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CONTRIBUTION OF ACADEMICIAN MOMIR POLENAKOVIC TO THE DEVELOPMENT OF NEPHROLOGY IN THE REPUBLIC OF MACEDONIA

OFFICIAL ADDRESS OF ACADEMICIAN V. SERAFIMOSKI, SECRETARY OF THE DEPARTMENT OF MEDICAL SCIENCES OF THE MACEDONIAN ACADEMY OF SCIENCES AND ARTS ON THE OCCASION OF THE 75TH ANNIVERSARY OF ACADEMICIAN MOMIR POLENAKOVIC

Vladimir Serafimoski

Macedonian Academy of Sciences and Arts, Skopje, R. Macedonia

Corresponding Author: Vladimir Serafimoski, Macedonian Academy of Sciences and Arts, Bul. Krste Misirkov, No. 2, Skopje, R. Macedonia

From left to right: V. Serafimoski (Skopje), Z. Popov (Skopje), N. Pop-Jordanova (Skopje), I. Filipce (Skopje)

Abstract

Academician Momir H. Polenakovic, MD, Ph.D. is an outstanding researcher, educator and scientist, one of the founders of the nephrology in the Republic of Macedonia. With more than 500 published papers in national and international journals, of which more than 189 are on the PubMed, he is one of the most fruitful medical worker in our country. With his participation in national and international congresses he has contributed to the transfer of the world nephrology in Macedonia, as well as, to the dissemination of the reputation of the Macedonian nephrology and science in the world. He has educated a number of specialists in internal medicine and subspecialists in nephrology. He has introduced new tests and methods in diagnosis and treatment of renal disease, which was a basis for his research and publication. Analyzing the life opus of Academician Momir Polenakovic we can say that he has dedicated his life and work to the research, diagnosis and treatment of kidney patients.

Key words: Macedonian nephrology, research, diagnosis, treatment of kidney patients

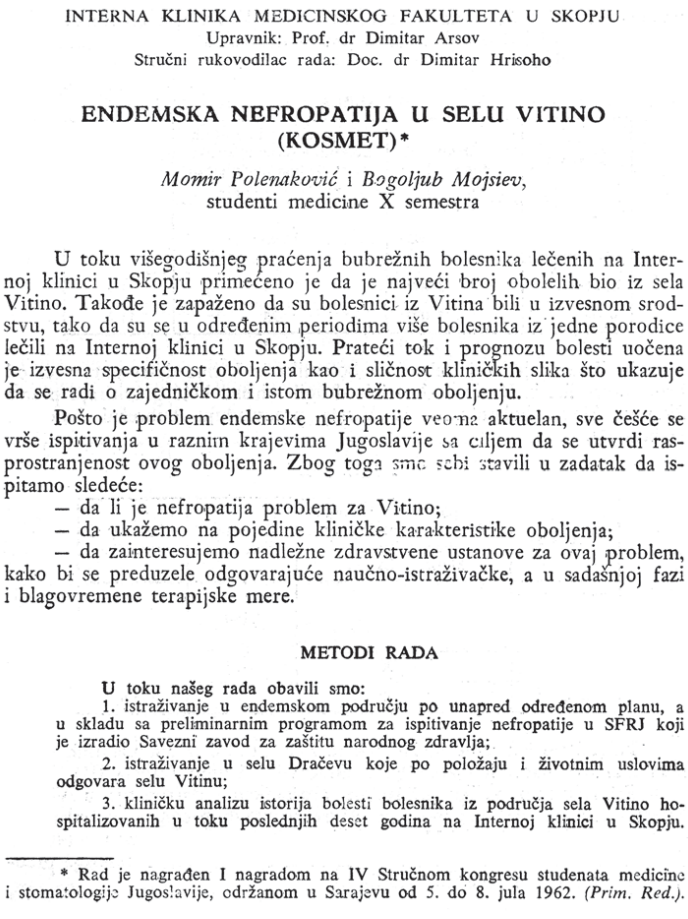
M. Polenakovic is a Professor of Medicine – Nephrology. He is an outstanding researcher, educator and scientist, one of the founders of the nephrology in the Republic of Macedonia.

Analyzing the life opus of Academician Momir Polenakovic we can say that he has dedicated his work to the research, diagnosis and treatment of kidney patients. Extremely well

educated at the most famous nephrology centers in Europe and the USA, he managed to transfer part of what he has learnt abroad to Macedonia at the Nephrology Clinic, where he spent his life. Besides being a superb clinician, physician-specialist, internist-nephrologist, he was also a great teacher who educated numerous students and doctors from the Republic of Macedonia and the surrounding countries. With his talent in organizing of the nephrology care and the contacts with the colleagues from Macedonia and abroad he created a strong nephrology organization and nephrology protection of the citizens in Macedonia, and has contributed for the Nephrology Clinic of the Medical Faculty in Skopje to become one of the "centers of excellence" according to the estimates of the Ministry of Education and Science of the Republic of Macedonia. By uniting his organizational, educational, scientific and research qualities he has developed into one of the most outstanding workers in the medical area in our country.

During his study at the Medical Faculty of the University of Ss. Cyril and Methodius in Skopje he has shown interest in research and he has been educated and supported by the best professors of the Faculty, as Acad. I. Tadger, Acad. D. Arsov, Prof. V. Dolgova, Prof. D. Hrisoho, Prof. D. Miovski and Prof. B. Karanfilski. Under their guidance he participated in the research and has prepared several papers published in the student journals of former Yugoslavia (see the bibliography of Acad. Momir Polenakovic http://manu.edu.mk/prilozi/editor.htm).

In the early 1960s, with his Prof. Hrisoho he described the new region with the Balkan Endemic Nephropathy (BEN), along the upper part of South Morava River in the village of Vitina, Kosovo, Serbia. The clinico-morphological examination of BEN became a life occupation of Prof. Polenakovic. He has published several papers about BEN and one chapter published in the Oxford Textbook of Nephrology, 1992.



INTERNA KLINIKA MEDICINSKOG FAKULTETA U SKOPJU
Upravnik: Prof. dr Dimitar Arsov
Stručni rukovodilac rada: Doc. dr Dimitar Hrisoho

ENDEMSKA NEFROPATIJA U SELU VITINO (KOSMET)*

Momir Polenaković i *Bogoljub Mojsiev*,
studenti medicine X semestra

U toku višegodišnjeg praćenja bubrežnih bolesnika lečenih na Internoj klinici u Skopju primećeno je da je najveći broj obolelih bio iz sela Vitino. Takođe je zapaženo da su bolesnici iz Vitina bili u izvesnom srodstvu, tako da su se u određenim periodima više bolesnika iz jedne porodice lečili na Internoj klinici u Skopju. Prateći tok i prognozu bolesti uočena je izvesna specifičnost oboljenja kao i sličnost kliničkih slika što ukazuje da se radi o zajedničkom i istom bubrežnom oboljenju.

Pošto je problem endemske nefropatije veoma aktuelan, sve češće se vrše ispitivanja u raznim krajevima Jugoslavije sa ciljem da se utvrdi rasprostranjenost ovog oboljenja. Zbog toga smo sebi stavili u zadatak da ispitamo sledeće:

– da li je nefropatija problem za Vitino;
– da ukažemo na pojedine kliničke karakteristike oboljenja;
– da zainteresujemo nadležne zdravstvene ustanove za ovaj problem, kako bi se preduzele odgovarajuće naučno-istraživačke, a u sadašnjoj fazi i blagovremene terapijske mere.

METODI RADA

U toku našeg rada obavili smo:

1. istraživanje u endemskom području po unapred određenom planu, a u skladu sa preliminarnim programom za ispitivanje nefropatije u SFRJ koji je izradio Savezni zavod za zaštitu narodnog zdravlja;
2. istraživanje u selu Dračevu koje po položaju i životnim uslovima odgovara selu Vitinu;
3. kliničku analizu istorija bolesti bolesnika iz područja sela Vitino hospitalizovanih u toku poslednjih deset godina na Internoj klinici u Skopju.

* Rad je nagrađen I nagradom na IV Stručnom kongresu studenata medicine i stomatologije Jugoslavije, održanom u Sarajevu od 5. do 8. jula 1962. *(Prim. Red.)*.

Fig. 1 – The paper about the Endemic Nephropathy in the village of Vitina (Kosmet) was awarded the first prize at the IV Congress of students of medicine held in Sarajevo from 5 to 8 July 1962. The paper has been published

in Medicinski podmladak. 1962/63; XIV(4): 363–71

OXFORD TEXTBOOK OF CLINICAL NEPHROLOGY

Edited by

STEWART CAMERON, ALEX M. DAVISON, JEAN-PIERRE GRÜNFELD, DAVID KERR, and EBERHARD RITZ

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VOLUME 2

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april 1992, Skopje

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1992

6.7 Balkan nephropathy

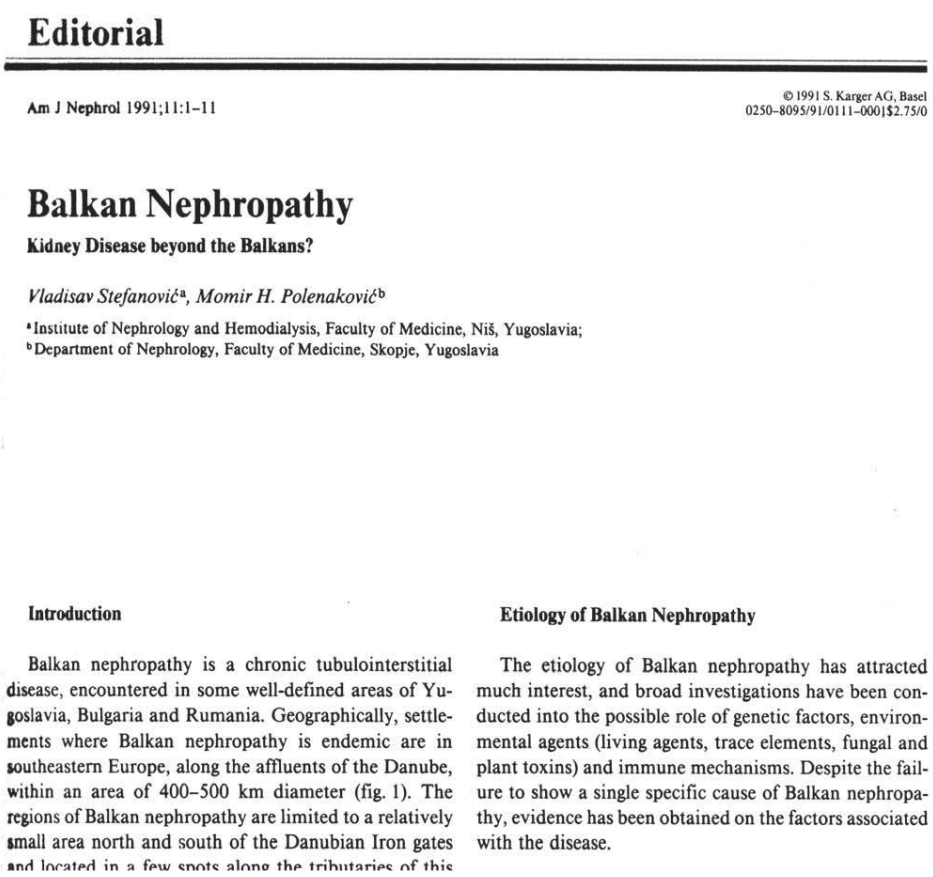
MOMIR H. POLENAKOVIĆ AND VLADISAV STEFANOVIĆ

Balkan nephropathy is a familial chronic tubulointerstitial disease, encountered in some restricted areas of Yugoslavia, Bulgaria, and Rumania. The first description of the disease in Yugoslavia was made by Danilović *et al.* (1957) and in Bulgaria by Tanchev *et al.* (1956). The earliest observation of an increased incidence of renal disease in some of the present endemic settlements was made by practising physicians in about 1941 and 1942.

