Quo Vadis Clinical Nephrology?

Prof. Andrzej Wiecek

Department of Nephrology, Transplantation and Internal Medicine
Medical University of Silesia, Katowice, Poland

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Quo Vadis Clinical Nephrology?

„Quo Vadis” = „Where are you going”

Translated on more than 60 languages, with many film versions

Edited by Polish writer Henryk Sienkiewicz in 1896
Nobel Prize Winner in 1905
Clinical Nephrology – can we predict the future?

“The best way to predict the future is to create it.”

Abraham Lincoln

16th President of the USA
Clinical Nephrology – can we predict the future?
Randomized clinical trials in various disciplines of medicine

Palmer S.C. i wsp., Am. J. Kidney Dis. 2011, 58, 335 - 337
Clinical Nephrology – can we predict the future?

How to predict the future
Clinical Nephrology – can we predict the future?

How to predict the future

• To ask a good witch
Clinical Nephrology – can we predict the future?

How to predict the future

• To ask a good witch

• To ask Google
Clinical Nephrology – can we predict the future?

How to predict the future

• To ask a good witch

• To ask Google

• To ask famous and experienced nephrologists

Prof. Raymond Vanholder
ERA-EDTA Past President
Dear Professor.................,

I was asked to give a lecture on a very fascinating and difficult topic, namely: „The future of Clinical Nephrology”. In order to prepare most comprehensive view on the future of nephrology, I would like to ask you and some other most influential and experienced nephrologists for kind support of this initiative and sending me a few thoughts concerning the future of clinical nephrology in the next 2-3 decades (including CKD patients, dialysis and transplantation).

I would greatly appreciate your help by receiving your reply not later than.....

During my presentation, I will certainly mention the list of supporters who were so kind and submit their opinions.

Best regards,

Andrzej Wiecek
Clinical Nephrology – can we predict the future?
List of nephrologists who responded to my e-mail

- R. Coppo (Italy)
- T. Drueke (France)
- J. Feehaly (U.K.)
- J. Floege (Germany)
- Z. Gaciong (Poland)
- M. Klinger (Poland)
- N. Lameire (Belgium)
- A. Levin (Canada)
- P. Li (Hong-Kong)
- B. Lindholm (Sweden)
- F. Locatelli (Italy)
- J. Mann (Germany)
- S. Moe (USA)
- K. Olgaard (Denmark)
- L. Pączek (Poland)
- C. Ronco (Italy)
- P. Ronco (France)
- M. Sever (Turkey)
- V. Tesar (Czech Rep.)
- R. Vanholder (Belgium)
- D. Wheeler (U.K.)
- C. Zoccali (Italy)

I thank all of them very much for their valuable contribution !!!
Clinical Nephrology – can we predict the future?
Different types of responses

The responses I received were:

• Their own vision of the future of the nephrology
• Their lectures on the same (similar) topics
• Their own articles, or articles published recently by other authors, on the same (similar) topic
Clinical Nephrology – can we predict the future?
Different types of response

A Future of Nephrology

Richard J. Glassock, MD, MACP
Emeritus Professor - The David Geffen School of Medicine at UCLA - Los Angeles, California

The title of this communication has been carefully chosen to indicate that it describes only one of many possible futures for the discipline of Nephrology. If the “past is prologue” then we can expect to observe many dramatic developments in a future of Nephrology. The author began his career in Nephrology more than 40 years ago, when the field was in its infancy. Who could have imagined the enormous scope and impact of developments that have transpired since the early 1960’s? The certain death sentence of end-stage renal disease (ESRD) has been lifted by dual therapies of chronic dialysis and transplantation. Untreatable diseases, such as glomerulonephritis and diabetic glomerulosclerosis, have yielded, at least in part, to innovative therapies. The armamentarium of diagnostic and prognostic tools has expanded greatly. New disease entities, hitherto unrecognized, have been delineated and extensively explored.
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Clinical Nephrology – can we predict the future?
Different typs of response

Artificial organs: current status and future directions

Andrea Remuzzi

1 IRCCS - Mario Negri Institute of Pharmacological Research, Anna Maria Astori Center, Bergamo - Italy
2 Department of Management, Information and Production Engineering, University of Bergamo, Dalmine (Bergamo) - Italy

