3rd Annual Southern California Kidney Symposium: Sex Differences in Kidney Health and Disease

Saturday
December 1, 2018
7:30 am – 5:15 pm

Sunday
December 2, 2018
8:30 am – 12:00 pm

Aresty Conference Center, USC Health Sciences Campus
Los Angeles, CA

Presented by:
Department of Medicine
Division of Nephrology and Hypertension
USC Office of Continuing Medical Education
# 3rd Annual Southern California Kidney Symposium: Sex Differences in Kidney Health and Disease

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Course Overview and Objectives

3rd Annual Southern California Kidney Symposium:
Sex Differences in Kidney Health and Disease

Course Description
This is the third annual Southern California Kidney Symposium with the theme Sex Differences in Kidney Health and Disease. Invited faculty from several Southern California academic institutions, as well as other institutions outside the area, will present before an audience of clinical and research faculty and trainees new clinical and research findings on topics in several broad areas, including the kidney in pregnancy and the effects of preeclampsia, sex differences in kidney physiology, sex differences in kidney disease and women and kidney replacement therapies, with emphasis on clinical and policy implications. Day two of this conference will cover the future development of clinical nephrology and kidney research.

Educational Objectives
At the conclusion of the program the participant will be able to:

- Assess the role of sex differences in the management of metabolic and kidney diseases.
- Identify potential dietary therapies to address these sex differences in kidney disease and hypertension.
- Discuss important considerations on the effects of kidney disease on pregnancy.
- Identify the causes and consequences of preeclampsia as it relates to the kidney.
- Understand how Medicare payment policies address gender differences in the chronic kidney disease patient population.
- Outline the current recommended management for the treatment of hypertension in patients with chronic kidney disease.
- Understand the current differences in causes and outcomes of acute kidney injury, hypertension and diabetes between men and women.
- Describe new initiatives to improve outcomes of pregnancy in patients with chronic kidney disease, patients undergoing dialysis or after kidney transplantation.
- Understand the current roadblocks to recruiting and retaining members of the nephrology and kidney research community and learning about potential solutions to these barriers.

Accreditation Statement
The Keck School of Medicine of the University of Southern California is accredited by the Accreditation Council for Continuing Medical Education (ACCME) to provide continuing medical education for physicians.

Credit Designation
The Keck School of Medicine of the University of Southern California designates this live activity for a maximum of 10.25 AMA PRA Category 1 Credits™. Physicians should claim only the credit commensurate with the extent of their participation in the activity.
NEEDS ASSESSMENT

It is well known that kidney disease is understudied relative to its impact on public health (1, 2). According to American Society of Nephrology, there are 26 million Americans (1 in 9 adults) have chronic kidney disease (CKD). More that 570,000 of them have kidney failure, also known as end-stage renal disease (ESRD) (3). Of note, many people who have CKD are not even aware that they have it. For many people who are diagnosed with CKD, there is no effective cure, and the only hope is to slow down the progression by multifactorial management. Most people who have ESRD rely on dialysis, which is a high-cost, low-efficiency and sometimes painful process. A key driver of this problem is the lack of innovation caused by shortfalls in support for research, education, the recruitment of kidney disease practitioners and public attention.

In California, we have more than 60,000 people with ESRD (4), with various underlying causes, including diabetic nephropathy, hypertension, glomerulonephritis, polycystic kidney disease, among others (5). In our own geographical area, the number of CKD patients seen at Keck Hospital of USC is about 500 annually for the past 20 years (6). There were 14,036 newly diagnosed chronic ESRD individuals in the state of California in 2013 (4).

It is particularly concerning that research on kidney disease in pregnancy or pregnancy in patients with chronic kidney disease remains an area that lacks significant progress (7). In addition, the molecular mechanisms that underlie sex differences in kidney disease and responses to treatment are still the subject of intense investigation (8,9).

As an area leader in research, education and patient care, we at the University of Southern California feel the need to promote the dissemination of new and innovative research findings in kidney disease and up-to-date clinical practices in kidney disease and hypertension management especially with respect to sex differences in kidney disease therapies to physicians, trainees, and other healthcare professionals who are on the front lines of patient care. In addition, we feel that a forum is needed to showcase cutting edge research and clinical initiatives in kidney disease that are occurring in Southern California and nationwide. Thus, we have organized this third annual Southern California Kidney Symposium with a goal to highlight cutting-edge research and clinical practice guidelines within the context of the theme of “Sex Differences in Kidney Health and Disease”. There are significant knowledge gaps in our understanding of how to best treat men vs. women in certain aspects of kidney disease. We have invited as speakers 12 faculty experts representing several Southern California academic institutions, including the Keck School of Medicine of USC, Cedars-Sinai Medical Center, UCLA Geffen School of Medicine, UC-Irvine, UC-San Diego, and additional outside experts from the U. of Alabama at
Birmingham, Harvard University and Georgetown University. These invited experts will present and moderate new and timely clinical and research talks on topics in several broad areas (including: metabolism, gastrointestinal, and renal disease; liver-kidney cross-talk; kidney transplantation; and the cardio-renal axis and the kidney in cardiovascular disease) before an audience of clinical and research faculty and trainees.

We anticipate that the symposium will:

(1) provide Continuing Medical Education (CME) to physicians and other health care professionals through the highlighting of new, up-to-date clinical practice guidelines in nephrology and hypertension with focus on: a) assessing the role of sex-differences in the management of metabolic and kidney diseases, b) identifying potential dietary therapies to address these sex differences in kidney disease and hypertension, c) discussing important considerations on the effects of kidney disease on pregnancy, d) identifying the causes and consequences of pre-eclampsia as it relates to the kidney, e) understanding how Medicare payment policies address gender differences in the chronic kidney disease patient population, f) outlining the current recommended management for the treatment of hypertension in patients with chronic kidney disease, g) understanding the current differences in causes and outcomes of acute kidney injury, hypertension and diabetes between men and women, h) describing new initiatives to improve outcomes of pregnancy in patients with chronic kidney disease, patients undergoing dialysis or after kidney transplantation and j) understanding the current roadblocks to recruiting and retaining members of the nephrology and kidney research community and learning about solutions to these barriers.