Geographical distribution

Balkan nephropathy is geographically located in the areas of south-eastern Europe, along the tributaries of the Danube (Fig. 1), within an area of about 400 to 500 km^2. The endemic areas in Yugoslavia, Bulgaria, and Rumania border on one another and the distance between them is not more than 100 km. The disease is limited to a relatively small region north and south of the Danubian Iron Gates and located in a few areas along the tributaries of this river in the plains and low hills at an altitude of 150 to 500 m above sea level, some distance from the mountainous regions of the Balkans and Carpathians. The region where Balkan nephropathy is detected generally have high humidity and high rainfall. No local geological peculiarities have been described.

Fig. 2 – Polenaković MH, Stefanović V. Balkan Nephropathy. In: Oxford Textbook of Clinical Nephrology. eds. Cameron S, Davison AM, Grünfeld J-P, Kerr D, Ritz E. Vol. 1–3. Oxford University Press; 1992: 857–66



Editorial

Am J Nephrol 1991;11:1–11

0250–8095/91/0111–000$2.75/0

Balkan Nephropathy

Kidney Disease beyond the Balkans?

Vladisav Stefanović[a], *Momir H. Polenaković*[b]

[a] Institute of Nephrology and Hemodialysis, Faculty of Medicine, Niš, Yugoslavia;
[b] Department of Nephrology, Faculty of Medicine, Skopje, Yugoslavia

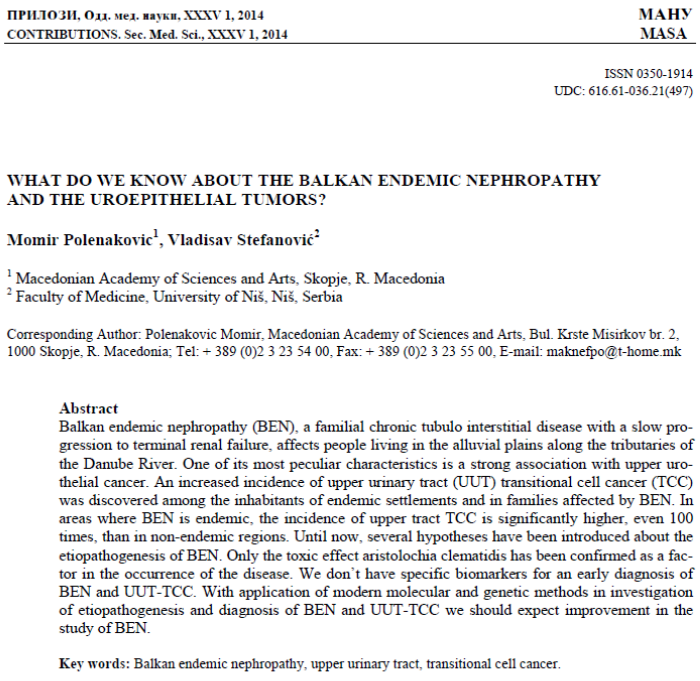
Introduction

Balkan nephropathy is a chronic tubulointerstitial disease, encountered in some well-defined areas of Yugoslavia, Bulgaria and Rumania. Geographically, settlements where Balkan nephropathy is endemic are in southeastern Europe, along the affluents of the Danube, within an area of 400–500 km diameter (fig. 1). The regions of Balkan nephropathy are limited to a relatively small area north and south of the Danubian Iron gates and located in a few spots along the tributaries of this

Etiology of Balkan Nephropathy

The etiology of Balkan nephropathy has attracted much interest, and broad investigations have been conducted into the possible role of genetic factors, environmental agents (living agents, trace elements, fungal and plant toxins) and immune mechanisms. Despite the failure to show a single specific cause of Balkan nephropathy, evidence has been obtained on the factors associated with the disease.

Fig. 3 – Stefanović V, Polenaković MH. Balkan Nephropathy: Kidney Disease Beyond the Balkans? American Journal of Nephrology. 1991; 11: 1–11



ПРИЛОЗИ, Одд. мед. науки, XXXV 1, 2014
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WHAT DO WE KNOW ABOUT THE BALKAN ENDEMIC NEPHROPATHY AND THE UROEPITHELIAL TUMORS?

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[2] Faculty of Medicine, University of Niš, Niš, Serbia

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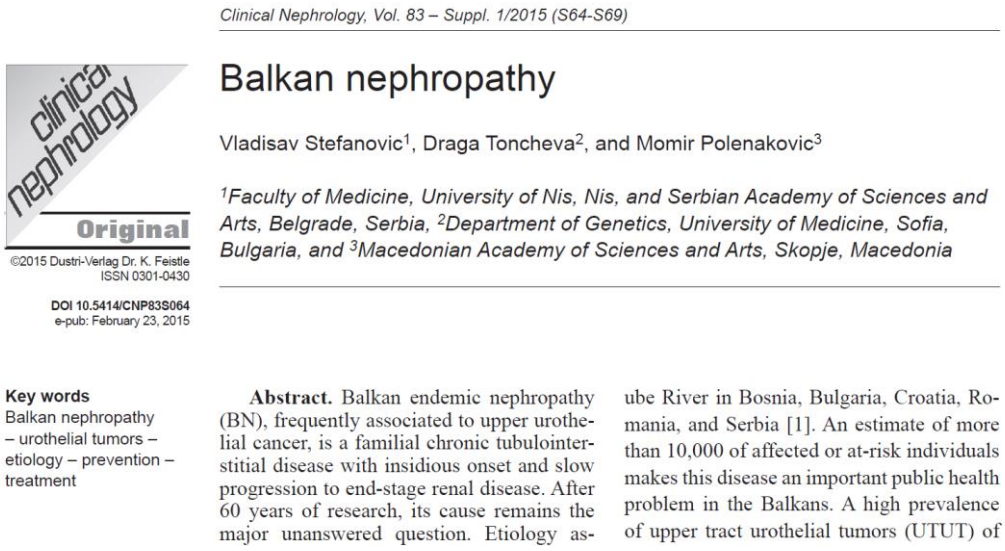
Abstract

Balkan endemic nephropathy (BEN), a familial chronic tubulo interstitial disease with a slow progression to terminal renal failure, affects people living in the alluvial plains along the tributaries of the Danube River. One of its most peculiar characteristics is a strong association with upper urothelial cancer. An increased incidence of upper urinary tract (UUT) transitional cell cancer (TCC) was discovered among the inhabitants of endemic settlements and in families affected by BEN. In areas where BEN is endemic, the incidence of upper tract TCC is significantly higher, even 100 times, than in non-endemic regions. Until now, several hypotheses have been introduced about the etiopathogenesis of BEN. Only the toxic effect aristolochia clematidis has been confirmed as a factor in the occurrence of the disease. We don't have specific biomarkers for an early diagnosis of BEN and UUT-TCC. With application of modern molecular and genetic methods in investigation of etiopathogenesis and diagnosis of BEN and UUT-TCC we should expect improvement in the study of BEN.

Key words: Balkan endemic nephropathy, upper urinary tract, transitional cell cancer.

Fig. 4 – Momir Polenakovic, Vladisav Stefanović. WHAT DO WE KNOW ABOUT THE BALKAN ENDEMIC NEPHROPATHY AND THE UROEPITHELIAL TUMORS? Prilozi: XXXV 1, 2014



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Balkan nephropathy

Vladisav Stefanovic[1], Draga Toncheva[2], and Momir Polenakovic[3]

[1]Faculty of Medicine, University of Nis, Nis, and Serbian Academy of Sciences and Arts, Belgrade, Serbia, [2]Department of Genetics, University of Medicine, Sofia, Bulgaria, and [3]Macedonian Academy of Sciences and Arts, Skopje, Macedonia

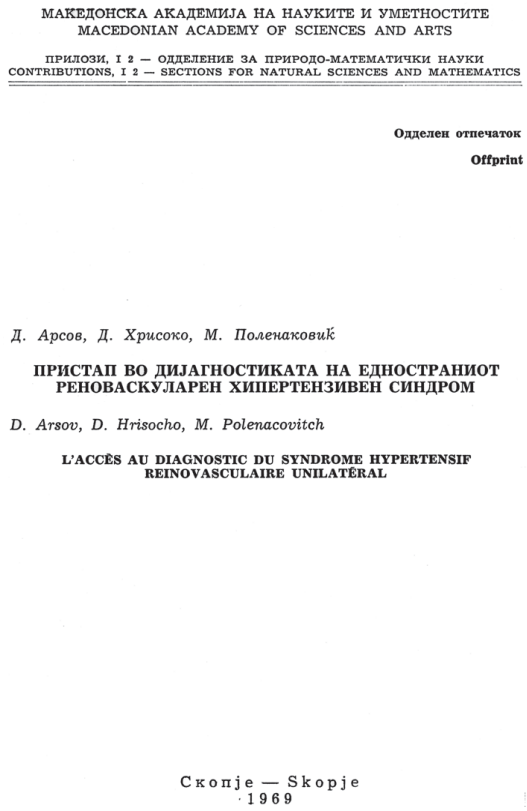
Key words
Balkan nephropathy – urothelial tumors – etiology – prevention – treatment

Abstract. Balkan endemic nephropathy (BN), frequently associated to upper urothelial cancer, is a familial chronic tubulointerstitial disease with insidious onset and slow progression to end-stage renal disease. After 60 years of research, its cause remains the major unanswered question. Etiology as-

ube River in Bosnia, Bulgaria, Croatia, Romania, and Serbia [1]. An estimate of more than 10,000 of affected or at-risk individuals makes this disease an important public health problem in the Balkans. A high prevalence of upper tract urothelial tumors (UTUT) of

Fig. 5 – Vladisav Stefanovic, Draga Toncheva, Momir Polenakovic. Balkan Nephorpathy. Clinical Nephrology. Vol. 83 – Suppl. 1/2015 (S64–S69)

With his colleagues he introduced the treatment of Acute (1965) and Chronic (1971) Kidney Failure with hemodialysis. He has published a number of papers about renal disease in national and international journals. He has a special interest in investigation of cuprophar membrane and PMMA in patients on hemodialysis. He participated in the first renal transplantation in the Republic of Macedonia in 1977.



МАКЕДОНСКА АКАДЕМИЈА НА НАУКИТЕ И УМЕТНОСТИТЕ
MACEDONIAN ACADEMY OF SCIENCES AND ARTS

ПРИЛОЗИ, I 2 — ОДДЕЛЕНИЕ ЗА ПРИРОДО-МАТЕМАТИЧКИ НАУКИ
CONTRIBUTIONS, I 2 — SECTIONS FOR NATURAL SCIENCES AND MATHEMATICS

Одделен отпечаток

Offprint

Д. Арсов, Д. Хрисоко, М. Поленаковиќ

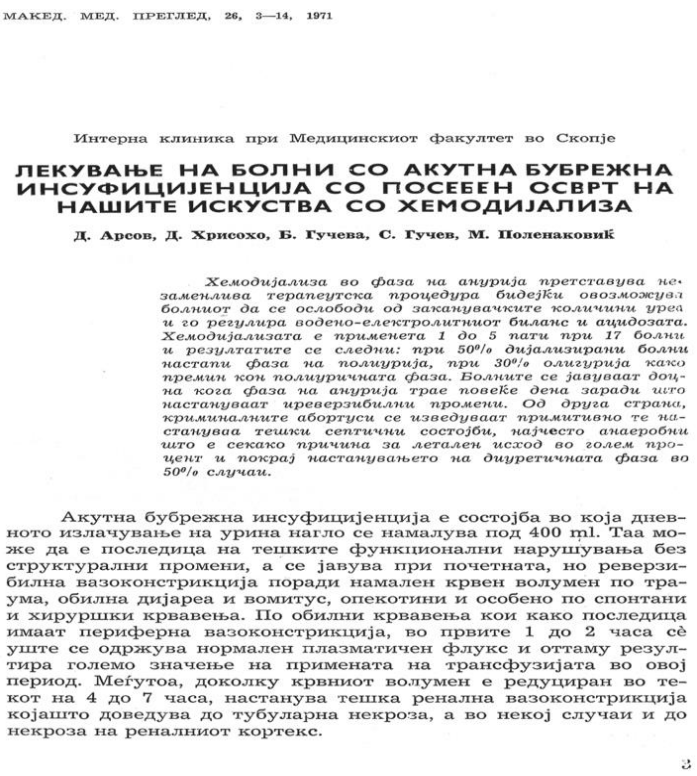
ПРИСТАП ВО ДИЈАГНОСТИКАТА НА ЕДНОСТРАНИОТ РЕНОВАСКУЛАРЕН ХИПЕРТЕНЗИВЕН СИНДРОМ

D. Arsov, D. Hrisocho, M. Polenacovitch

L'ACCÈS AU DIAGNOSTIC DU SYNDROME HYPERTENSIF REINOVASCULAIRE UNILATÉRAL

Скопје — Skopje
1969

*Fig. 6 – Arsov D., Hrisoho D., Polenakovic M. **L'accès au diagnostic du syndrome hypertensif reinovasculaire unilatéral**. Prilozi. Sections for natural sciences and mathematics MANU 1969; I(2): 23–33*