At the end of 2016, the International Journal of Artificial Organs will publish the final issue of its 39th volume. The journal has traditionally been a longstanding witness of the history of artificial organs, chronicling their development and applications, from the bioengineering of new technologies used in artificial organs to their clinical applications. During this time period, a lot of changes have taken place in the field. This evolution characterizes the present status of research increase respectively over, in this 17-year period. On the contrary, publications related to total artificial heart and artificial liver did not increase and remained constant over the same period. An interesting growth in the number of publications per year can be found in PubMed for the artificial pancreas, with a modest number of publications as an absolute value, but increasing significantly over the past 5 years. While the absolute values of the publications reflect the clinical relevance of the
Clinical Nephrology — can we predict the future?
Different types of response

Nephrology research—the past, present and future

Jürgen Floege, Robert H. Mak, Bruce A. Molitoris, Giuseppe Remuzzi and Pierre Ronco

Abstract | Important advances have been made in basic and clinical nephrology research over the past decade, with improved pathological insights into various disease processes and the introduction of new treatments for diseases such as atypical haemolytic uraemic syndrome. However, many challenges remain. In this Viewpoint, we asked five Nature Reviews Nephrology Advisory Board members, who have been associated with the journal since its launch in November 2005, to reflect on the progress and roadblocks of the past 10 years. They also comment on areas where effort and money should be invested and how they expect the field to progress in the next 10 years.


In your opinion, what have been the most important findings in basic nephrology research in the past 10 years?

Concerns the identification of the elusive permeability factor(s) in minimal change glomerulonephritis and focal segmental glomerulosclerosis. Rare genetic diseases associated with hypertension has led to further insight into the pathophysiology of hypertension.

Robert H. Mak. The most notable progress in basic nephrology research has been in the field of polycystic kidney disease (PKD). The onset, progression and severity of autosomal dominant polycystic kidney disease (ADPKD) is now known to be determined by the dosage and nature of mutations in PKD1 and PKD2; the genetic background of other cilia-associated modifier genes such as the autosomal recessive PKD gene PKHD1; as well as ‘second hit’ somatic mutations. Downstream mechanisms involving cilia motility, intracellular calcium and cyclic nucleotide signalling, cell cycle regulation and cross-talk between the epithelial cell and the cytoskeleton all contribute to cystogenesis. Furthermore, complex environmental factors including mechanical stress, paracrine responses and inflammation add to the pathogenesis of ADPKD progression. A systems-based approach of genotype-
Clinical Nephrology – can we predict the future?
Different types of response

VIEWPOINT

Nephrology research—the past, present and future

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Clinical Nephrology – can we predict the future?
Different types of response

Future Avenues to Decrease Uremic Toxin Concentration

Raymond C. Vanholder, MD, PhD, Sunny Eloot, MSc, PhD, and Griet L.R.L. Glorieux, MSc, PhD

In this article, we review approaches for decreasing uremic solute concentrations in chronic kidney disease and in particular, in end-stage renal disease (ESRD). The rationale to do so is the straightforward relation between concentration and biological (toxic) effect for most toxins. The first section is devoted to extracorporeal strategies (kidney replacement therapy). In the context of high-flux hemodialysis and hemodiafiltration, we discuss increasing dialyzer blood and dialysate flows, frequent and/or extended dialysis, adsorption, bioartificial kidney, and changing physical conditions within the dialyzer (especially for protein-bound toxins). The next section focuses on the intestinal generation of uremic toxins, which in turn is stimulated by uremic conditions. Therapeutic options are probiotics, prebiotics, synbiotics, and intestinal sorbents. Current data are conflicting, and these issues need further study before useful therapeutic concepts are developed. The following section is devoted to preservation of (residual) kidney function. Although many therapeutic options may overlap with therapies provided before ESRD, we focus on specific aspects of ESRD treatment, such as the risks of too-strict blood pressure and glycemic regulation and hemodynamic changes during dialysis. Finally, some recommendations are given on how research might be organized with regard to uremic toxins and their effects, removal, and impact on outcomes of uremic patients.


INDEX WORDS: Uremic toxins; uremic toxin removal; dialysis adequacy; intestinal generation; microbiome; residual kidney function; dialysate; kidney failure; hemodialysis; end-stage renal disease (ESRD); review.