(2) showcase cutting edge research and clinical initiatives in kidney disease that are occurring in the Southern California area and beyond;

(3) serve as a forum for kidney disease researchers and clinicians to foster new relationships that will help bridge the divide between researchers and clinical practitioners;

(4) serve as a forum for networking and mentoring that will benefit trainees and established clinicians and investigators alike; and

(5) promote the establishment of new scientific collaborations that will aid in the establishment of new translational research projects and regional cores that are relevant to kidney disease, an underserved area of medical research.
References:

2. Link: http://jasn.asnjournals.org/content/early/2016/04/27/ASN.2015090976.full.pdf+html
7. https://calv-i2b2appdev.med.usc.edu/webclient/
3rd Annual Southern California Kidney Symposium: Sex Differences in Kidney Health and Disease

The American Board of Medical Specialties (ABMS) and the Accreditation Council of Graduate Medical Education (ACGME) have embarked on a joint initiative to quantify and evaluate a set of 6 physician core competencies by which the individual physician will be measured for Residency Certification, Board Certification and more recently, Maintenance of Certification (MOC).

It is the intent of the Office of Continuing Medical Education at the Keck School of Medicine of USC to develop our CME activities in the context of desirable physician attributes.

The following are a list of Core Competencies that will be covered in one or more of the presentations at this symposium.

- **Patient Care** that is compassionate, appropriate, and effective for the treatment of health problems and the promotion of health.

- **Medical Knowledge** about established and evolving biomedical, clinical, and cognate (e.g. epidemiological and social-behavioral) sciences and the application of this knowledge to patient care.

- **Practice-Based Learning and Improvement** that involves investigation and evaluation of their own patient care, appraisal and assimilation of scientific evidence, and improvements in patient care.

- **Interpersonal and Communication Skills** that result in effective information exchange and teaming with patients, their families, and other health professionals.

- **Professionalism**, as manifested through a commitment to carrying out professional responsibilities, adherence to ethical principles, and sensitivity to a diverse patient population.

- **Systems-Based Practice**, as manifested by actions that demonstrate an awareness of and responsiveness to the larger context and system of health care and the ability to effectively call on system resources to provide care that is of optimal value.
ACKNOWLEDGES EXHIBIT SUPPORT

Cardinal Level

Alexion
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UKRO Foundation
The USC Department of Medicine/Division of Nephrology and Hypertension is grateful to the Manfred Mosk Foundation for an educational grant in support of the symposium. A special recognition to UKRO for all their support of this symposium.
CLAIMING CME / CEU?

Next week you will be receiving an email containing detailed instructions about claiming & printing your certificate.

**Step 1: Log-In**

Visit [https://cmetracker.net/KECKUSC/Archive](https://cmetracker.net/KECKUSC/Archive) & click on the certification button of the program you attended. Log-in using your email and password.

**Step 2: Complete Online Evaluation**

Feedback is important which is why we strongly encourage all attendees to participate in the online evaluation.

**Step 3: Download & Print Certificate**

By clicking submit you will be prompted to enter your participation credits, download & print your certificate.

For questions or concerns please contact the Keck School of Medicine’s Office of CME at 323-442-2555.
INSTRUCTIONS ON THE ANNOTATION OF PDF FILES

To view, print and annotate your syllabus you will need Adobe Reader version 7 (or higher). This program is freely available for a whole series of platforms that include PC, Mac, and UNIX and can be downloaded from [http://get.adobe.com/reader/](http://get.adobe.com/reader/). The exact system requirements are given at the Adobe site: [http://www.adobe.com/products/reader/tech‐specs.html](http://www.adobe.com/products/reader/tech‐specs.html).

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<td>To make annotations in the PDF file, go to the main Adobe tool bar and change the cursor from a hand symbol to the normal cursor by clicking on the ‘Select’ button in the menu bar at the top (versions 7 and 8). When you open the PDF file using Adobe Reader, the Commenting tool bar should be displayed automatically; if not, click on ‘Tools’, select ‘Comment &amp; Markup’ (or ‘Commenting’ in version 7), then click on ‘Show Comment &amp; Markup tool bar’ (or ‘Commenting tool bar’ in version 7, or ‘Show Commenting bar’ on the Mac). If these options are not available in your Adobe Reader menus then it is possible that your Adobe Acrobat version is lower than 7 or the PDF has not been prepared properly.</td>
<td>To make annotations in the PDF file, open the PDF file using Adobe Reader X, click on ‘Comment’. If this option is not available in your Adobe Reader menus then it is possible that your Adobe Acrobat version is lower than X or the PDF has not been prepared properly. This opens a task pane and, below that, a list of all Comments in the text. These comments initially show all the changes made by our copyeditor to your file.</td>
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(PC, Adobe Reader version 7)

(PC, Adobe Reader version 8, right-click on title bar (Comment & Markup) to show additional icons)

(Mac)

**PDF ANNOTATIONS (Adobe Reader version 9)**

The default for the Commenting tool bar is set to ‘off’ in version 9. To change this setting select ‘Edit | Preferences’, then ‘Documents’ (at left under ‘Categories’), then select the option ‘Never’ for ‘PDF/A View Mode’ (the Commenting tool bar is the same as in version 8).

(Changing the default setting, Adobe version 9)
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<td>Click the ‘Insert Text’ icon <img src="image" alt="Insert Text" /> on the Commenting tool bar. Click to set the cursor location in the text and simply start typing. The text will appear in a commenting box. You may also cut-and-paste text from another file into the commenting box. Close the box by clicking on ‘x’ in the top right-hand corner.</td>
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<td>Click the ‘Replace (Ins)’ icon <img src="image" alt="Replace" /> on the Commenting tool bar. To highlight the text to be replaced, click and drag the cursor over the text. Then simply type in the replacement text. The replacement text will appear in a commenting box. You may also cut-and-paste text from another file into this box. To replace formatted text (an equation for example) please Attach a file (see below).</td>
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<td>Attach a file</td>
<td>Click on the ‘Attach a File’ button <img src="image" alt="Attach a File" /> on the Commenting tool bar. Click on the figure, table or formatted text to be replaced. A window will automatically open allowing you to attach the file. To make a comment, go to ‘General’ in the ‘Properties’ window, and then ‘Description’. A graphic will appear in the PDF file indicating the insertion of a file.</td>
<td>Click on the ‘Attach File’ icon <img src="image" alt="Attach File" /> on the Commenting tool bar. Click on the figure, table or formatted text to be replaced. A window will automatically open allowing you to attach the file. A graphic will appear indicating the insertion of a file.</td>
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DEPARTMENT OF MEDICINE
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The Keck School of Medicine of USC takes responsibility for the content, quality and scientific integrity of this CME activity.

