius V, Pius VI, Leo XII.
- John XXI (1276-1277) died of crush syndrome. On August 10, 1277 the ceiling of his office fell down. He was severely injured. Extracted alive from the rubble he died a few days later.
- 8 Popes died of kidney and bladder stones: Boniface IX, Gregory XIV, Clement IX, Innocent XII, Innocent XIII, Pius V, Pius VI, Leo XII.
- 4 Popes had nephritis: Marcellus II, Hadrian VI, Clement X, Pius VII.
- 4 Popes had prostate disease: Clement XI, Pius VII, Paul VI, John Paul II.
- 2 Popes had infections originating in the urinary tract: Clement VI had severe gonorrhoea, Julius II had syphilis.
- 5 Popes underwent cardiac death: Clement XIII, Pius X, Pius XI, Paul VI, John Paul I.

Ages of Popes at death were above mean for their times. Many were martyred (no. 28), some underwent violent death (no. 9), and 2 were imprisoned (Celestine V, Pius VI). Among 264 Popes, prevalence of deaths originating in diseases of the urinary tract and of the heart was 17.4%.

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