МАКЕД. МЕД. ПРЕГЛЕД, 26, 3—14, 1971

Интерна клиника при Медицинскиот факултет во Скопје

ЛЕКУВАЊЕ НА БОЛНИ СО АКУТНА БУБРЕЖНА ИНСУФИЦИЈЕНЦИЈА СО ПОСЕБЕН ОСВРТ НА НАШИТЕ ИСКУСТВА СО ХЕМОДИЈАЛИЗА

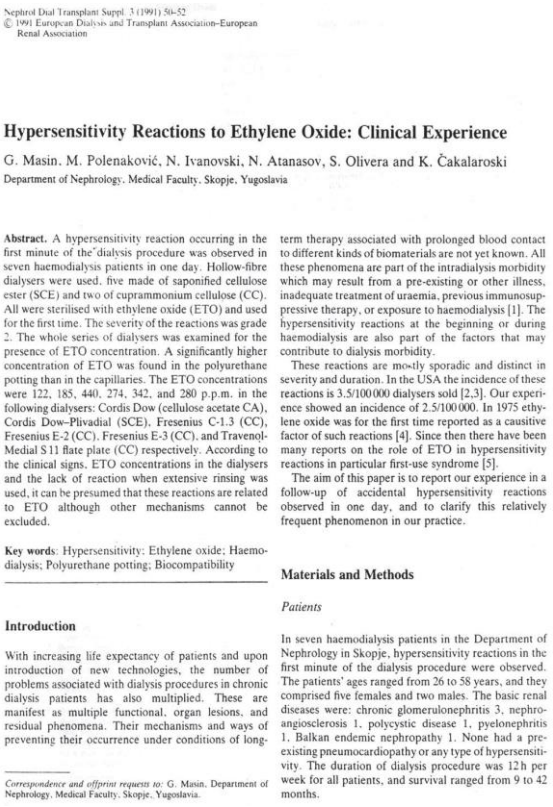
Д. Арсов, Д. Хрисохо, Б. Гучева, С. Гучев, М. Поленаковиќ

Хемодијализа во фаза на анурија претставува незаменлива терапеутска процедура бидејќи овозможува болниот да се ослободи од заканувачките количини урея и го регулира водено-електролитниот биланс и ацидозата. Хемодијализата е применета 1 до 5 пати при 17 болни и резултатите се следни: при 50% дијализирани болни настапи фаза на полиурија, при 30% олигурија како премин кон полуричната фаза. Болните се јавуваат доцна кога фаза на анурија трае повеќе дена заради што настануваат иреверзибилни промени. Од друга страна, криминалните аборгуси се изведуваат примитивно те настанува тешки септични состојби, најчесто анаеробни што е секако причина за летален исход во голем процент и покрај настанувањето на диуретичната фаза во 50% случаи.

Акутна бубрежна инсуфицијенција е состојба во која дневното излачување на урина нагло се намалува под 400 ml. Таа може да е последица на тешките функционални нарушувања без структурални промени, а се јавува при почетната, но реверзибилна вазоконстрикција поради намален крвен волумен по траума, обилна дијареа и вомитус, опекотини и особено по спонтани и хируршки крварења. По обилни крварења кои како последица имаат периферна вазоконстрикција, во првите 1 до 2 часа сè уште се одржува нормален плазматичен флукс и оттаму резултира големо значење на примената на трансфузијата во овој период. Меѓутоа, доколку крвниот волумен е редуциран во текот на 4 до 7 часа, настанува тешка ренална вазоконстрикција којашто доведува до тубуларна некроза, а во некој случаи и до некроза на реналниот кортекс.

3

Fig. 7 – Arov D., Hrisoho D, Guceva B., Gucev S. Polenakovic M. Treatment of Patients with Acute Renal Insufficiency with Special Reference to our Experience with Haemodialysis. Macedonian Medical Review 1971; XXVI(1–2): 3–14



Nephrol Dial Transplant Suppl. 3 (1991) 50-52

Hypersensitivity Reactions to Ethylene Oxide: Clinical Experience

G. Masin, M. Polenaković, N. Ivanovski, N. Atanasov, S. Olivera and K. Čakalaroski
Department of Nephrology, Medical Faculty, Skopje, Yugoslavia

Abstract. A hypersensitivity reaction occurring in the first minute of the dialysis procedure was observed in seven haemodialysis patients in one day. Hollow-fibre dialysers were used, five made of saponified cellulose ester (SCE) and two of cuprammonium cellulose (CC). All were sterilised with ethylene oxide (ETO) and used for the first time. The severity of the reactions was grade 2. The whole series of dialysers was examined for the presence of ETO concentration. A significantly higher concentration of ETO was found in the polyurethane potting than in the capillaries. The ETO concentrations were 122, 185, 440, 274, 342, and 280 p.p.m. in the following dialysers: Cordis Dow (cellulose acetate CA), Cordis Dow–Plivadial (SCE), Fresenius C-1.3 (CC), Fresenius E-2 (CC), Fresenius E-3 (CC), and Travenol-Medial S 11 flate plate (CC) respectively. According to the clinical signs, ETO concentrations in the dialysers and the lack of reaction when extensive rinsing was used, it can be presumed that these reactions are related to ETO although other mechanisms cannot be excluded.

Key words: Hypersensitivity; Ethylene oxide; Haemodialysis; Polyurethane potting; Biocompatibility

Introduction

With increasing life expectancy of patients and upon introduction of new technologies, the number of problems associated with dialysis procedures in chronic dialysis patients has also multiplied. These are manifest as multiple functional, organ lesions, and residual phenomena. Their mechanisms and ways of preventing their occurrence under conditions of long-term therapy associated with prolonged blood contact to different kinds of biomaterials are not yet known. All these phenomena are part of the intradialysis morbidity which may result from a pre-existing or other illness, inadequate treatment of uraemia, previous immunosuppressive therapy, or exposure to haemodialysis [1]. The hypersensitivity reactions at the beginning or during haemodialysis are also part of the factors that may contribute to dialysis morbidity.

These reactions are mostly sporadic and distinct in severity and duration. In the USA the incidence of these reactions is 3.5/100 000 dialysers sold [2,3]. Our experience showed an incidence of 2.5/100 000. In 1975 ethylene oxide was for the first time reported as a causitive factor of such reactions [4]. Since then there have been many reports on the role of ETO in hypersensitivity reactions in particular first-use syndrome [5].

The aim of this paper is to report our experience in a follow-up of accidental hypersensitivity reactions observed in one day, and to clarify this relatively frequent phenomenon in our practice.

Materials and Methods

Patients

In seven haemodialysis patients in the Department of Nephrology in Skopje, hypersensitivity reactions in the first minute of the dialysis procedure were observed. The patients' ages ranged from 26 to 58 years, and they comprised five females and two males. The basic renal diseases were: chronic glomerulonephritis 3, nephroangiosclerosis 1, polycystic disease 1, pyelonephritis 1, Balkan endemic nephropathy 1. None had a pre-existing pneumocardiopathy or any type of hypersensitivity. The duration of dialysis procedure was 12 h per week for all patients, and survival ranged from 9 to 42 months.

Correspondence and offprint requests to: G. Masin, Department of Nephrology, Medical Faculty, Skopje, Yugoslavia.

Fig. 8 – Masin G, Polenaković M, Ivanovski N, Atanasov N, Stojčeva O, Čakalarovski K. Hypersensitivity Reactions to Ethylene Oxide: Clinical Experience. Nephrology Dialysis Transplantation. 1991; 6 (Suppl. 3): 50–2

THE LANCET

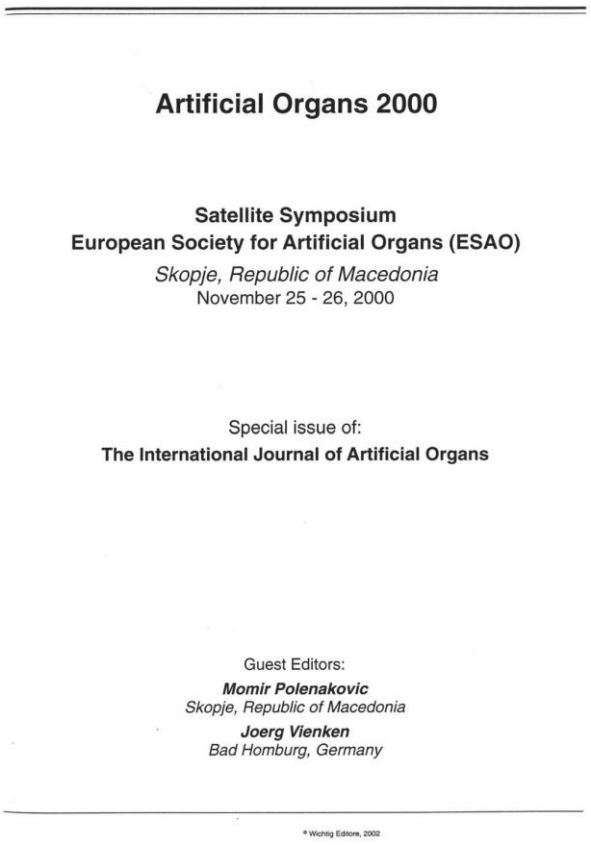
Haemodialysis-membrane biocompatibility and mortality of patients with dialysis-dependent acute renal failure: a prospective randomised multicentre trial

Achim Jörres Gerhard M Gahl Clemens Dobis Momir H Polenakovic Koco Cakalaroski Boleslaw Rutkowski Ewa Kisielnicka Detlef H Krieter K Wolfgang Rumpf Christian Guenther Wilhelm Gaus Josef Hoegel for the International Multicentre Study Group

Reprinted from THE LANCET Saturday 16 October 1999 Vol. 354 No. 9187 Pages 1337–1341

THE LANCET 42 BEDFORD SQUARE LONDON WC1B 3SL UK

Fig. 9 – Jörres A, Gahl GM, Dobis C, Polenakovic MH, Cakalaroski K, Rutkowski B, Kisielnicka E, Krieter DH, Rumpf KW, Guenther C, Gaus W, Hoegel J. Haemodialysis-membrane biocompatibility and mortality of patients with dialysis-dependent acute renal failure: a prospective randomised multicentre trial. The Lancet. 1999; 354(9187): 1337–41



Artificial Organs 2000

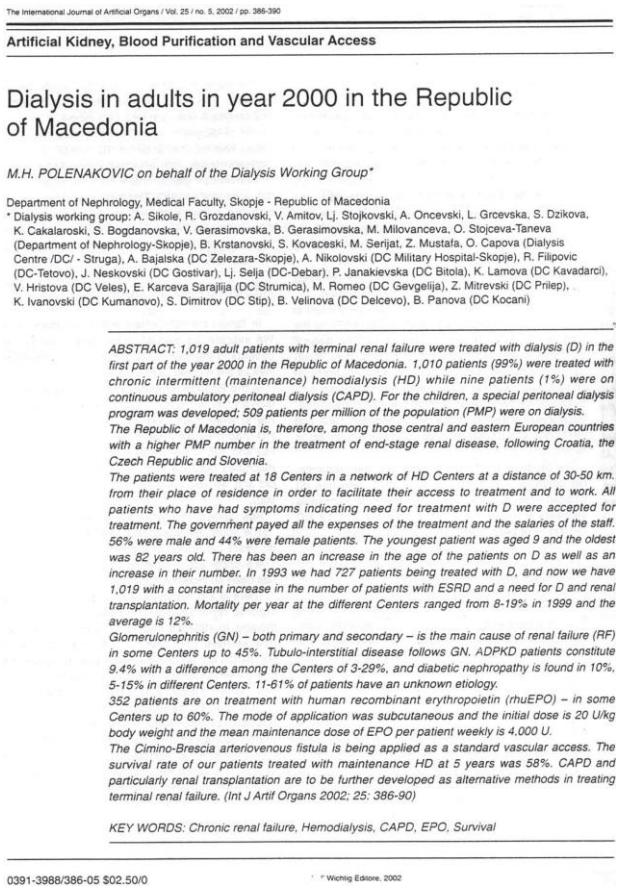
Satellite Symposium
European Society for Artificial Organs (ESAO)
Skopje, Republic of Macedonia
November 25 - 26, 2000