As part of the new commercial guidelines, we are required to disclose any real or apparent commercial conflict(s) of interest (COI) of all persons in control of educational content for this activity, specifically, but not limited to: faculty/presenters, CME committee members and/or planners. Any disclosed real or apparent commercial conflict(s) of interest (COI) have been resolved through a conflict resolution process prior to the beginning of this activity.

The Keck School of Medicine further requires that, if applicable, faculty/presenters disclose to the audience their intention to discuss the off label and/or investigational (not yet approved for any purpose) use of pharmaceuticals or medical devices at the beginning of their presentation.

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<td>All CME planners</td>
<td>The CME planners have no relevant financial relationships with any commercial interests</td>
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Aresty Conference Center, USC Health Sciences Campus
December 1-2, 2018

Presented by: Department of Medicine, Division of Nephrology & Hypertension & USC Office of Continuing Medical Education

DECEMBER 1, 2018 – DAY I: Sex Differences in Kidney Health and Disease

7:30 am Registration and Continental Breakfast
8:20 am Welcome
Núria M. Pastor-Soler, MD, PhD

Session I: Sex Differences in Kidney Physiology
Moderator: Núria M. Pastor-Soler, MD, PhD
8:30 am Sex Differences in Sodium and Potassium Handling
Alicia A. McDonough, PhD
9:20 am AMPK Is a Potential Target to Improve Outcomes After Kidney Donation
Núria M. Pastor-Soler, MD, PhD
10:00 am Break, Networking and Mentoring

Session II: Diseases that Specifically Target the Female Kidney
Moderator: Alicia A. McDonough, PhD
10:15 am Risk of Cardiovascular Disease, End-Stage Renal Disease, and Stroke in Postpartum Women and their Fetuses After a Hypertensive Pregnancy
Mark W. Cunningham Jr., PhD, MBA
10:50 am Preeclampsia and Atypical Hemolytic Uremic Syndrome: How Do They Complement Each Other?
Richard M. Burwick, MD, MPH
11:30 am Intravital Imaging Reveals New Clues on Lupus Nephritis Pathomechanism
Janos Peti-Peterdi, MD, PhD and Co-Author Chaim Jacob, MD, PhD
12:15 pm Lunch, Networking and Mentoring

Session III: Sex Differences in Kidney Disease
Moderator: Hui Yi Shan, MD
1:00 pm Sex and Gender Differences in Diabetic Kidney Disease
Susanne B. Nicholas, MD, PhD
1:40 pm Basic Science Understanding of Sex Differences in Acute Kidney Injury
Lisa M. Curtis, PhD
2:40 pm The Role of Sex Differences and Metabolic Changes in Polycystic Kidney Disease
Kenneth R. Hallows, MD, PhD
3:00 pm Break

Session IV: Women and Kidney Replacement Therapies: Clinical and Policy Implications
Moderator: Thin Thin Maw, MD, MS
3:15 pm Dialysis and Pregnancy
Madeleine V. Pahl, MD
3:45 pm Sex Differences in Transplantation
Deborah B. Adey, MD
4:15 pm Gender and the Medicare Payment Policy in Kidney Diseases
Eugene Lin, MD
4:45 pm Panel Discussion and Closing Remarks
5:15 pm Adjourn
DECEMBER 2, 2018 – DAY II: Career Development in Nephrology and Kidney Research

Co-Sponsored by Women in Nephrology

Trainees and Junior Faculty Welcome
8:30 am Continental Breakfast, Networking and Mentoring
9:00 am Welcome
   Núria M. Pastor-Soler, MD, PhD

Session I: Basics of Career Development
Moderator: Lisa M. Curtis, PhD
9:10 am Essentials of Leadership and Business in Nephrology
   Cynthia M. Miracle, MD
9:45 am Mentoring and Coaching in Clinical Nephrology and Kidney Research
   Núria M. Pastor-Soler, MD, PhD and Lisa M. Curtis, PhD
10:15 am Break, Networking and Mentoring

Session II: Nephrology at the Crossroads
Moderator: Susanne B. Nicholas, MD, PhD
10:45 am Emerging Subspecialties Within Nephrology: The Example of Onconephrology
   Umut Selamet, MD
11:15 am The Future of the Workforce in Clinical Nephrology and Kidney Research
   Li-Li Hsiao, MD, PhD
11:45 am Closing Panel: Questions and Answers
12:00 pm Adjourn

Organizing Committee:
Kenneth R. Hallows, MD, PhD
Taneisha Jackson, Course Coordinator
Thin Thin Maw, MD, MS
Alicia A. McDonough, PhD
Núria M. Pastor-Soler, MD, PhD, Chair

ACKNOWLEDGEMENT:
The USC Department of Medicine/Division of Nephrology and Hypertension is grateful to the Manfred Mosk Foundation for an educational grant in support of the symposium. A special recognition to UKRO for all their support of this symposium.
Sex Differences in Sodium and Potassium Handling

Alicia A. McDonough, PhD

December 1, 2018

8:30 am – 9:20 am
Sex is a significant biological variable:

- Female physiology is optimized for successful reproduction which entails fluctuations in vascular, hemodynamic and renal function

Beyond reproduction and lactation, women:

- have lower BP than men pre-menopause
- exhibit better renal ischemia tolerance
- are protected from CV and renal disease pre-menopause

Aims:

- Generate a quantitative profile of renal Na\(^+\) transporters, channels, claudins, (phosphorylation and cleavage) in female and male rats and mice at baseline
- Address the in vivo physiologic consequences of the differences identified

Sodium transporters and channels along the nephron:

- PT:
  - NHE3
  - NaPi2
  - AQP1

- TALH:
  - NKCC2
  - NKCC2p
  - NHE3
  - Cld-2

- DCT:
  - NCC, NCCp, Cld-7

- CNT:
  - ENaC
  - ENaC cleaved

- CD:
  - AQP2

Apical transporter regulation can be assessed with specific antibodies:

- ↓↑ # transporters/channels in plasma membrane
- ↓↑ total abundance
- Phosphorylation, proteolysis, other modifications
**APPROACH**

Adult female and male Sprague Dawley rats (n=6 each)

**Methods**

- Urine and plasma [Na⁺], [K⁺] and [Li⁺] by flame photometry
- Endogenous lithium clearance: $C_{Li} = \frac{[U/P] \times (V_{Li}/BW)}{t}$
- Immunoblotting: homogenates run at 1 and ½ amounts to validate linearity
- Confocal microscopy
- Micropuncture for JHCO₃⁻ transport

**Overnight fasting + H₂O metabolic cages**

Collect:
- Blood
- Urine: in cage + bladder
- Kidneys: Dissect cortex, medulla
- Females: Vaginal smear*

**3 hr feeding with 0% K⁺ diet**

**DAY 0: 3pm**

**DAY 1: 7-10am**

**DAY 1: 10am**

**DAY 7: 10 am**

**Saline challenge:**
- Under isoflurane
- 7% b.w. saline i.p.
- Collect UV and UNa in metabolic cage

**Part 1)**

Proximal nephron physiology and transporters

**Female rats exhibit less proximal tubule bicarbonate reabsorption than males, a marker of NHE3 activity**

**Proximal tubule NHE3 location in microvilli exhibits sexual differences**

Female rats excrete an acute saline load (7% body weight, i.p.) more rapidly than males. Urine collected in conscious rats in metabolic cages

**Quantitative Immunoblot**

考慮するとき、プロテインの丸まることを免疫斑

- Estrus cycle in rats, occurs over 4 or 5 days: P= proestrus, E= estrus, M= metestrus, D= diestrus.
- Vaginal smears taken between 10 AM -12 PM.
- No apparent correlation between the stage of the estrus cycle and these transporters proteins abundance or phosphorylation

**Female rats**

| Estrus cycle stage | NHE3 | JHCO3⁻ | Lithium clearance *
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>F = proestrus</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>E = estrus</td>
<td>0.8</td>
<td>0.8</td>
<td>0.8</td>
</tr>
<tr>
<td>M = metestrus</td>
<td>0.6</td>
<td>0.6</td>
<td>0.6</td>
</tr>
<tr>
<td>D = diestrus</td>
<td>0.4</td>
<td>0.4</td>
<td>0.4</td>
</tr>
</tbody>
</table>

* Determined by in vivo stationary microperfusion via continuous measurement of luminal pH

AC Girardi, Heart Institute (InCor), Univ. of São Paulo

**Less proximal reabsorption?**

**Proximal tubule NHE3 location in microvilli exhibits sexual differences**

In males, NHE3 (green) and villin (red) co-localized in the body of the villi (yellow)

In females, NHE3 distributed to the base of the microvilli below villin. More abundant NHE3pS552, which localizes to base of microvilli

* NHE3 is less active at the base of the microvilli: Brain JC, AJP Renal, 2014
Part 2) Distal nephron physiology and transporters
- Do distal transporters “compensate” for increased delivery in females?
- Does the compensation affect the potassium set-point?
- Female: NCC2 in cTAL, NCC, ENaC, ROMK, BK, Cldn7
- *o/n fast and OK meal before euthanasia

Higher abundance of distal transporters in Female vs. Male
- Proximal tubule: ↑NHE3p (less active) ↓NaPi2, ↓Cldn2, ↓AQP1
- Female: lower plasma [K+] associated with higher NCC, NCCp
- Female: more rapid natriuresis and diuresis in response to saline load
- CONCLUSION: Lower proximal Na+ transport in females expedites secretion of a saline challenge and provides higher distal Na+ transporters’ abundance which may facilitate K+ secretion and lower plasma [K+] set-point

Physiologic consequences of higher distal ENaC in females:
- Lower plasma [K+] in females after overnight fast, no difference in aldosterone
- Higher ENaC abundance and flow may drive more K+ secretion
- Higher NCC and claudins to limit K+ secretion?
- Lower plasma [K+] set point. Protection from hyperkalemia during pregnancy?
Transporter profiles of adult C57BL/6 mice post o/n fast

Similarities between female mice and rats:
- Lower proximal: NHE3, NHE3p, NaPi2, Cldn2, villin, myosin VI
- NHE3 at base of microvilli
- Higher distal: NKCC2, NKCC2p, NCC, NCCp, SPAK*, Cldn7

Differences between female mice and rats:
- Higher AQP1 in female vs. male mice
- Natriuretic response to saline challenge not greater in female mice
- No difference in ENaC in female vs. male mice
- No difference in plasma [K+] in female vs. male mice

Experimental AngII infusion hypertension used in thousands of studies
AngII → vasoconstriction, renal excess sodium, ↑intrarenal AngII, Inflammation
Rise in blood pressure is error signal to activate pressure natriuresis, normalize ECV

Part 3) Angiotensin II Hypertension in Females

Aim
Test the hypothesis that the female transporter profile blunts the rise in blood pressure during AngII hypertension (400 ng/kg/min, 14 d)

Protocol

<table>
<thead>
<tr>
<th>DAY 0</th>
<th>DAY 1-14</th>
<th>DAY 14</th>
</tr>
</thead>
</table>
| Overnight baseline urine collection in metabolic cages | Control - renal surgery Ang II - osmotic minipumps Blood pressure by tail cuff | C/N metabolic cage for urine Under isoflurane collect: blood, kidneys, do renal trans 

AngII Hypertension and Renal Injury

Breakdown filtration barrier:
- Podocyte injury
- Inhibition of nephrin production
- Chronic vasoconstriction → hypoxia
Ang II hypertension is similar in males and females (~ 195 mmHg)

Albuminuria significantly increased in males, n.s. in females

Male  F e m a l e s
0  2  0  4  0  6  0
M i c r o a l b u m i n u r i a  ( m g / d l)

ELISA Assays

Albuminuria assessed in 0.02% o/n urine

M a l e s  F e m a l e s
0  2  0  4  0  6  0
R a t s e r u m  a l b u m i n  ( g / d l)

ELISA Assays

Albuminuria assessed in 0.02% o/n urine

M a l e s  F e m a l e s
0  2  0  4  0  6  0
R a t s e r u m  a l b u m i n  ( g / d l)

Does proteinuria of Ang II–hypertension activate ENaC?