Clinical Nephrology – can we predict the future?

Different types of response

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Clinical Nephrology — can we predict the future?

Different types of response

Research and Future of Nephrology

Carmine Zoccali
Clinical Nephrology – can we predict the future?

Different types of response
Clinical Nephrology – can we predict the future?

Quo vadis clinical nephrology?

- High costs and decreasing interest in nephrology
- Future of (non-invasive) clinical nephrology
- Future of haemodialysis
- Future of peritoneal dialysis
- Future of transplantation
Clinical Nephrology – can we predict the future?

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Estimated global prevalence of CKD
Estimated global prevalence of CKD

One in 10 people worldwide will develop chronic kidney disease in their lifetime!
Estimated global prevalence of CKD

One in 10 people worldwide will develop chronic kidney disease in their lifetime!
Figure 1 | **The burden of chronic kidney disease (CKD)***. a | Percentage distribution of the various stages of CKD. b | CKD in the global population. The fraction of patients who undergo renal replacement therapy (RRT) is very small. *Global approximations, extracted from various databases*.5,12-18.

Vanholder R. et al. NATURE REVIEWS | NEPHROLOGY, 2017, in press
Clinical Nephrology – can we predict the future?
Costs of treatment of CKD patients

Table 1
CKD: Average estimated all-cause cost per patent in 2016

<table>
<thead>
<tr>
<th>Condition</th>
<th>Commercial insurance</th>
<th>Medicare</th>
</tr>
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<tbody>
<tr>
<td>No CKD</td>
<td>$7,500</td>
<td>$8,100</td>
</tr>
<tr>
<td>Stage 3a CKD</td>
<td>$27,200</td>
<td>$20,500</td>
</tr>
<tr>
<td>Stage 4–5 CKD</td>
<td>$77,000</td>
<td>$46,100</td>
</tr>
</tbody>
</table>

Clinical Nephrology – can we predict the future?
Costs of treatment of CKD patients

Reducing the costs of chronic kidney disease while delivering quality health care: a call to action

Raymond Vanholder¹, Lieven Annemans², Edwina Brown³, Ron Gansevoort⁴, Judith J. Gout-Zwart⁵, Norbert Lameire¹, Rachael L. Morton⁶, Rainer Oberbauer⁷, Maarten J. Postma⁸,⁹, Marcello Tonelli¹⁰, Wim Van Biesen¹ and Carmine Zoccali¹¹ on behalf of the European Kidney Health Alliance

Abstract | The treatment of chronic kidney disease (CKD) and of end-stage renal disease (ESRD) imposes substantial societal costs. Expenditure is highest for renal replacement therapy (RRT), especially in-hospital haemodialysis. Redirection towards less expensive forms of RRT (peritoneal dialysis, home haemodialysis) or kidney transplantation should decrease financial
Clinical Nephrology – can we predict the future?
Costs of treatment of CKD patients

Key points

- The treatment of chronic kidney disease (CKD) and of end-stage kidney disease (ESRD) has a high societal cost
- Insufficient efforts are being made to promote the use of cost-effective renal replacement therapies (RRT), such as transplantation and home dialysis (including peritoneal dialysis)
- In CKD and in many other chronic diseases, the time has come to decrease investment in curative approaches and to focus on prevention
- The relative costs and benefits of each approach should be carefully analysed before a preventive or curative method is favoured
- A need exists for more health-economic studies of primary and secondary prevention in CKD to be conducted, and for the quality of such research to be improved

Vanholder R. et al., NATURE REVIEWS | NEPHROLOGY, 2017, in press
Clinical Nephrology – can we predict the future?
Costs of treatment of CKD patients

<table>
<thead>
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Vanholder R. et al., NATURE REVIEWS | NEPHROLOGY, 2017, in press
Clinical Nephrology – can we predict the future?
Costs of treatment of CKD patients

Key points

- The treatment of chronic kidney disease (CKD) and of end-stage kidney disease (ESRD) has a high societal cost.
- Insufficient efforts are being made to promote the use of cost-effective renal replacement therapies (RRT), such as transplantation and home dialysis (including peritoneal dialysis).
- In CKD and in many other chronic diseases, the time has come to decrease investment in curative approaches and to focus on prevention.
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- A need exists for more health-economic studies of primary and secondary prevention in CKD to be conducted, and for the quality of such research to be improved.