Special issue of:
The International Journal of Artificial Organs

Guest Editors:
Momir Polenakovic
Skopje, Republic of Macedonia
Joerg Vienken
Bad Homburg, Germany

® Wichtig Editore, 2002

Fig. 10 – Artificial Organs 2000



The International Journal of Artificial Organs / Vol. 25 / no. 5, 2002 / pp. 386-390

Artificial Kidney, Blood Purification and Vascular Access

Dialysis in adults in year 2000 in the Republic of Macedonia

*M.H. POLENAKOVIC on behalf of the Dialysis Working Group**

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ABSTRACT: 1,019 adult patients with terminal renal failure were treated with dialysis (D) in the first part of the year 2000 in the Republic of Macedonia. 1,010 patients (99%) were treated with chronic intermittent (maintenance) hemodialysis (HD) while nine patients (1%) were on continuous ambulatory peritoneal dialysis (CAPD). For the children, a special peritoneal dialysis program was developed; 509 patients per million of the population (PMP) were on dialysis.
The Republic of Macedonia is, therefore, among those central and eastern European countries with a higher PMP number in the treatment of end-stage renal disease, following Croatia, the Czech Republic and Slovenia.
The patients were treated at 18 Centers in a network of HD Centers at a distance of 30-50 km. from their place of residence in order to facilitate their access to treatment and to work. All patients who have had symptoms indicating need for treatment with D were accepted for treatment. The governrhent payed all the expenses of the treatment and the salaries of the staff. 56% were male and 44% were female patients. The youngest patient was aged 9 and the oldest was 82 years old. There has been an increase in the age of the patients on D as well as an increase in their number. In 1993 we had 727 patients being treated with D, and now we have 1,019 with a constant increase in the number of patients with ESRD and a need for D and renal transplantation. Mortality per year at the different Centers ranged from 8-19% in 1999 and the average is 12%.
Glomerulonephritis (GN) – both primary and secondary – is the main cause of renal failure (RF) in some Centers up to 45%. Tubulo-interstitial disease follows GN. ADPKD patients constitute 9.4% with a difference among the Centers of 3-29%, and diabetic nephropathy is found in 10%, 5-15% in different Centers. 11-61% of patients have an unknown etiology.
352 patients are on treatment with human recombinant erythropoietin (rhuEPO) – in some Centers up to 60%. The mode of application was subcutaneous and the initial dose is 20 U/kg body weight and the mean maintenance dose of EPO per patient weekly is 4,000 U.
The Cimino-Brescia arteriovenous fistula is being applied as a standard vascular access. The survival rate of our patients treated with maintenance HD at 5 years was 58%. CAPD and particularly renal transplantation are to be further developed as alternative methods in treating terminal renal failure. (Int J Artif Organs 2002; 25: 386-90)

KEY WORDS: Chronic renal failure, Hemodialysis, CAPD, EPO, Survival

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Fig. 11 – Polenaković MH on behalf of the Dialysis Working Group. Dialysis in adults in year 2000 in the Republic of Macedonia. The International Journal of Artificial Organs. 2002; 25(5): 386–90

МАК МЕД ПРЕГЛЕД 2001; 55 (СУПЛЕМЕНТ 49): 255-256

Еритропоетин во лекувањето на бубрежна анемија

Поленаковиќ М.

Richard Bright во 1835 год. прв ја опишал поврзаноста помеѓу анемијата и хроничната бубрежна инсуфициенција. Понатамошните студии потврдиле дека еритропоезата е поврзана со бубрезите преку продукцијата на хормонот еритропоетин кој е главен регулатор на создавањето на еритроцитите во коскениот мозок. Секое оштетување на бубрезите кое ги вклучува и клетките одговорни за синтеза на еритропоетинот и неговата физиолошка контрола ќе предизвика хипопролиферативна анемија чиј што интензитет корелира со степенот на намалување на бубрежната функција. Многу од регистрираниот морбидитет и морталитет кај пациентите со бубрежна инсуфициенција се должи на последиците од анемијата.

Кај возрасна машка особа хемоглобинот е 13,5-18 г/дл, а кај женска 11,5-16 г/дл. Кај мажи хематокритот изнесува 0,40-0,54%, а кај жени 0,37-0,47%, еритроцитите кај мажи се помеѓу 4.500.000-6.500.000/мм³, а кај жени помеѓу 3.900.000 и 5.600.000/мм³. Овие основни вредности треба да се имаат на ум при оцена на постоење на анемија и започнување на лекувањето на истата со еритропоетин.

Во 1986 год. за прв пат е клинички употребен, произведен по пат на генетско инженерство, рекомбинантен хуман еритропоетин (rHu EPO), во лекување на анемијата кај хроничната бубрежна инсуфициенција. Бројни мултицентрични студии и широка примена на еритропоетинот во лекувањето на анемијата кај хроничната бубрежна инсуфициенција ги покажаа сите позитивни и негативни дејства на еритропоетинот како и неговата незаменлива улога во лекувањето на болни со хронична бубрежна инсуфициенција. Организирана примена на rHu EPO во лекувањето на бубрежната анемија започна во 1990 год. во Р.Македонија. Имавме можност да учествуваме во интернационалната мултицентрична студија со rHu EPO кај пациенти на хемодијализа насловена: „Контролирана клиничка студија за влијанието на субкутаната ЕПО терапија врз морбидитетот и клиничката толеранција кај пациенти со терминална бубрежна инсуфициенција на лекување со хемодијализа". Еритропоетинот, Recormon (R), употребен за клиничките испитувања го обезбеди производителот Boehringer-Mannheim од Германија. 40 пациенти лекувани со хемодијализа од Клиниката за нефрологија влегоа во студијата. Анемија со хематокрит пониок од 28 вол% беше критериум за вклучување во студијата. Се целеше со субкутано давање на ЕПО – Recormon (R), 3 x 20 единици на килограм телесна тежина, на 10 минути пред секоја хемодијализа да се достигне саканиот хематокрит од 30-35 вол%. Карактеристично за оваа мултицентрична студија, во која земаа учество клиники од Бугарија, Чехословачка, Полска, Источна Германија, Советскиот Сојуз, Унгарија и Југославија, партиципираше само Клиниката за нефрологија од Скопје, беше субкутано давање на ЕПО и бавно покачување на хематокритот за да се избегнат несаканите дејства. Нашето искуство од оваа студија за прв пат го соопштивме во текот на Научниот симпозиум по повод 20 години хронична хемодијализа во Македонија – „Нефрологија денес и утре", одржан во Македонската академија на науките и уметностите, на 16 и 17. 05. 1991 г. а отпечатен во Македонски медицински преглед, Суплемент 12, стр. 65-74, 1993. Нашите резултати и искуства во лекувањето на бубрежната анемија со ЕПО ги соопштивме во повеќе домашни и странски списанија. Дел од резултатите беа соопштени во текот на Првиот Конгрес на Македонското здружение за нефрологија, дијализа, трансплантација и вештачки органи и отпечатен како Зборник на трудови во Македонски медицински преглед, суплемент 14, 1994, насловен „Нефрологија '93" и под заглавие „Еритропоетин". Кардиоваскуларните ефекти на терапијата со еритропоетин се дадени на Табела 1.

Fig. 12 – Polenakovic M. Erythropoietin in treatment of renal anemia Nefrologija 2000, Macedonian Medical Review. 2001; 55 (suppl. 49): 255–6

He introduced the treatment with erithropoetin (EPO) in patients with anemia and chronic renal disease, as well as on hemodialysis. His publications about the survival of red blood cells and EPO and heart morphology before and after treatment with EPO are well known.

Artificial Organs
17(12):977–984, Blackwell Scientific Publications, Inc., Boston

Analysis of Heart Morphology and Function Following Erythropoietin Treatment of Anemic Dialysis Patients

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Fig. 13 – Sikole A, Polenakovic M, Spirovska V, Polenakovic B, Masin G. Analysis of Heart Morphology and Function Following Erythropoietin Treatment of Anemic Dialysis Patients. Artificial Organs. 1993; 17(12): 977–84


Is Erythropoietin a Survival Factor for Red Blood Cells?

Fig. 14 – Polenakovic M, Sikole A. Is Erythropoietin a Survival Factor for Red Blood Cells? Journal of the American Society of Nephrology. 1996; 7(8): 1178–82

In the beginning of 1970s, he introduced the percutaneous renal biopsy and the examination of the received renal tissue with light, fluorescent and electronic microscopy, among the first in former Yugoslavia. That way, he performed the classification of primary and secondary glomerulonephritis. Thanks to these methods the treatment of glomerulonephritis improved with the most advanced therapy, with immunosuppressive therapy and plasmapheresis.

УНИВЕРЗИТЕТ „КИРИЛ И МЕТОДИЈ“ — СКОПЈЕ

М. Поленаковиќ, Д. Хрисохо, Д. Димчевски

ИЗВЕДУВАЊЕ НА ПЕРКУТАНА БУБРЕЖНА БИОПСИЈА СО „TRU-CUT“ ИГЛА ЗА БИОПСИЈА СО ПОМОШ НА ДИЈАСКОПИЈА НА TV МОНИТОР

ГОДИШЕН ЗБОРНИК НА МЕДИЦИНСКИОТ ФАКУЛТЕТ СКОПЈЕ, 1975

ТОМ XXI VOL. XXI

ИНТЕРНА КЛИНИКА — НЕФРОЛОШКИ ОДДЕЛ И ИНСТИТУТ ЗА РАДИОЛОГИЈА И ОНКОЛОГИЈА ПРИ МЕДИЦИНСКИОТ ФАКУЛТЕТ — СКОПЈЕ

ИЗВЕДУВАЊЕ НА ПЕРКУТАНА БУБРЕЖНА БИОПСИЈА СО „TRU-CUT“ ИГЛА ЗА БИОПСИЈА СО ПОМОШ НА ДИЈАСКОПИЈА НА TV МОНИТОР

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Перкутаната бубрежна биопсија (PBB) е метода којашто придонесува за поставувањето морфолошка и имунолошка дијагноза, а со тоа и на евалуацијата на дифузните бубрежни болести во текот на животот на пациентот.

Од првите пишувани сопштувања за PBB — 1950[1] и 1952[2] година техниката на PBB се усовршила и се упростила, така што таа денеска е составен и незаменлив дел на клинички-морфолошката оцена на пациентите со бубрежни болести.[3, 4, 5, 6, 7]

Целта на овој труд е да се изнесе нашето клиничко искуство и резултатите што се добиени со примената на „TRU-CUT“ иглата за PBB, користејќи ја при работата дијаскопијата на TV мониторот.

МЕТОД

Внимателен избор на пациент за PBB, пред и по биопсионата нега, како и изведувањето на самата PBB е можно само од опитен лекар.

Индикациите, контраиндикациите како и компликациите врзани за PBB се познати.[3, 4, 5, 8]

Основниот услов за успешната PBB е точната локализација на позицијата на бубрегот и неговата длабочина, избегнување озледа на бубрегот и околните органи, како и добивање доволен број гломерули за адекватна морфолошка оцена.