Leaked proteins include plasminogen which is activated to plasmin in tubular fluid by uPA (a plasminogen activator). Plasmin removes an inhibitory peptide from γ-ENaC → full activation of the ENaC channel

More urinary plasminogen and angiotensinogen in M vs. F during Ang II-HTN:

During Ang II-HTN: cleaved α-ENaC and β-ENaC are increased similarly in M and F γ-ENaC cleaved twice as much in M, associated with urinary plasmin Predictive of more ENaC activation in M vs. F

Part 3) Conclusions:

Urine and plasma:
• Hypertension similar during AngII in M and F
• Albuminuria increased in M, unchanged in F
• Lower serum albumin in M vs. F

Transporter activation:
• NHE3: decreases in M, increases in F
• NCC: increases in M, not females
• NKCC2: activation in both males and females
• ENaC: more γ-ENaC cleavage in M than F, associated with proteinuria and plasmin

Yet, ENaC N, P0 and P0 did not reveal a difference between sexes; measured by M. Momenko (U. Augusta)

Diana L. Torres
3rd year Keck Med student
#: SA-PO1011
Sex differences in response to high salt
AMPK Is a Potential Target to Improve Outcomes After Kidney Donation

Núria M. Pastor-Soler, MD, PhD

December 1, 2018

9:20 am – 10:00 am
Risk of Cardiovascular Disease, End-Stage Renal Disease, and Stroke in Postpartum Women and their Fetuses After a Hypertensive Pregnancy

Mark W. Cunningham Jr., PhD, MBA

December 1, 2018

10:15 am – 10:50 am
Preeclampsia and Atypical Hemolytic Uremic Syndrome: How Do They Complement Each Other?

Richard M. Burwick, MD, MPH

December 1, 2018

10:50 am – 11:30 am
Intravital Imaging Reveals New Clues on Lupus Nephritis Pathomechanism

Janos Peti-Peterdi, MD, PhD and Co-Author Chaim Jacob, MD, PhD

December 1, 2018

11:30 am – 12:15 pm
Sex and Gender Differences in Diabetic Kidney Disease

Susanne B. Nicholas, MD, PhD

December 1, 2018

1:00 pm – 1:40 pm
Basic Science Understanding of Sex Differences in Acute Kidney Injury

Lisa M. Curtis, PhD

December 1, 2018
1:40 pm – 2:40 pm
The Role of Sex Differences and Metabolic Changes in Polycystic Kidney Disease

Kenneth R. Hallows, MD, PhD

December 1, 2018

2:40 pm – 3:00 pm
Dialysis and Pregnancy

Madeleine V. Pahl, MD

December 1, 2018

3:15 pm – 3:45 pm
Help! My Dialysis Patient is Pregnant

Madeleine V. Pahl, MD, FASN
University of California, Irvine

Disclosures

- I am a nephrologist
- I know more about renal physiology than I do about pregnancy
- Oh yes, and I have no financial disclosures to report

Pregnancy in Dialysis Patients

“Show me a method of birth control more effective that ESRD”
Roger Rodby MD, 1991

Factors Affecting Fertility

- Menstrual irregularities, endocrine abnormalities and sexual dysfunction affect fertility in ESRD
- most women are anovulatory, even those who menstruate
- estradiol levels are appropriate for the follicular phase
- LH, FSH do not surge
- progesterone levels remain low
- 70-90% are hyperprolactinemic
- Early literature (Obstet Gyn 51:552, 1978) reported only 10% of women of childbearing age menstruated but more recent study reports 42%
- Frequency of pregnancy is increasing in dialysis patients

Pregnancy Rates

<table>
<thead>
<tr>
<th>Reference</th>
<th># pregnancies/ # women</th>
<th>Incidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Souquiyyeh; AJKO (Saudi Arabia) 1992</td>
<td>27/360</td>
<td>7%</td>
</tr>
<tr>
<td>Hou; AJKO (US) 1994</td>
<td>58/1281</td>
<td>1.5%</td>
</tr>
<tr>
<td>Okundaye; AJKO (US Registry) 1998</td>
<td>184/6230</td>
<td>2.2%</td>
</tr>
<tr>
<td>Bagon; AJKO (Belgium) 1998</td>
<td>15/1472</td>
<td>1%</td>
</tr>
<tr>
<td>Toma; ANZA Registry Japan 1999</td>
<td>172/5000</td>
<td>3.4%</td>
</tr>
</tbody>
</table>

- Incidence in PD is 2-3X lower, maybe due to dialysate in peritoneum, adhesions from peritonitis

ANZA Registry

- Data from 1966-2008 on dialyzed women aged 15-49 yrs.
- 23,700 person years (PY) with 49 pregnancies
- Overall Rates: 2.07/1000 PY
- Significant increase in pregnancy rate for 1996-2008 period (3.3/1000 PY vs 0.54 and 0.67 in 1976-85 and 1986-95)
- Patient on PD less likely to achieve a pregnancy
Pregnancy Outcome with Hemodialysis
(series with > 20 patients; improvement over time)

<table>
<thead>
<tr>
<th>Site</th>
<th>Termination (%)</th>
<th>Losses (%)</th>
<th>Live births (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Europe 1980</td>
<td>39</td>
<td>28</td>
<td>23</td>
</tr>
<tr>
<td>Saudi Arabia 1992</td>
<td>0</td>
<td>63</td>
<td>37</td>
</tr>
<tr>
<td>US 1994</td>
<td>8</td>
<td>52</td>
<td>37</td>
</tr>
<tr>
<td>US 1998</td>
<td>11</td>
<td>46</td>
<td>42</td>
</tr>
<tr>
<td>Japan 1999</td>
<td>19</td>
<td>24</td>
<td>40</td>
</tr>
<tr>
<td>Australia-New Zealand 2008</td>
<td>15</td>
<td>30</td>
<td>53</td>
</tr>
<tr>
<td>Japan 2009</td>
<td>-</td>
<td>36</td>
<td>64</td>
</tr>
<tr>
<td>Brazil 2010</td>
<td>-</td>
<td>13</td>
<td>87</td>
</tr>
</tbody>
</table>

ANZA Registry: Outcomes

- Data from 1966-2008, on dialyzed women aged 15-49 yrs, 23,700 person years (PY) with 49 pregnancies, 30 live births, 11 medical terminations, 3 spontaneous abortions, 5 still births.
- 68% maintained on HD, 32% on PD (no information on dialysis prescription during pregnancy).
- Overall live birth rate 1.26/1000 PY or 79% excluding terminations.
- Preeclampsia rate was 19.4%.
- No maternal deaths.
- 55% low birth weight (< 2.5 kg).
- 35% very low birth weight (< 1.5 kg).