Vanholder R. et al., NATURE REVIEWS | NEPHROLOGY, 2017, in press
Clinical Nephrology – can we predict the future?

Global distribution of nephrologists per million population

Figure 2. Global Distribution of Nephrologists Per 1 Million Population

Published online April 21, 2017
Clinical Nephrology – can we predict the future?
Different types of response

The global nephrology workforce: emerging threats and potential solutions!

Muhammad U. Sharif¹,², Mohamed E. Elsayed¹,², and Austin G. Stack¹,²,³

¹Division of Nephrology, Department of Medicine, University Hospital Limerick, Limerick, Ireland, ²Graduate Entry Medical School, University of Limerick, Limerick, Ireland, and ³Health Research Institute (HRI), University of Limerick, Limerick, Ireland

Correspondence to: Austin G. Stack; E-mail: austin.stack@ul.ie
Clinical Nephrology – can we predict the future?

Global distribution of nephrologists per million population

Clinical Nephrology – can we predict the future?

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Clinical Nephrology – can we predict the future?
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Clinical Nephrology – can we predict the future?
Global distribution of nephrologists per million population
Clinical Nephrology – can we predict the future?

Decreasing interest in nephrology

Trends of ESKD prevalence in USA and number of Nephrologists per 1000 ESKD patients

Clinical Nephrology – can we predict the future?
Decreasing interest in nephrology
Clinical Nephrology – can we predict the future?

Decreasing interest in nephrology

Clinical Nephrology – can we predict the future?
Decreasing interest in nephrology

Ross M.J. and Braden G. for the ASN Match Committee
Clinical Nephrology – can we predict the future?
Decreasing interest in nephrology

- The global nephrology workforce has failed to expand in order to meet the growing healthcare needs of this vulnerable patient population.

- In truth, this shortage of nephrologists is seen in many parts of the world, including North America, Europe, Australia, New Zealand, Asia and the African continent.

- Moreover, expert groups on workforce planning as well as national and international professional organizations predict further reductions in the nephrology workforce over the next decade, with potentially serious implications.

Clinical Nephrology – can we predict the future?

Decreasing interest in nephrology

Sharif M.U. et al.,
Clinical Nephrology – can we predict the future?

Decreasing interest in nephrology

Potential Threats to Nephrology Workforce

- Reliance on foreign graduates
- Cultural and ethnic disparities between patients and care providers
- Aging workforce
- Rising incidence and prevalence of CKD and ESKD
- Uncertainty about future employment
- Rising costs of medical education and specialist training
- Lack of exposure to nephrology among students and residents
- Inadequate training
- Erosion of nephrology practice scope by other specialists
- Inflexible work schedules

Declining interest in nephrology among trainees

Sharif M.U. et al.,
Clinical Nephrology – can we predict the future?
Decreasing interest in nephrology

- It is likely that each country will evolve its own way of dealing with the issue consistent with the availability of specialized training and the systems of healthcare delivery. **General or Family Practitioners** may be called upon to deliver a significant portion of care for ESRD and dialysis, **supported by a small cadre of Nephrology consultants.**

- This has already occurred **in some developing countries, as a response to a deficit in trained Nephrologists**, without any apparent detrimental effect on outcome (mortality and morbidity).
Quo vadis clinical nephrology?

- High costs and decreasing interest in nephrology
- Future of (non-invasive) clinical nephrology
- Future of haemodialysis
- Future of peritoneal dialysis
- Future of transplantation
Mature induced-pluripotent-stem-cell-derived human podocytes reconstitute kidney glomerular-capillary-wall function on a chip

Samira Musah1,2,3, Akiko Mammoto4, Thomas C. Ferrante1, Sauveur S. F. Jeanty1, Mariko Hirano-Kobayashi1,4, Tadanori Mammoto4, Kristen Roberts1, Seyoon Chung1, Richard Novak1, Miles Ingram1, Tohid Fatanat-Didar1, Sandeep Koshy1, James C. Weaver1, George M. Church1,2,3 and Donald E. Ingber1,3,4,5*