За изведувањето на PBB ја користиме техниката што е опишана од Карк и соработниците[3, 4, 5]. Употребена е „Tru-Cut“ игла за биопсија, произведена од Travenol; наменета е само за една употреба (Diaposable biopsy geedle). Иглата се состои од два метални цилиндрични дела. Надворешниот е празен. Тој е како цевка, а се вика какула. Во него влегува внатрешниот цилиндричен дел којшто е од полн метал. Овој дел ја затво-

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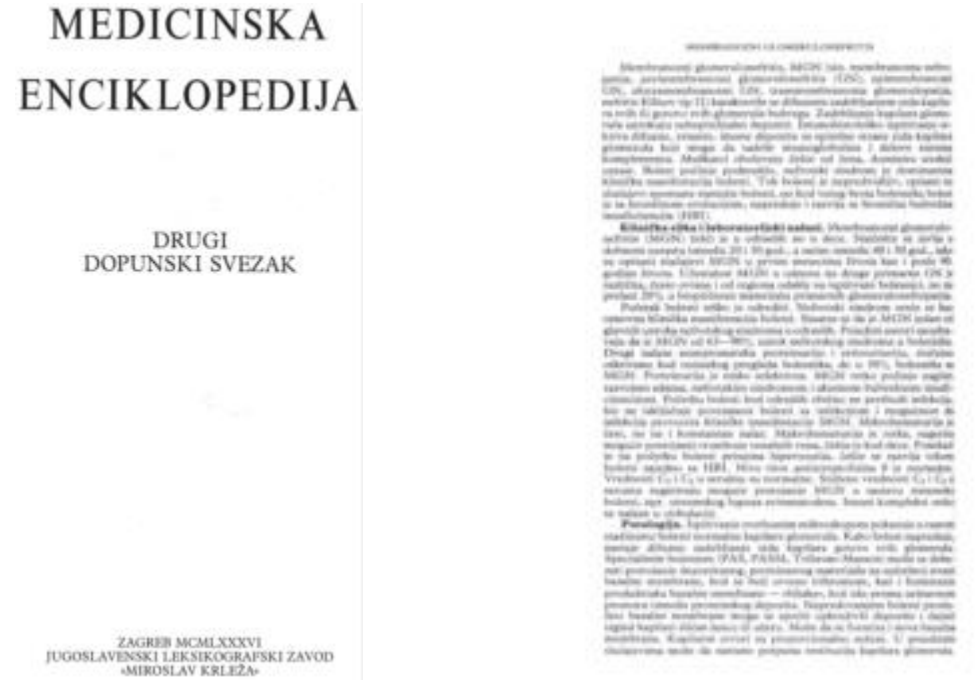
Fig. 15 – Polenakovic M., Hrisoho D., Dimchevski D. Application and Clinical Experience in Performing Percutaneous Renal Biopsy Using the "Tru–Cut" Renal Biopsy Needle and Television Monitored Fluoroscopy. Annual of the Medcial Faculty in Skopje. 1975; XXI: 71–7

Having in mind his experience in research of glomerulonephritis he was invited by the editors of the Medical Encyclopedia from Zagreb, Croatia to write a chapter about Membranous nephropathy and IgA nephropathy in the *Medicinska enciklopedija* (Jugoslavenski leksikografski zavod, Zagreb, Medical Encyclopedia).

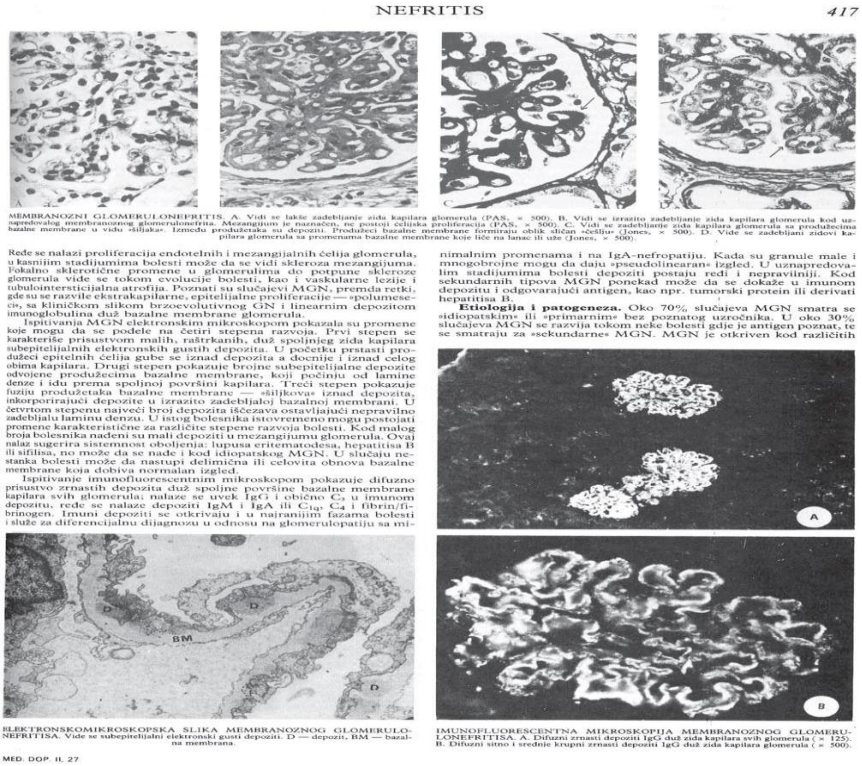


MEDICINSKA ENCIKLOPEDIJA

DRUGI DOPUNSKI SVEZAK

ZAGREB MCMLXXXVI
JUGOSLAVENSKI LEKSIKOGRAFSKI ZAVOD «MIROSLAV KRLEŽA»

Fig. 16 – Medicinska enciklopedija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MEMBRANOZNI GLOMERULONEFRITIS. A. Vidi se lakše zadebljanje zida kapilara glomerula (PAS, × 500). B. Vidi se izrazito zadebljanje zida kapilara glomerula kod uznapredovalog membranoznog glomerulonefritisa. Mezangijum je nepromenjen, ne postoji ćelijska proliferacija (PAS, × 500). C. Vidi se zadebljanje zida kapilara glomerula sa produženim bazalne membrane u vidu »šiljaka«. Između produženja su depoziti. Produženi bazalne membrane formiraju oblik sličan »češlju« (Jones, × 500). D. Vide se zadebljani zidovi kapilara glomerula sa promenama bazalne membrane koje liče na lanac ili uže (Jones, × 500).

Rede se nalazi proliferacija endotelnih i mezangijalnih ćelija glomerula, u kasnijim stadijumima bolesti može da se vidi skleroza mezangijuma. Fokalno skleротične promene u glomerulima do potpune skleroze glomerula vide se tokom evolucije bolesti, kao i vaskularne lezije i tubulointersticijalna atrofija. Poznati su slučajevi MGN, premda retki, gde su se razvile ekstrakapilarne, epitelijalne proliferacije — »polumesec«, sa kliničkom slikom brzoevolutivnog GN i linearnim depozitom imunoglobulina duž bazalne membrane glomerula.

Ispitivanja MGN elektronskim mikroskopom pokazala su promene koje mogu da se podele na četiri stepena razvoja. Prvi stepen se karakteriše prisustvom malih, raštrkanih, duž spoljnjeg zida kapilara subepitelijalnih elektronskih gustih depozita. U početku prstasti produženi epitelnih ćelija gube se iznad depozita a docnije i iznad celog obima kapilara. Drugi stepen pokazuje brojne subepitelijalne depozite odvojene produženima bazalne membrane, koji počinju od lamine densе i idu prema spoljnoj površini kapilara. Treći stepen pokazuje fuziju produžetaka bazalne membrane — »šiljkova« iznad depozita, inkorporirajući depozite u izrazito zadebljalu bazalnoj membrani. U četvrtom stepenu najveći broj depozita iščezava ostavljajući nepravilno zadebljalu lamina densu. U istog bolesnika istovremeno mogu postojati promene karakteristične za različite stepene razvoja bolesti. Kod malog broja bolesnika nađeni su mali depoziti u mezangijumu glomerula. Ovaj nalaz sugerira sistemnost oboljenja: lupusa eritematodesa, hepatitisa B ili sifilisa, no može da se nađe i kod idiopatskog MGN. U slučaju nestanka bolesti može da nastupi delimična ili celovita obnova bazalne membrane koja dobiva normalan izgled.

Ispitivanje imunofluorescentnim mikroskopom pokazuje difuzno prisustvo zrnastih depozita duž spoljne površine bazalne membrane kapilara svih glomerula: nalaze se uvek IgG i obično C_3 u imunom depozitu, rede se nalaze depoziti IgM i IgA ili C_{1q}, C_4 i fibrin/fibrinogen. Imuni depoziti se otkrivaju i u najranijim fazama bolesti i služe za diferencijalnu dijagnozu u odnosu na glomerulopatiju sa minimalnim promenama i na IgA-nefropatiju. Kada su granule male i mnogobrojne mogu da daju »pseudolinearan« izgled. U uznapredovalim stadijumima bolesti depoziti postaju redi i nepravilniji. Kod sekundarnih tipova MGN ponekad može da se dokaže u imunom depozitu i odgovarajući antigen, kao npr. tumorski protein ili derivati hepatitisa B.

Etiologija i patogeneza. Oko 70% slučajeva MGN smatra se »idiopatskim« ili »primarnim« bez poznatog uzročnika. U oko 30% slučajeva MGN se razvija tokom neke bolesti gde je antigen poznat, te se smatraju za »sekundarne« MGN. MGN je otkriven kod različitih

ELEKTRONSKOMIKROSKOPSKA SLIKA MEMBRANOZNOG GLOMERULONEFRITISA. Vide se subepitelijalni elektronski gusti depoziti. D — depoziti, BM — bazalna membrana.

IMUNOFLUORESCENTNA MIKROSKOPIJA MEMBRANOZNOG GLOMERULONEFRITISA. A. Difuzni zrnasti depoziti IgG duž zida kapilara svih glomerula (× 125). B. Difuzni sitno i srednje krupni zrnasti depoziti IgG duž zida kapilara glomerula (× 500).

MED. DOP. II, 27

Fig. 17 – Polenaković M. Membranous Glomerulonephritis. Medicinska enciklopedija, Drugi dopunski svezak, Zagreb, Jugoslavenski Leksikografski zavod "Miroslav Krleža", MCMLXXXVI: 416–8

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infektivnih bolesti kao npr. hepatitisa B, sifilisa (kongenitalni i sekundarni), lepre, šistosomijaze, filarijaze; kod multisistemskih bolesti, npr. sistemskog lupusa eritematodesa, reumatoidnog artritisa, mešovite bolesti vezivnog tkiva, dermatomiozitisa, sarkoidoze; kod neoplazmi — karcinoma (pluća, kolona, želuca i dr.), limfoma i rede leukemija; za vreme primene lekova, npr. zlata, žive, D-penicilamina, trietadiona, probenecida i kaptoprila. MGN je zapažen kod heredofamilijarnih i metabolnih bolesti kao i kod hroničnog odbacivanja bubrega. Ovi »sekundarni« MGN služe kao model za stvaranje imunokompleksa GN, gde može da se otkrije specifični antigen sugeriran kliničkom slikom, za razliku od »idiopatskog« MGN gde to nije, za sada, moguće.

Mišljenja o patogenezi MGN su kontroverzna. Morfološke karakteristike MGN idu u prilog imunokompleksa GN. Sugerira se da endogeni ili egzogeni antigeni izazivaju formiranje protutela, zatim se stvaraju u cirkulaciji imuni kompleksi koji se talože iz cirkulacije duž kapilara glomerula i uzrokuju GN. Druga teorija sugerira mogućnost kombinacije slobodnih protutela iz cirkulacije sa antigenima prethodno lociranim na epitelnoj strani zida kapilara glomerula i in situ stvaranjem imunih kompleksa koji dalje uzrokuju GN. Ispitivanje sistema HLA sugerira da postoji genetska osnova za osetljivost prema bolesti. Saopštava se da je idiopatski MGN povezan sa HLA-B_8, B_{18} ili sa DR3. Saopštava se da je HLA-DR 3 nađen u 67—76% bolesnika sa MGN u odnosu na 21% zdravih belaca. Ispitivanja učinjena u Velikoj Britaniji ukazuje na povezanost MGN s haplotipom HLA-DR 3, B_{18} i BF_1. Ustanovljena je i znatno veća učestalost MT 2 kod bolesnika sa idiopatskim MGN no kod zdravih lica.