Complications

- Risk of death does not appear to be increased by pregnancy.
- Preeclampsia common in CKD and rises with severity, 19-54% and a challenge to diagnose.
- BP increases, fetal growth restriction, altered placental Doppler blood flows, HELLP, visual changes, seizure.
- Associated with poor fetal outcomes.
- Polyhydramnios in 30-70%, may be associated with favorable fetal outcome (Luders AJKD, 2010).
- Intra-uterine growth retardation.
- Pre-term labor and delivery with low birth-weight infants.

Pregnancy Outcome in Peritoneal Dialysis

- Early series suggested PD preferred modality (Redrow, Medicine 1988), theoretical benefit: gentle daily UF, fewer fluctuations in solutes.
- US Registry showed no statistical difference in HD vs. PD in birth rates.

<table>
<thead>
<tr>
<th>HD</th>
<th>PD</th>
</tr>
</thead>
<tbody>
<tr>
<td>83/117</td>
<td>70.9%</td>
</tr>
<tr>
<td>9/14</td>
<td>64.2%</td>
</tr>
<tr>
<td>0.61</td>
<td></td>
</tr>
</tbody>
</table>

Successful delivery

Birth weight (g): 1483 ± 116 vs. 1623 ± 320, 0.04

Children of a Lesser God or Miracles?

- Emotional/behavioral profile of children born to mothers on dialysis: Kidney and Pregnancy Study Group in Italy.
- 23 mothers, 24 live-born children, ages 2-13 yrs.
- Emotional/behavioral outcome was normal in most children. None had chronic diseases or permanent disability but developmental disorders mainly involving communication skills.
- Mothers were less stressed when compared with others with chronic diseases: authors termed it a “positive defense” (Piccoli AOT 2015, 30(7):1190-1202)

Dialysis Management

- Dialysis prescription
- Dry weight
- BP control
- Anemia management
- Mineral-bone metabolism concerns
- Nutrition/pre-natal vitamin supplements
- Dialyzers /dialysate
- OB/fetal monitoring
Dialysis Prescription

- Early Australia CKD data (Mackay, Aust NZ J Obs, 3:21-24, 1963) noted single most important factor in fetal outcome was level BUN, recent targets BUN < 50 improved outcomes (AACM et al., Kidney International 2009;75: 1217-32).
- US Registry: 12 pts dialyzed > 20 hr/wk, 83% pregnancies successful vs. 46% in those dialyzed < 14 hrs/week and US Registry update: 75% of those dialyzed for > 20 hrs/week had successful outcome vs. 38% dialyzed for < 19 hrs/week (Hou, J Am Soc Nephrol 2002).
- Report (Heise et al., Nephrol Dial Transplant 2005) 26/257) Mean weekly Kt/V of 0.6 ± 0.4 and Urea Reduction Rate 54.8% ± 29.4% in 5 patients: 100% successful gestational age 32.8 ± 3.3 wks, birth weight 1765 ± 554g.

A Large Series Spanning 20 years

- 52 pregnancies from 1988-2008 (Lugers AJKD, 2010)
- 87% overall successful rate
  - Gestational age 32.7 ± 3.1 wk
  - Preeclampsia a poorer prognosis (60 vs 92.9%)
- Approach to Care:
  - 28 women conceived pre-dialysis: dialyzed 12 hrs/wk
  - 24 conceived while on dialysis: dialyzed 15 hrs/wk
  - No outcome differences in birth weight, gestational age, % pre-term births, surviving infants
  - Pre-dialysis BUN < 75 associated with better fetal outcomes and higher birth weight

Experience on Nocturnal Dialysis

- 6 pregnancies; women conceived while maintained on nocturnal dialysis (36 hr/wk)
- Increased to 48 ± 5 hrs/wk
- All infants survived, 1 born at < 36 wks
- Mean weight 2417.5 ± 657 g

Weight Management

- Dry weight: regularly evaluated and allow for steady increase, 1st trimester minimum gain of 1-1.5 kg, in 2nd and 3rd trimester, increase 0.5 kg/wk
- Suggestion to consider fetal weight and growth from ultrasound in 3rd trimester
- Observed weight changes from start of pregnancy in 5 cases (Haase, Nephrol Dial Trans 2005)

<table>
<thead>
<tr>
<th>Weight</th>
<th>Gestational Age (wks)</th>
<th>Baby Weight (g)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>195</td>
<td>1274</td>
</tr>
<tr>
<td>2</td>
<td>105</td>
<td>2215</td>
</tr>
<tr>
<td>3</td>
<td>430</td>
<td>1240</td>
</tr>
<tr>
<td>4</td>
<td>540</td>
<td>2465</td>
</tr>
<tr>
<td>5</td>
<td>140</td>
<td>1630</td>
</tr>
</tbody>
</table>
Blood Pressure Control

- HTN extremely common: 79% are HTN's and 48% had BP > 170/110
- Diastolic BP targets of 80-90 mmHg
- Mainstay of treatment volume control to dry weight
- Aggressive ultrafiltration has rarely been reported to cause hypotension and fetal distress (Unzelman Tran Am Soc Art Int Org 1973)
- Avoid ACEi/ARB