An in vitro model of the human kidney glomerulus—the major site of blood filtration—could facilitate drug discovery and illuminate kidney-disease mechanisms. Microfluidic organ-on-a-chip technology has been used to model the human proximal tubule, yet a kidney-glomerulus-on-a-chip has not been possible because of the lack of functional human podocytes—the cells that regulate selective permeability in the glomerulus. Here, we demonstrate an efficient (over 90%) and chemically defined method for directing the differentiation of human induced pluripotent stem (hiPS) cells into podocytes that express markers for a mature phenotype (nephrin+, WTI+, podocin+, PAX2-) and that exhibit primary and secondary foot processes. We also show that the hiPS-cell-derived podocytes produce glomerular basement-membrane collagen and recapitulate the natural tissue-tissue interface of the glomerulus, as well as the differential clearance of albumin and inulin, when co-cultured with human glomerular endothelial cells in an organ-on-a-chip microfluidic device. The glomerulus-on-a-chip also mimics adriamycin-induced albuminuria and podocyte injury. This in vitro model of human glomerular function with mature human podocytes may facilitate drug development and personalized-medicine applications.

Musah S. et al., Nature Biomed. Engin., 2017, 1, 0069
Clinical Nephrology – can we predict the future?
(Non-invasive) clinical nephrology

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Musah S. et al., Nature Biomed. Engin., 2017, 1, 0069
Clinical Nephrology — can we predict the future?
(Non-invasive) clinical nephrology

Advances in the treatment of frequent causes of CKD:

- Diabetic nephropathy
- ADPKD
- AKI (regenerative nephrology)
Clinical Nephrology – can we predict the future?
(Non-invasive) clinical nephrology

Vallon, Thomson, Diabetologia 2017; 60:215-225
Figure 3 | Aberrant signalling pathways that have been implicated in the pathogenesis of polycystic kidney disease and potential drugs that act on targets in these pathways. Abbreviations: AVP, arginine vasopressin; CDK, cyclin-dependent kinase; CFTR, cystic fibrosis transmembrane conductance regulator; P2R, purinergic P2 receptor; PyR, pyridine receptor; SST, somatostatin; TKI, tyrosine kinase inhibitor; TZD, thiazolidinedione; V2R, vasopressin V2 receptor. Republished with permission of the American Society of Nephrology, from Antignac, C. et al. The future of polycystic kidney disease research—as seen by the 12 Kaplan awardees. doi:10.1681/ASN.2014121192 (2015); permission conveyed through Copyright Clearance Center, Inc.
Treatment of ADPKD

Figure 3: Aberrant signalling pathways that have been implicated in the pathogenesis of polycystic kidney disease and potential drugs that act on targets in these pathways. Abbreviations: AVP, arginine vasopressin; CDK, cyclin-dependent kinase; CFTR, cystic fibrosis transmembrane conductance regulator; P2R, purinergic P2 receptor; PyR, pyramidal receptor; SST, somatostatin; TKI, tyrosine kinase inhibitor; T2D, thiazolidinedione; V2R, vasopressin V2 receptor. Republished with permission of the American Society of Nephrology, from Antignac, C. et al. The future of polycystic kidney disease research—as seen by the 12 Kaplan awardees. doi:10.1681/ASN.2014121192 (2015); permission conveyed through Copyright Clearance Center, Inc.

Klotho May Ameliorate Proteinuria by Targeting TRPC6 Channels in Podocytes

Ji-Hee Kim,* Jian Xie,† Kyu-Hee Hwang,* Yueh-Lin Wu,‡‡ Noelynn Oliver,§ Minseob Eom,‖ Kyu-Sang Park,*‖ Nestor Barreuzeta,§ In-Deok Kong,*§ R. Paul Fracasso,§ Chou-Long Huang,† and Seung-Kuy Cha*§

*Departments of Physiology and Global Medical Science, †Department of Pathology, and ‡Institute of Lifestyle Medicine, Yonsei University Wonju College of Medicine, Wonju, Republic of Korea; ‡Division of Nephrology, Department of Internal Medicine, University of Texas Southwestern Medical Center, Dallas, Texas; ‖Division of Nephrology, Department of Internal Medicine, Taipei Medical University Hospital, Taipei, Taiwan; and §Cardiometabolic Disease Research, Boehringer Ingelheim Pharmaceuticals Inc., Ridgefield, Connecticut