Tok i prognoza. MGN je bolest sa nepredvidljivim tokom, ona ne zavisi mnogo od primenjene terapije. Spontana remisija može da nastane do u 25% slučajeva bolesnika; 25—50% bolesnika dugo vremena mogu da imaju samo početne manifestacije bez evolucije u hroničnu bubrežnu insuficijenciju (HBI). Ima slučajeva povlačenja nefrotskog sindroma, no sa dugotrajnim ostacima blage proteinurije. Bolest u značajnom broju slučajeva evoluira do HBI; tako tokom 5—10 god., od otkrivanja MGN, oko 25% bolesnika razvija HBI, a drugi posle 10—20 god., čak i docnije. Kod odraslih se saopštava o razvoju HBI u 30—60% bolesnika sa MGN. Kod dece prognoza je bolja, osobito ako su mlada od 5 god., evolucija prema HBI je do 10%. Hipertenzija, koja je retko prisutna u početku bolesti, razvija se tokom bolesti i do u 30% bolesnika. Tromboza renalnih vena češća je kod MGN no kod ostalih GN. Često je klinički latentna, pogoršava tok MGN i može da izazove tromboembolične komplikacije; prevladava mišljenje da je sekundarna na MGN. Izračunato je da do 76% bolesnika sa MGN preživljava prvih 10 god., od otkrivanja bolesti.

Lečenje. Saopštava se da je davanje kortikosteroida u početku idiopatskog MGN sa nefrotskim sindromom i sačuvanom bubrežnom funkcijom reduciralo proteinuriju i usporilo pojavu HBI. Uloga citostatika u lečenju još nije tačno definisana. Kod sekundarnih formi MGN primenjuje se lečenje osnovne bolesti. Rekurentnost MGN na presađeni bubreg nije kontraindikacija za transplantaciju.

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M. Polenaković

NEFROPATIJA IgA

IgA-nefropatiju (sin. IgA-IgG-glomerulonefritis, IgA-nefritis, IgA-IgG nefropatija, mezangijalni IgA-glomerulonefritis, Bergerova bolest) prvi put su opisali 1968. god. Berger i Hinglais. Nađen je karakterističan imunohistološki nalaz, konstantno i dominantno prisustvo zrnastih depozita IgA u mezangijumu svih glomerula, bez obzira na histološke promene, u oduševa sistemske bolesti. Pacijenti, češće muškog pola, obično u drugoj ili trećoj deceniji života, imaju rekurentnu makroskopsku hematuriju ili mikroskopsku hematuriju sa proteinurijom. Tok bolesti je hroničan, sa sporom evolucijom ka hroničnoj bubrežnoj insuficijenciji.

Klinička slika i laboratorijski nalazi. Učestalost IgA-nefropatije varira između 3,8—25% u bioptičnom materijalu primarnih glomerulonefrita. U Francuskoj je jedna od najčešćih glomerulskih bolesti, slična je incidentnost i u Australiji, Italiji i Japanu, dok je manje zastupljena u Severnoj Americi i Velikoj Britaniji. I u našoj zemlji sponinje se među učestalijim glomerulonefritima.

Otkriva se u mladih osoba, najčešće uzrasta između 19—30 god., iako su opservirani slučajevi i kod dece uzrasta od 3—8 god., i kod starijih osoba. Muškarci češće obolevaju od žena. Familijarna zastupljenost je retka.

Rekurentna ili perzistentna hematurija najčešće se sreću kao klinička prezentacija bolesti. Jedna trećina bolesnika ima makrohematuriju koja je obično povezana sa infekcijama gornjeg respiratornog trakta,

NEFROPATIJA IgA. Proliferacija mezangija glomerula (PAS × 200).

gastrointestinalnog ili urinarnog sistema. Ređa je posle ekstremnog fizičkog napora ili posle imunizacije. Učestalija je na početku bolesti nego kasnije. Karakteristično je da se makrohematurija pojavljuje posle infekcije ili napora u toku nekoliko časova, najčešće tokom prva dva dana. Ovaj kratki interval razlikuje IgA-nefropatiju od poststreptokokog glomerulonefritisa, kod kojega interval između infekcije i hematurije obično traje između 10—14 dana. Makrohematuriju mogu da prate bolovi u abdomenu, slabinama, mišićima, rede dizurija, osećaj malaksalosti a povremeno i povišena telesna temperatura. Između pojava makrohematurije obično perzistira mikrohematurija i proteinurija, iako povremeno mogu da budu odsutne. Vremenski intervali između pojava makrohematurije su različiti. Kod polovine bolesnika postoji na početku bolesti samo proteinurija i mikrohematurija. U ovih bolesnika bolest može da se otkrije samo preko analize urina. IgA-nefropatija rede počinje kao akutni glomerulonefritis, sa hematurijom, edemima, bubrežnom insuficijencijom i hipertenzijom. Ponekad bolest može da se otkrije pri ispitivanju uzroka hipertenzije i hronične bubrežne insuficijencije.

Proteinurija je umerena, obično nije veća od 1 g/24 h, retko je tako obilna da izazove nefrotski sindrom. Nalaz eritrocita i granuliranih cilindara u urinu ukazuje na parenhimno oštećenje bubrega a ne na urološku genezu hematurije za kojom se često nepotrebno traga. Nivo IgA, kao i povišeni nivo IgA-imunokompleksa. C_3 i C_4 u serumu obično su normalni. C_3 proaktivator (Faktor B) je normalan. Mogu se naći IgA, kao i povišeni nivo IgA imunokompleksa. C_3 i C_4 u serumu obično su normalni. C_3 proaktivator (Faktor B) je normalan. Mogu se naći uvećene vrednosti fragmenata C_3 u serumu što sugerira aktivaciju C_3 in vivo najverovatnije alternativnim putem. Kod ove nefropatije opisana je aktivacija sistema komplementa alternativnim putem, pomoću hlađenja. Zapaženo je da su HLA-antigeni, i to HLA-Bw 35 u Francuskoj, B 12 u SAD i HLA-DR_4 u Japanu učestaliji u ovih bolesnika no u ostaloj populaciji.

Patologija. Ispitivanjem bubrežne biopsije svetlosnim mikroskopom vidi se karakteristično uvećanje mezangijuma, koje difuzno zahvata skoro sve lobuluse glomerula. Konstantno je povećan mezangijalni matriks, pridružen nejednakom proliferacijom mezangijalnih ćelija u tubulusima. Ovaj nalaz ranije je često opisivan kao fokalni glomerulonefritis. Bojenje trihromom (Masson) pokazuje »fibrinoidne« depozite u mezangijumu. Ako ne postoje segmentne lezije, dobija se izgled mezangijalnog glomerulonefritisa, a u blagim slučajevima pro-

ELEKTRONSKOMIKROSKOPSKA SLIKA NEFROPATIJE IgA. Mezangijalni elektronski gusti depoziti. D — depozit, M — mezangij, UP — urinarni prostor, KL — kapilarni lumen (× 14 600, prof. Grozdev).

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Unilateral Renal Vein Occlusion in Rats[1]

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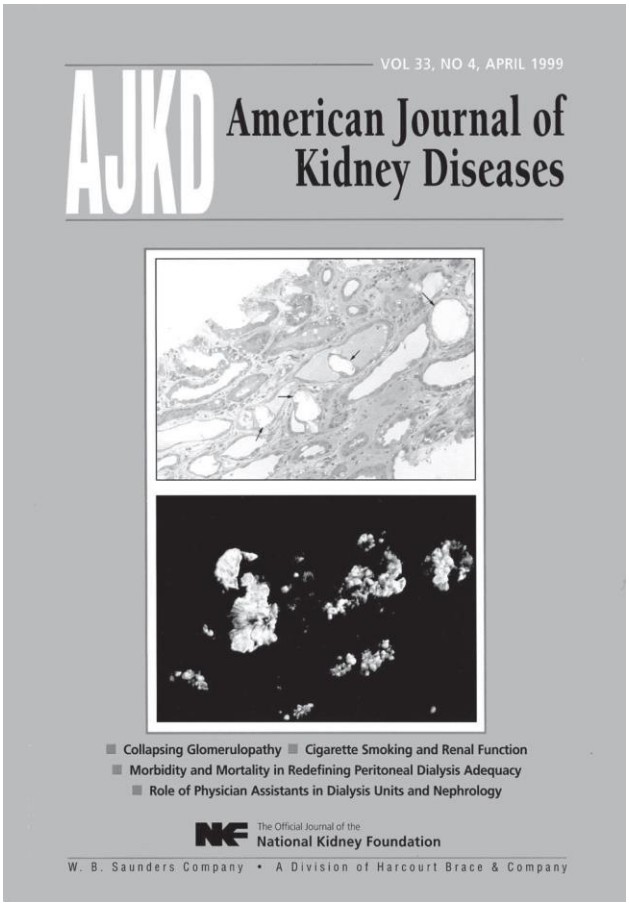
Key Words. Renal vein · Thrombosis · Occlusion · Rats · Experimental electromicroscopic immunofluorescent

Abstract. To study the relationship of renal vein thrombosis to membranous glomerulonephritis with the nephrotic syndrome, we attempted to simulate the former by occluding to 0.5 mm one renal vein in rats. Although increased proteinuria did occur during the first 3 days after such occlusion, there was little difference from control animals in the amount of proteinuria thereafter, up to 46 days, and no evidence of membranous glomerulonephritis by light, immunofluorescent, or electron microscopy.

Fig. 19 – Polenaković M, Ganote ChE, Potter EV, Jennings RB. Unilateral Renal Vein Occlusion in Rats. Nephron. 1985; 40: 91–5




ORIGINAL INVESTIGATIONS

Collapsing Glomerulopathy: Clinical Characteristics and Follow-Up

Ladislava Grcevska, MD, and Momir Polenakovik, MD

Editorial, p. 801

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Treatment and Long-Term Follow-Up of Patients With Stage II to III Idiopathic Membranous Nephropathy

Momir H. Polenakovik, MD, PhD, and Ladislava Grcevska, MD

• Many important aspects of the therapeutic approach to patients with idiopathic membranous nephropathy are still controversial. There are several reports that the effectiveness of therapy depends on histological staging and severity of interstitial mononuclear cell infiltration. We used several different treatments in 39 patients with stage II to III primary membranous nephropathy with proteinuria more than 2.5 g/d, without hypertension and chronic renal failure at biopsy. Ten patients were not treated, 13 were treated with only steroids, 13 with alternate use of steroids and chlorambucil, and three with cyclosporine A. The follow-up period was 5 to 10 years. Statistics included Kruskall-Wallis and one-way ANOVA analysis. A significant decrease in proteinuria was noted in patients treated with steroids ($P < 0.01$), from 8.45 ± 1.04 g/d (mean ± SEM) to 1.42 ± 0,45 g/d after follow-up of 5 years and in patients treated with steroids and chlorambucil (12.9 ± 2.4 g/d [mean ± SEM] to 2.46 ± 1.38 g/d). Compared with patients treated with steroids (15.3%) and patients treated with steroids and chlorambucil (15.3%), untreated patients had a high frequency of chronic renal failure after 5 years of follow-up (70%) and had a significant increase in mean serum creatinine ($P = 0.008$). We conclude that steroid therapy alone, or associated with chlorambucil, is effective in patients with stage II to III membranous nephropathy. Patients responded with a decrease of proteinuria and stable renal function during the long-term follow-up period. The group of patients treated with cyclosporine A was too small to analyze.

INDEX WORDS: Membranous nephropathy; steroids; chlorambucil.

IDIOPATHIC MEMBRANOUS nephropathy is a common cause of nephrotic syndrome in adults.[1-5] Renal function may remain stable for long periods, and spontaneous remissions of nephrotic syndrome can occur, but there also are patients who are disabled by or even die of complications related to nephrotic syndrome or progressive chronic renal failure.[4-7] The role of steroid and cytotoxic agents for treating idiopathic membranous nephropathy remains controversial.[7-18] Research studies have shown varying degrees of effectiveness of steroid therapy on different stages of glomerular changes in membranous nephropathy and different degrees of interstitial infiltration.[10,17]

To avoid the influence of histological staging and severity of tubulointerstitial changes, several treatment methods were used for 39 patients with stage II to III idiopathic membranous nephropathy, without significant tubulointerstitial changes, with proteinuria more than 2.5 g/d, and without hypertension and chronic renal failure at the start of treatment.