Anemia

- Safety of EPO and intravenous iron has not been established but is common practice
  - EPO (MW 30,400) is not expected to cross placenta
  - However animal data conflicting: 
    - 125I-EPO found in fetal rats but not fetal lambs after treatment of mother
  - Small study in humans noted normal EPO levels and HCT in neonates exposed to intrauterine exogenous EPO (Acta Ob Gyn Scand 75:449, 1996)

- US Registry Data, 90% had HCT > 30%
  - 26% of EPO treated did not require transfusions; 77% of those who did not receive EPO did
  - Targets 10-11 g/dl usually require 50% increase in EPO dose
  - Maintenance IV iron will likely be required

Mineral Bone Metabolism

- Avoid hypocalcemia and post-treatment hypercalcemia, 2.5 mEq/L dialysate calcium may be preferable
- Calcitriol preparations are usually continued
  - Placental converts 25(OH)2 to 1,25(OH)2 which may be required
  - High doses used in 1 patient without ill effects to the fetus
  - Calcitriol safety unclear but in pregnant animals safe with no adverse fetal effects
  - 1 case with primary HPT treated in the 32nd week of pregnancy (J Pediatr Endocrinol Metab. 2009 Aug;22(8):741-9)
  - 2 pregnancies in 1 patient with PTH malignancy and hypercalcemia, no fetal adverse events (Endocr Case Rep. 2014; 2014: 140056)

- Prenatal vitamins / folate (2mg/day). Maintain nl B12/folate levels and MCV
- Some provide additional B-complex and trace mineral supplements
- Magnesium: maintain nl levels, with preeclampsia can add Mg to dialysate to reach levels of 5-7 mg/dl (J Obstet Gynecol Surv. 1991.)

Nutrition and Vitamin Supplements

- Little information available regarding protein intake but most prescribe additional for fetal development
  - Suggest 1.8 g/kg/day with 3000 kcal/day
  - Prenatal vitamins folic (2mg/day). Maintain ni B12/folate levels and MCV
  - Some provide additional B-complex and trace mineral supplements
  - Magnesium: maintain ni levels, with preeclampsia can add Mg to dialysate to reach levels of 5-7 mg/dl (J Obstet Gynecol Surv. 1991.)
Dialyzer/Dialysate Considerations

- Biocompatible, non-re-use dialyzers, avoid formaldehyde or ethylene oxide exposure due to potential fetal malformations
- Attention to K concentration (3 mEq/L)
- Bicarbonate bath: may need to be lowered to maintain physiologic level
- Anticoagulation with unfractionated heparin as required

Dialysis prescription
- High flux membranes
- No re-use of dialyzers
- Avoid formaldehyde or ethylene oxide treated dialyzers

Dialysate
- 3 mEq/L potassium bath
- 25 mEq/L bicarbonate bath
- 2.5-3.5 mEq/L calcium bath

Dialysis dose
- >20 hours/week
- 6 HD treatments a week
- Target BUN < 50 mg/dl

Dry weight
- Increase 1-1.5 kg in the first 12 weeks
- Increase 0.5 kg weekly thereafter

Anemia
- Target Hg 10-11 g/dl
- Continue erythropoietin, expect increase in dose
- Continue parenteral iron as required

MBD
- Continue vitamin D preparations
- No clear data on use of cinacalcet

Nutrition
- 1.8 g protein/kg/day
- Multivitamin use
- Folate 2.5 mg/day

Summary

- The 1 yr survival for women of childbearing age on dialysis has been reported to be 90% and risk of death does not appear to be increased by pregnancy
- Outcome of pregnancy in dialysis patients has improved but it is difficult to determine what changes in care are responsible, but increased dialysis prescription may play a role
- Further improvements will require meticulous documentation and close collaboration between nephrologist and obstetrician

Hemodialysis management in pregnancy

<table>
<thead>
<tr>
<th>Dialysis prescription</th>
<th>Dialysate</th>
<th>Dialysis dose</th>
<th>Dry weight</th>
<th>Anemia</th>
<th>MBD</th>
<th>Nutrition</th>
</tr>
</thead>
<tbody>
<tr>
<td>High flux membranes</td>
<td>3 mEq/L potassium</td>
<td>&gt;20 hours/week</td>
<td>Increase 1-1.5 kg in the first 12 weeks</td>
<td>Target Hg 10-11 g/dl</td>
<td>Continue vitamin D preparations</td>
<td>1.8 g protein/kg/day</td>
</tr>
<tr>
<td>No re-use of dialyzers</td>
<td>25 mEq/L bicarbonate</td>
<td>6 HD treatments a week</td>
<td>Increase 0.5 kg weekly thereafter</td>
<td>Continue erythropoietin, expect increase in dose</td>
<td></td>
<td>Multivitamin use</td>
</tr>
<tr>
<td>Avoid formaldehyde or ethylene oxide treated dialyzers</td>
<td>2.5-3.5 mEq/L calcium bath</td>
<td>Target BUN &lt; 50 mg/dl</td>
<td></td>
<td>Continue parenteral iron as required</td>
<td></td>
<td>Folate 2.5 mg/day</td>
</tr>
</tbody>
</table>
Sex Differences in Transplantation

Deborah B. Adey, MD

December 1, 2018

3:45 pm – 4:15 pm
Gender and the Medicare Payment Policy in Kidney Diseases

Eugene Lin, MD

December 1, 2018

4:15 pm – 4:45 pm
Overview

- Incidence/Prevalence of ESRD
- History of ESRD payment
- Construction of the ESRD PPS
- Gender differences in ESRD costs
- Controversies in risk-adjustment

Disclosures

- NIH NIDDK K08DK118213
- University Kidney Research Organization (UKRO)
- Limited consultancy with Acumen, LLC

The content in this presentation do not represent official views of the NIH, CMS, or the UKRO

Incidence/Prevalence of ESRD

Incidence of ESRD


Incidence of ESRD (2016)

Prevalence of ESRD

![Prevalence of ESRD](image)

**ESRD cost to Medicare**

![ESRD cost to Medicare](image)

**History of ESRD payment**

![History of ESRD payment](image)

### Timeline

- 1973: Medicare covers ESRD irrespective of age
- 1983: Dialysis composite rate introduced
- 1989: Erythropoietin approve for dialysis
- 2011: Implementation of the ESRD PPS