ABSTRACT
Klotho is a type-1 membrane protein predominantly produced in the kidney, the extracellular domain of which is secreted into the systemic circulation. Membranous and secreted Klotho protect organs, including the kidney, but whether and how Klotho directly protects the glomerular filter is unknown. Here, we report that secreted Klotho suppressed transient receptor potential channel 6 (TRPC6)-mediated Ca$^{2+}$ influx in cultured mouse podocytes by inhibiting phosphoinositide 3-kinase-dependent exocytosis of the channel. Furthermore, soluble Klotho reduced ATP-stimulated actin cytoskeletal remodeling and trans-epithelial albumin leakage in these cells. Overexpression of TRPC6 by gene delivery in mice induced albuminuria, and exogenous administration of Klotho ameliorated the albuminuria. Notably, immunofluorescence and in situ hybridization revealed Klotho expression in podocytes of mouse and human kidney. Heterozygous Klotho-deficient CKD mice had aggravated albuminuria compared with that in wild-type CKD mice with a similar degree of hypertension and reduced clearance function. Finally, disrupting the integrity of glomerular filter by saline infusion-mediated extracellular fluid volume expansion increased urinary Klotho excretion. These results reveal a potential novel function of Klotho in protecting the glomerular filter, and may offer a new therapeutic strategy for treatment of proteinuria.

Klotho may prevent podocyte destruction

Will the next decade be that of regenerative medicine in nephrology?

- The field now seems poised to advance rapidly with the discovery that multipotent renal stem cells exist in the mammalian kidney and that progenitor cells seem to persist in the adult glomerulus and tubules.

- Mesenchymal stem cells are already used in clinical trials to prevent AKI.

- Embryonic and induced pluripotent stem cells represent other very powerful tools that hold considerable promise for the future.
Clinical Nephrology – can we predict the future?
(Non-invasive) clinical nephrology

Additional suggestions from experts:

• CKD patients will be managed by primary care physicians in a protocol driven fashion with "triggers" for referral to nephrologist for diagnostic studies or preparation for RRT.
• Gene therapy for correcting the genetic disorders.
• Development of personalized nephrology, based on specific biomarkers for the major types of acute and chronic kidney diseases.
• Treatment of premature vascular ageing in CKD.
• New methods of treatment (prevention?) of kidney fibrosis.
• Treatment of immune dysfunction in uremia.
Quo vadis clinical nephrology?

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- Future of haemodialysis
- Future of peritoneal dialysis
- Future of transplantation
One of my patients who had received a kidney transplant in 1998 returned to dialysis in 2016 and immediately commented that nothing has changed.

Although dialysis is undoubtedly already at a very high technical level, there is no doubt that it is not perfect with many aspects such as intradialytic stability, efficacy and individualization of therapy as well as affordability of treatment offering room for improvement.
Clinical Nephrology — can we predict the future?
Haemodialysis

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<thead>
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<td>1,947</td>
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<td>Artificial Heart</td>
<td>64</td>
<td>65</td>
<td>63</td>
<td>91</td>
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<tr>
<td>Artificial Liver</td>
<td>83</td>
<td>107</td>
<td>58</td>
<td>62</td>
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<td>Artificial Organs</td>
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VAD = ventricular assist device; ECMO = extracorporeal membrane oxygenation.
Clinical Nephrology – can we predict the future?
Haemodialysis

<table>
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<td>Artificial Liver</td>
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Portable and wearable dialysis devices for the treatment of patients with end-stage kidney failure: Wishful thinking or just over the horizon?

Andrew Davenport

Abstract Dialysis is a life-sustaining treatment for patients with end-stage kidney disease. In a different context, for many patients this treatment is the focal point around which their life revolves, not only due to the time spent travelling to and from treatment sessions and the time dedicated to the dialysis treatment itself, but also due to the accompanying dietary

War [1]. However it was only in the 1960s following advances in vascular access, dialysers [2] and dialysis machine design [3] that HD started to become available as a treatment for patients with advanced chronic kidney disease (CKD). The many limitations on patient life style at that time, particularly the strict dietary and fluid restrictions required, were readily

The WAK has both a blood side and a dialysate side, with spent dialysate regenerated by passage through a series of sorbents, followed by the addition of bicarbonate and electrolytes.
Wearable and portable dialysis devices
Clinical Nephrology – can we predict the future?