PATIENTS AND METHODS

Patient Selection

Thirty-nine white patients (26 men and 13 women; ages 33.2 ± 11.5 years) with stage II to III idiopathic membranous nephropathy documented by standard histopathologic procedures were included in the study. Stage II to III membranous nephropathy was defined by optical microscopy silver stain which showed interruption of the outer aspects of capillary loop interrupted by numerous basement membrane "spikes," and by the presence of numerous epimembranous electron-dense immune deposits separated by "spikes" of basement membrane material on electron microscopy (Fig 1). Tubulointerstitial changes were absent or slight and were graded semiquantitatively as 0 or ±. Both glomerular and tubulointerstitial changes were analyzed by two pathologists. The total number of glomeruli per section for optical microscopy was 10 to 25, for electron microscopy, 1 to 3. All patients had normal renal function and no hypertension at biopsy, and all had greater than 2.5 g/d proteinuria. Patients with systemic disorders (eg, malignancies, diabetes, chronic infections, rheumatologic diseases, and congestive heart failure) were excluded. Proteinuria equal to or greater than 3.5 g/d was considered nephrotic. Chronic renal failure was defined as serum creatinine higher than 110 μmol/L or a 50% reduction in clearance from normal. End-stage renal failure was the start of hemodialysis treatment.

Treatment Protocols

Group 1. Ten patients were treated with a low-salt diet and, if necessary, diuretics and plasma infusions. Eight of these patients refused specific treatment, and treatment was believed to be contraindicated in the other two patients

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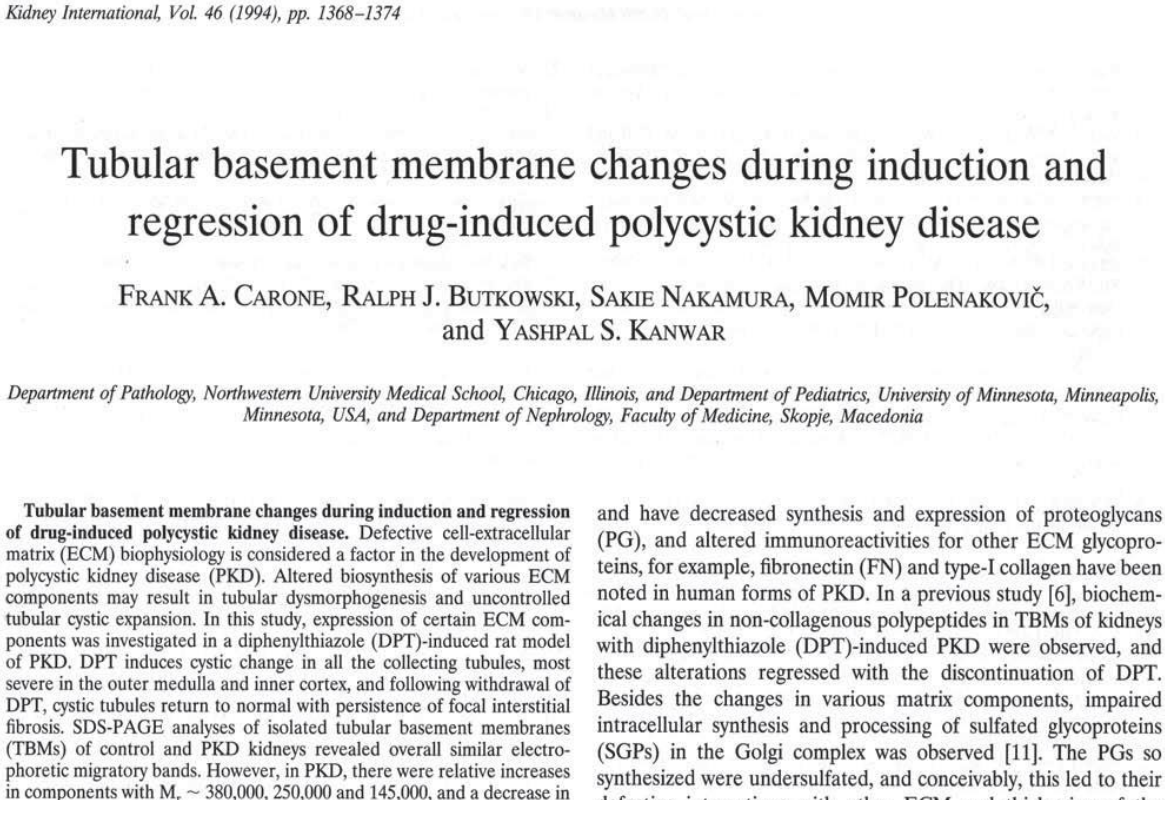

Kidney International, Vol. 46 (1994), pp. 1368–1374

Tubular basement membrane changes during induction and regression of drug-induced polycystic kidney disease

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Tubular basement membrane changes during induction and regression of drug-induced polycystic kidney disease. Defective cell-extracellular matrix (ECM) biophysiology is considered a factor in the development of polycystic kidney disease (PKD). Altered biosynthesis of various ECM components may result in tubular dysmorphogenesis and uncontrolled tubular cystic expansion. In this study, expression of certain ECM components was investigated in a diphenylthiazole (DPT)-induced rat model of PKD. DPT induces cystic change in all the collecting tubules, most severe in the outer medulla and inner cortex, and following withdrawal of DPT, cystic tubules return to normal with persistence of focal interstitial fibrosis. SDS-PAGE analyses of isolated tubular basement membranes (TBMs) of control and PKD kidneys revealed overall similar electrophoretic migratory bands. However, in PKD, there were relative increases in components with M, ~ 380,000, 250,000 and 145,000, and a decrease in and have decreased synthesis and expression of proteoglycans (PG), and altered immunoreactivities for other ECM glycoproteins, for example, fibronectin (FN) and type-I collagen have been noted in human forms of PKD. In a previous study [6], biochemical changes in non-collagenous polypeptides in TBMs of kidneys with diphenylthiazole (DPT)-induced PKD were observed, and these alterations regressed with the discontinuation of DPT. Besides the changes in various matrix components, impaired intracellular synthesis and processing of sulfated glycoproteins (SGPs) in the Golgi complex was observed [11]. The PGs so synthesized were undersulfated, and conceivably, this led to their

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Nephrol Dial Transplant (2003) 18 [Suppl 5]: v26–v27
DOI: 10.1093/ndt/gfg1039

Nephrology
Dialysis
Transplantation

The incidence of biopsy-proven primary glomerulonephritis in the Republic of Macedonia—long-term follow-up

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Abstract

In order to define the type of renal disease, renal biopsy was performed in 1304 patients, aged 14–72 years. Their biopsies were processed for light and immunofluorescence microscopy, and electron microscopy in some cases. The diagnosis of primary glomerular disease was confirmed in 716 patients with the following incidence: minimal change nephrotic syndrome in 52 (7.2%), focal segmental glomerulosclerosis in 72 (9.9%), membranous nephropathy in 97 (13.5%), IgA nephropathy in 85 (11.8%), diffuse mesangial glomerulonephritis (GN) without IgA in 32 (4.4%), focal mesangial GN in 97 (13.5%), membranoproliferative GN in 59 (8.4%), acute GN in 88 (12.3%), crescentic GN in 53 (7.4%) and sclerosing GN in 46 patients (6.4%).

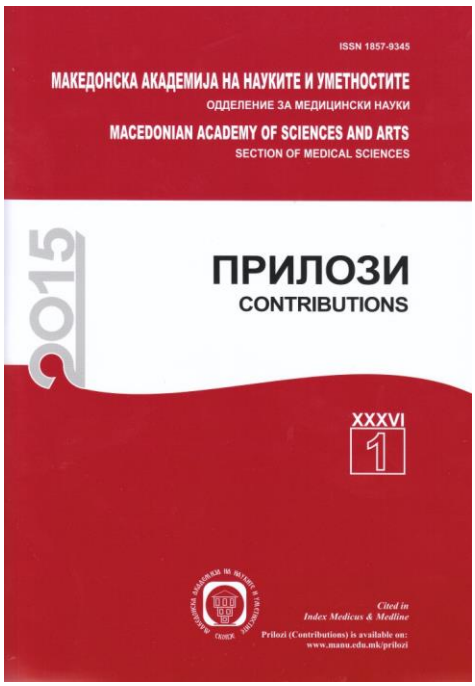
Subjects and methods

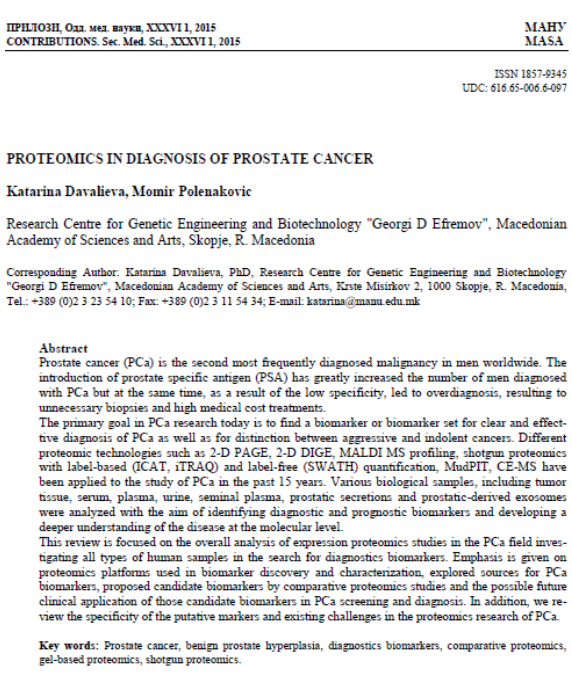
This is a single-centre retrospective study. Renal biopsy specimens of adult patients with primary GN were selected from 1304 percutaneous renal biopsies, performed at the Department of Nephrology, Skopje, Macedonia over a period of 26 years (1975–2001). All the biopsies were evaluated by light microscopy and immunofluorescence, using standard procedures. Electron microscopy was only available during 1980–1983 and 1993–1998. Churg (WHO) classification was performed after exclusion of systemic diseases or underlying abnormalities [8].

Results

Fig. 23 – Polenakovic MH, Grcevska L, Dzikova S. The incidence of biopsy-proven primary glomerulonephritis in the Republic of Macedonia – long-term follow-up. Nephrology Dialysis Transplantation. 2003; 18(Suppl 5): 26–7

In the last years, Acad. Momir Polenakovic as Head of the Research Center for Genetic Engineering and Biotechnology at the Macedonian Academy of Sciences and Arts is mainly involved in the genetic and proteomic investigation of HCV and prostate cancer.





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PROTEOMICS IN DIAGNOSIS OF PROSTATE CANCER

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Abstract

Prostate cancer (PCa) is the second most frequently diagnosed malignancy in men worldwide. The introduction of prostate specific antigen (PSA) has greatly increased the number of men diagnosed with PCa but at the same time, as a result of the low specificity, led to overdiagnosis, resulting to unnecessary biopsies and high medical cost treatments.