Haemodialysis

Implantable artificial kidney?
World's First Implantable Artificial Kidney Could Enter Human Trials By 2017

By Suzanne Hodsden

A team of university scientists has developed the world’s first artificial kidney technology to be implanted in the body. Their bio-hybrid approach uses living kidney cells in tandem with a series of specialized microchips powered by the human heart to filter waste from the blood stream.

The National Kidney Foundation estimates that over 100,000 patients are on the waiting list for a donor kidney, and over 3,000 are added list each year. The average patient spends 3.6 years waiting for a viable transplant, and may be treated with dialysis while they wait, but only one in three dialysis patient survives longer than five years without a transplant.
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Additional suggestions from experts:

• Improve prevention, early detection, and good management of AKI.
• Return of the nephrologist into the ICU not only for advising on RRT in AKI but also on consulting on fluid electrolyte disturbances, changed pharmacokinetics of drugs in both AKI and CKD.
• Home-based/self-care monitoring of CKD and its complications – much more than today can be performed by patients in their home using new devices and ICT technology.
• Reduce the cost of dialysis.
• New drugs e.g. for anaemia management (HIF stabilares – p.o).
Clinical Nephrology – can we predict the future?

Peritoneal Dialysis

Quo vadis clinical nephrology?

- High costs and decreasing interest in nephrology
- Future of (non-invasive) clinical nephrology
- Future of haemodialysis
- Future of peritoneal dialysis
- Future of transplantation
Clinical Nephrology – can we predict the future?
Peritoneal Dialysis

- Alternative osmotic agents
- Better catheters
- Home assistance
- Telemedicine
- Wearable cyclers for continuous flow peritoneal dialysis (cfpd)
Clinical Nephrology – can we predict the future?
Peritoneal Dialysis

Wearable cyclers for continuous flow peritoneal dialysis (cfpd)

2017 sent for FDA approval
Additional suggestions from experts:

• Peritoneal dialysis will become less popular in developed healthcare systems.

• For patients reaching end-stage between the ages of 65-85 who are unsuitable for kidney transplantation, we will offer no peritoneal dialysis but rather haemodiafiltration.
PD prevalence in Europe

**APC = Annual Percentage Change**

**HD**
- Period: 1993-2000, APC: +4.5 (+4.4; +4.7)
- Period: 2000-2004, APC: +3.0 (+2.8; +3.3)
- Period: 2004-2009, APC: +1.5 (+1.3; +1.7)
- Period: 2009-2012, APC: -0.2 (-0.5; +0.2)

**PD**
- Period: 1993-2000, APC: +3.5 (+3.1; +3.9)
- Period: 2000-2007, APC: 0.0 (-0.5; +0.5)
- Period: 2007-2012, APC: -2.8 (-3.4; -2.2)

**Tx**
- Period: 1993-1999, APC: +5.2 (+5.1; +5.4)
- Period: 1999-2004, APC: +3.8 (+3.5; +4.1)
- Period: 2004-2012, APC: +3.2 (+3.1; +3.3)

Trends in the prevalence of patients on PD in Asia between 1999 and 2013

Li. Ph., et al., Nature Rev. Nephrol., 2017; Ahead of print
Clinical Nephrology – can we predict the future?

Transplantation

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Clinical Nephrology – can we predict the future?

Transplantation

Research review paper

3D bioprinting for engineering complex tissues

Christian Mandrycky a,1, Zongjie Wang b,1, Keeyoung Kim b,*, Deok-Ho Kim a,**

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b School of Engineering, The University of British Columbia, Kelowna, BC V1V 1V7, Canada

A R T I C L E   I N F O

Article history:
Received 5 August 2015
Received in revised form 10 December 2015
Accepted 22 December 2015
Available online 23 December 2015

Keywords:
Bioprinting
Bioprinting
Tissue engineering
3D printing
Hydrogel
Drug screening
Regenerative medicine

A B S T R A C T

Bioprinting is a 3D fabrication technology used to precisely disperse cell-laden biomaterials for the construction of complex 3D functional living tissues or artificial organs. While still in its early stages, bioprinting strategies have demonstrated their potential use in regenerative medicine to generate a variety of transplantable tissues, including skin, cartilage, and bone. However, current bioprinting approaches still have technical challenges in terms of high-resolution cell deposition, controlled cell distributions, vascularization, and innervation within complex 3D tissues. While no one-size-fits-all approach to bioprinting has emerged, it remains an on-demand, versatile fabrication technique that may address the growing organ shortage as well as provide a high-throughput method for cell patterning at the micrometer scale for broad biomedical engineering applications. In this review, we introduce the basic principles, materials, integration strategies and applications of bioprinting. We also discuss the recent developments, current challenges and future prospects of 3D bioprinting for engineering complex tissues. Combined with recent advances in human pluripotent stem cell technologies, 3D-bioprinted tissue models could serve as an enabling platform for high-throughput predictive drug screening and more effective regenerative therapies.
Clinical Nephrology – can we predict the future?

Transplantation

Mandrycky C. et al., Biotechnology Advances, 2016, 34, 422–434
Clinical Nephrology – can we predict the future?

Transplantation

Yue Z. et al., Curr. Opin. Organ. Transplant., 2016, 21:467–475
Clinical Nephrology – can we predict the future?

Transplantation

<table>
<thead>
<tr>
<th>Tissue</th>
<th>Cell sources</th>
<th>Materials</th>
<th>Printing method</th>
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<tr>
<td>Vessel</td>
<td>Smooth muscle cells</td>
<td>Carbon nanotube encapsulated alginate</td>
<td>Extrusion</td>
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<tr>
<td></td>
<td>Smooth muscle cells and aortic valve</td>
<td>Gelatin and alginate</td>
<td>Extrusion</td>
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<td>leaflet interstitial cells</td>
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<td>Human umbilical vein endothelial</td>
<td>PEG-DA, Matrigel, fibrin gel, alginate, agarose, and GelMA</td>
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<td>cells (HUVEC)</td>
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<td>Rat heart endothelial cells</td>
<td>Alginate</td>
<td>Extrusion</td>
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<td>Ea.hy926 endothelial cells</td>
<td>Nano-hydroxyapatite</td>
<td>Laser-assisted</td>
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<td>Fibroblasts (L929), mouse endothelial</td>
<td>Acrylated hyaluronic acid-PEG (HA-PEG), and Matrigel</td>
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<td>Stereolithography</td>
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<td>Bone</td>
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<td>MG-63 cells</td>
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<td>Equine chondrocytes and mesenchymal</td>
<td>PCL, GelMA, and GelMA-gellan hydrogels</td>
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<td>Adipose tissue</td>
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<td>Gelatin-alginate-fibrinogen hydrogel</td>
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Mandrycky C. et al., Biotechnology Advances, 2016, 34, 422–434
Clinical Nephrology – can we predict the future?

Transplantation

Perfusion decellularization of porcine and human kidneys

Xenotransplantation: where do we stand in 2016?

Gisella L. Puga Yung\textsuperscript{a}, Robert Rieben\textsuperscript{b}, Leo Bühler\textsuperscript{c}, Henk-Jan Schuurman\textsuperscript{c}, Jörg D. Seebach\textsuperscript{a}

\textsuperscript{a} Division of Immunology and Allergology, University Hospital and Faculty of Medicine, University of Geneva, Switzerland
\textsuperscript{b} Department of Clinical Research, University of Bern, Switzerland
\textsuperscript{c} Department of Surgery, University Hospital and Faculty of Medicine, University of Geneva, Switzerland
Clinical Nephrology – can we predict the future?

Transplantation

Xenotransplantation - Possible ???? When ???

Swiss Med Wkly. 2017;147:w14403
The imminent generation of genetically modified pigs raised in germ-free facilities, in addition to the promising preclinical results using these pigs, heralds the next, promising phase of xenotransplantation, based on the huge in-vestments made in the past.

Clinical Nephrology – can we predict the future?
Transplantation

Additional suggestions from experts:

• Most young patients will have identified a live donor before reaching ESKD and will undergo pre-emptive transplantation.

• Transplanted kidneys will last 30 years.

• New immunosuppressive drugs that will bring us closer to a stage of tolerance of kidney allografts.

• Optimal kidney ready for transplantation without the need of immunosuppression.
„While every generation believes that they lived in and experienced a “Golden Era”, for myself I believe that the best is yet to come !!!”

Richard J. Glassock
(USA)
Andrzej Więcek
Katowice