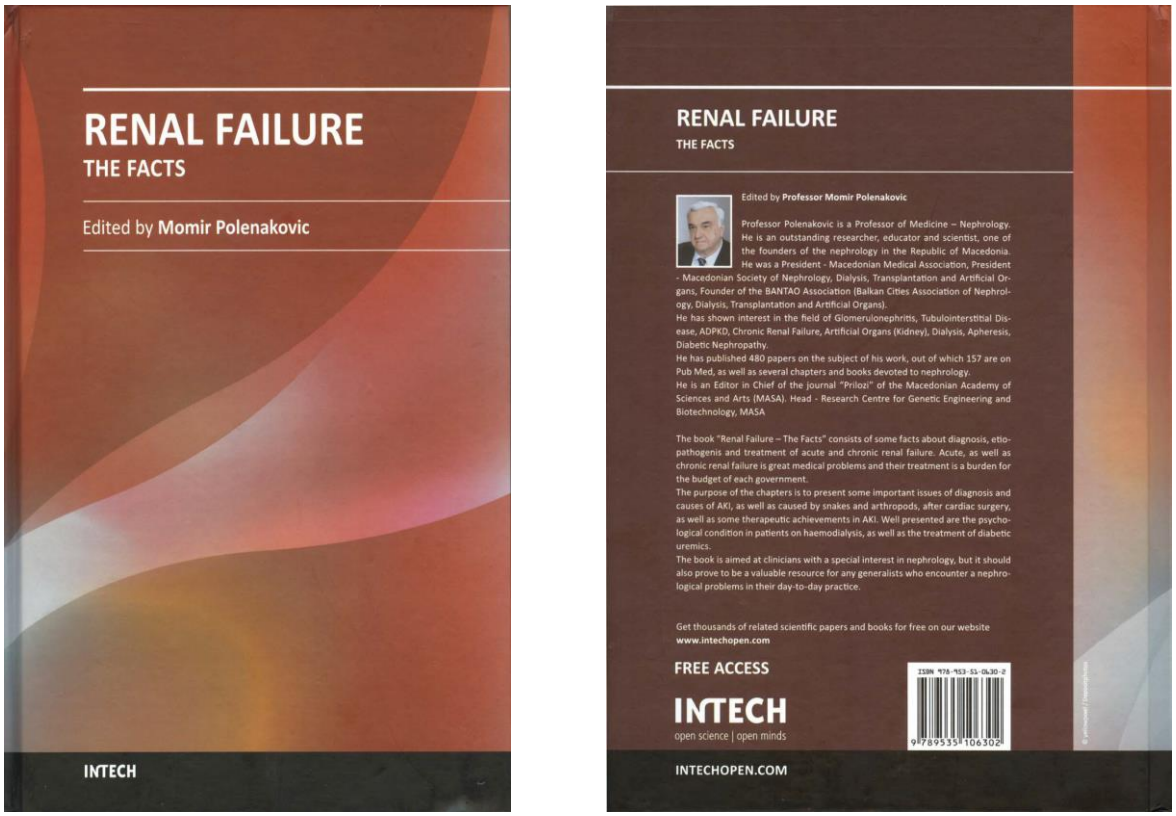
The primary goal in PCa research today is to find a biomarker or biomarker set for clear and effective diagnosis of PCa as well as for distinction between aggressive and indolent cancers. Different proteomic technologies such as 2-D PAGE, 2-D DIGE, MALDI MS profiling, shotgun proteomics with label-based (ICAT, iTRAQ) and label-free (SWATH) quantification, MudPIT, CE-MS have been applied to the study of PCa in the past 15 years. Various biological samples, including tumor tissue, serum, plasma, urine, seminal plasma, prostatic secretions and prostatic-derived exosomes were analyzed with the aim of identifying diagnostic and prognostic biomarkers and developing a deeper understanding of the disease at the molecular level.

This review is focused on the overall analysis of expression proteomics studies in the PCa field investigating all types of human samples in the search for diagnostics biomarkers. Emphasis is given on proteomics platforms used in biomarker discovery and characterization, explored sources for PCa biomarkers, proposed candidate biomarkers by comparative proteomics studies and the possible future clinical application of those candidate biomarkers in PCa screening and diagnosis. In addition, we review the specificity of the putative markers and existing challenges in the proteomics research of PCa.

Key words: Prostate cancer, benign prostate hyperplasia, diagnostics biomarkers, comparative proteomics, gel-based proteomics, shotgun proteomics.

Fig. 24 – Katarina Davalieva, Momir Polenakovic. Proteomics in diagnosis of prostate cancer. Prilozi: XXXVI 1, 2015

Prof. Polenakovic has published several books, alone, and with his colleagues.



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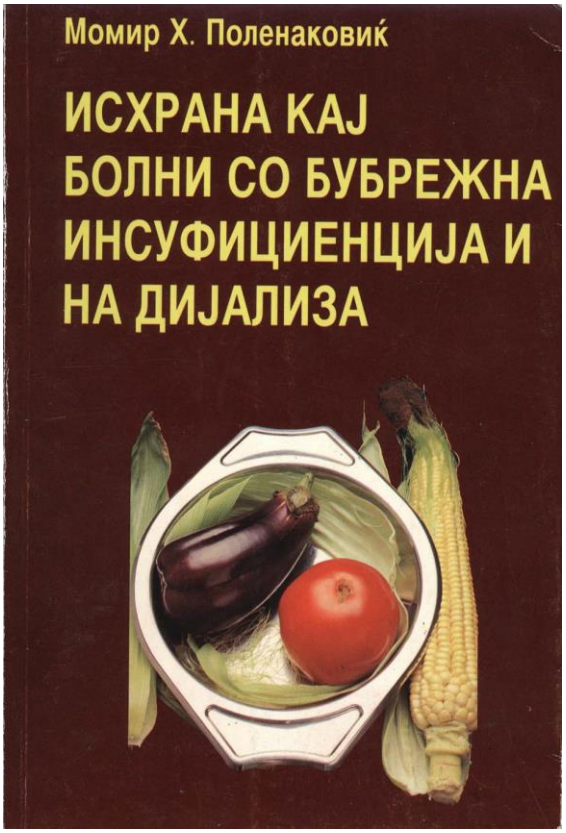

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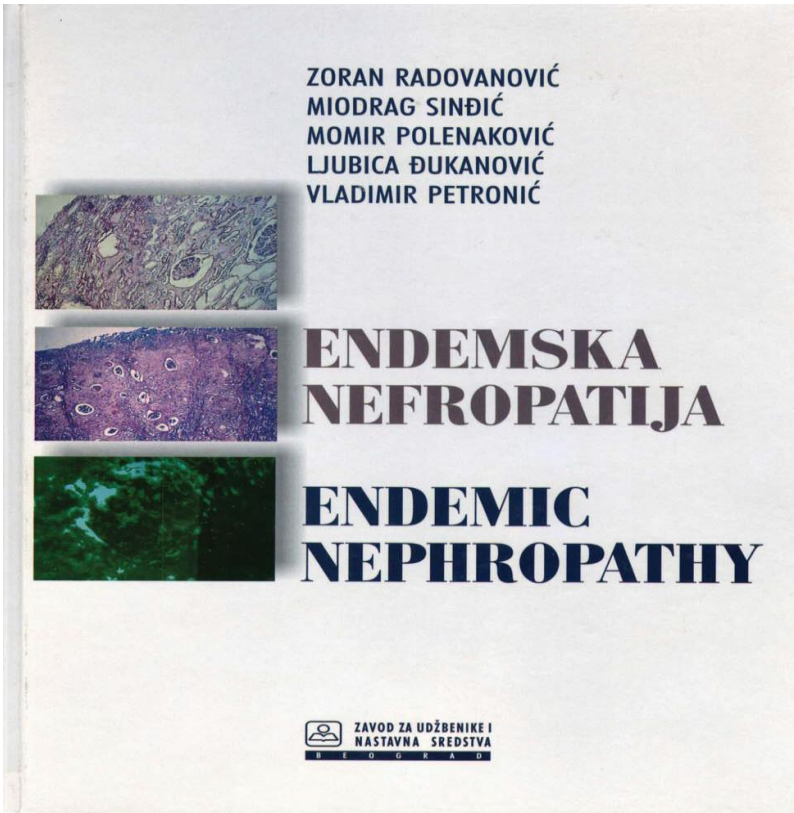

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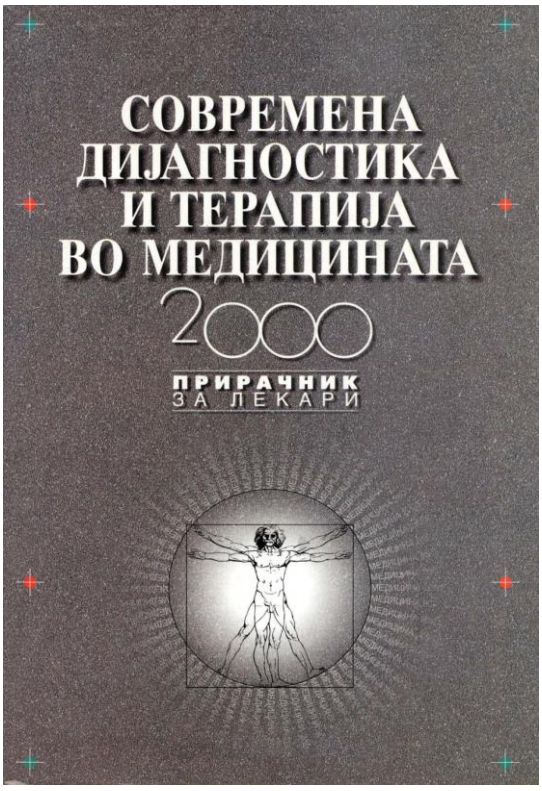


Глава 11

НЕФРОЛОГИЈА

Одговорен уредник:
акад. проф. д-р Момир Поленаковиќ

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Fig. 29 – Internal Medicine

Fig. 30 – Internal Propedeutics

Fig. 31 – Ivan Dejanov, Momir Polenakovic, Petar Dejanov. Infections, Haemostatic Disturbances and Antibiotic Therapy in Patients on Haemodialysis. SKopje: Macedonian Academy of Sciences and Arts; 2004: 84

He is an ***Editor in chief of the Journal Prilozi*** of the Macedonian Academy of Sciences and Arts; ***Associate editor of BANTAO Journal; Member of the Advisory Board of Actual Nephrology:*** *Kidney Foundation, Varna – Bulgaria;* ***Aktuality v nefrologii (Current concepts in nephrology), Czech Republic****; Former Member of the Advisory Board of:* ***Nephrology, Dialysis, Transplantation*** *(NDT), and* ***JAMA*** *(Journal of American Medical Association) – Yugoslav Edition.*

He has established international scientific joint collaborations: Department of Nephrology, Rostock-Germany; Department of Nephrology, Antwerpen-Belgium; Department of Nephrology, Freie Universitaet – Berlin; Departments of Medicine, Nephrology and Infectious Disease – Northwestern University Chicago and Wright State University – Dayton, USA; the International Centre for Genetic Engineering and Biotechnology, Trieste, Italy and the Department of Psychiatry, Columbia University Medical Center, New York, USA.

He was the principal investigator in several national and international projects.

We have partially presented the scientific work of Acad. Polenakovic. Having in mind that he has published more than 500 papers, of which more than 189 papers are on the PubMed, several hundred abstracts, several books and book chapters we can say that he is really a Nestor of the Macedonian nephrology and one of the most active and distinguished medical workers in the Republic of Macedonia.

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Р е з и м е

ПРИДОНЕСОТ НА АКАДЕМИК МОМИР ПОЛЕНАКОВИЌ ЗА РАЗВОЈОТ НА НЕФРОЛОГИЈАТА ВО РЕПУБЛИКА МАКЕДОНИЈА

ОФИЦИЈАЛНО ОБРАЌАЊЕ НА АКАДЕМИК ВЛАДИМИР СЕРАФИМОВСКИ, СЕКРЕТАР НА ОДДЕЛЕНИЕТО ЗА МЕДИЦИНСКИ НАУКИ НА МАКЕДОНСКАТА АКАДЕМИЈА НА НАУКИТЕ И УМЕТНОСТИТЕ, ПО ПОВОД 75 ГОДИНИ ОД РАЃАЊЕТО НА АКАДЕМИК МОМИР ПОЛЕНАКОВИЌ

Владимир Серафимоски

Македонска академија на науките и уметностите

Академик Момир Х. Поленаковиќ е познат истражувач, едукатор и научник, еден од основачите на нефрологијата во Република Македонија. Со повеќе од 500 објавени труда во домашни и во меѓународни списанија, од кои повеќе од 180 се на PubMed, тој е еден од најплодните медицински работници во нашата земја. Со своето учество на национални и на меѓународни конгреси академик Поленаковиќ придонесе за трансфер на светската нефрологија во Македонија, како и ширење на угледот на македонската нефрологија и наука во светот. Тој има образовано голем број специјалисти по интерна медицина и супспецијалисти по нефрологија. Академик Поленаковиќ воведе нови тестови и методи за дијагноза и третман на бубрежните болести, кои беа основа за неговото истражување и објавување. Анализирајќи го животниот опус на академик Момир Поленаковиќ, можеме да кажеме дека тој се посветил на истражувањето, дијагностицирањето и лекувањето на бубрежните болни.

Клучни зборови: македонска нефрологија, истражувања, дијагностика, третман на бубрежно болни