### 1973-1983

- Dialysis treatments reimbursed through “reasonable charges”
- Reimbursement per treatment:

<table>
<thead>
<tr>
<th>Patient 1</th>
<th>Patient 2</th>
<th>Patient 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Capital</td>
<td>Labor</td>
<td>Heparin</td>
</tr>
<tr>
<td>Capital</td>
<td>Labor</td>
<td>Heparin</td>
</tr>
<tr>
<td>Capital</td>
<td>Labor</td>
<td>Heparin</td>
</tr>
</tbody>
</table>

**Swaminathan S, et al. 2012. Health Affairs.**
1983: Composite rate introduced

- Treatments based on “average”

<table>
<thead>
<tr>
<th>Patient 1</th>
<th>Capital</th>
<th>Labor</th>
<th>Heparin</th>
<th>Supplies</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patient 2</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patient 3</td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

1983: Composite rate introduced

<table>
<thead>
<tr>
<th>Patient 1</th>
<th>Composite Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>Patient 2</td>
<td>Composite Rate</td>
</tr>
<tr>
<td>Patient 3</td>
<td>Composite Rate</td>
</tr>
</tbody>
</table>

1989: Introduction of Epo

- Erythropoietin / other meds reimbursed separately

<table>
<thead>
<tr>
<th>Patient 1</th>
<th>Composite Rate</th>
<th>Erythropoietin</th>
<th>Vitamin D</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patient 2</td>
<td>Composite Rate</td>
<td>Erythropoietin</td>
<td>Vitamin D</td>
</tr>
<tr>
<td>Patient 3</td>
<td>Composite Rate</td>
<td>Erythropoietin</td>
<td>Vitamin D</td>
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1989: Introduction of Epo

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<td>Patient 3</td>
<td>Composite Rate</td>
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2011: ESRD PPS Implementation

- Bundled separately billable medications into a bundled payment: the “base rate”

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2011: ESRD PPS Implementation

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Where does variation come from?

Risk adjustment...

ESRD Prospective Payment System

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ESRD PPS Risk Adjustment

- MedPAC. 2016-Outpatient Dialysis Services Payment System.
Patient Level Risk Adjusters

- Age
- BSA
- BMI
- Comorbidities
  - Incident (< 120 days on dialysis)
  - Hereditary Hemolytic or Sickle Cell Anemia
  - Myelodysplastic Syndrome
  - GI Bleed
  - Pericarditis

Gender differences in ESRD costs

CMS. 2018. ESRD PPS Patient-Level Adjustments.
Dialysis adequacy and gender

- Kt/V may underestimate dialysis adequacy in women and small men

**Anemia and gender**

![Graph showing anemia and gender comparison](image)

Spalding EM, et al. 2008. KI.

**Spalding EM, et al. 2008. KI.**

Anemia and gender

![Graph showing anemia and gender comparison](image)

Frankenfield DL, et al. 1999. AJKD.

**Frankenfield DL, et al. 1999. AJKD.**

Anemia and gender

![Graph showing anemia and gender comparison](image)

Ifudu O, et al. 2001. AJKD.

**Ifudu O, et al. 2001. AJKD.**

Controversies in risk-adjustment

![Table showing controversies in risk-adjustment](image)

Bladé O, et al. 2001. AJKD.

**Bladé O, et al. 2001. AJKD.**

Should gender be included?

- Key questions:
  - Are there biologic (intrinsic) differences between men and women?
  - Can a different variable (such as BSA) serve as a “proxy” for gender?
  - What are the risks and benefits of including gender into payment adjustment?

**Benefits of including gender**

- Reduces risk of cherry-picking / lemon dropping
- Accounts for differences in facility case-mix

**Kick School of Medicine of USC**

**Kick School of Medicine of USC**

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Risks of including gender

- Risk-adjustment could mask underlying differences in quality of care, entrenching disparities in care
- Potentially penalizes providers for taking care of predominantly male populations (e.g., facilities accepting VA patients)

Conceptual model

Risk Adjustment is helpful

Adapted from NQF. 2014. Risk Adjustment for Socioeconomic Status or Other Sociodemographic Factors.

Women require different therapies
Outcome

2. J.

Risk Adjustment isn’t as crucial (i.e., risk adjust for BSA or other factors)

Adapted from NQF. 2014. Risk Adjustment for Socioeconomic Status or Other Sociodemographic Factors.

Conceptual model

Adapted from NQF. 2014. Risk Adjustment for Socioeconomic Status or Other Sociodemographic Factors.

Conceptual model

Adapted from NQF. 2014. Risk Adjustment for Socioeconomic Status or Other Sociodemographic Factors.

References


6. Risk Adjustment isn’t as crucial (i.e., risk adjust for BSA or other factors)

Women are treated differently

Risk Adjustment isn’t helpful

Women require different therapies

Women are treated differently

Risk Adjustment is not helpful

Acknowledgements

• Some data reported here have been supplied by the United States Renal Data System (USRDS). The interpretation and reporting of these data are the responsibility of the presenter and in no way should be seen as an official policy or interpretation of the U.S. government.

Conclusions

• Women with dialysis are more costly

• Current risk-adjustment models omit gender, which may lead to cherry-picking

• Risk-adjustment is complex, and it is not always obvious to include all variables

• This is not unique to the ESRD PPS
Essentials of Leadership and Business in Nephrology

Cynthia M. Miracle, MD

December 2, 2018

9:10 am – 9:45 am
Mentoring and Coaching in Clinical Nephrology and Kidney Research

Núria M. Pastor-Soler, MD, PhD and Lisa M. Curtis, PhD

December 2, 2018

9:45 am – 10:15 am
Emerging Subspecialties Within Nephrology: The Example of Onconephrology

Umut Selamet, MD

December 2, 2018

10:45 am – 11:15 am
The Future of the Workforce in Clinical Nephrology and Kidney Research

Li-Li Hsiao, MD, PhD

December 2, 2018

11:15 am – 11:45 am
State and Federal Law

Federal Civil Rights Act: 42 U.S. Code § 1981 - Equal rights under the law
(a) Statement of equal rights. All persons within the jurisdiction of the United States shall have the same right in every State and Territory to make and enforce contracts, to sue, be parties, give evidence, and to the full and equal benefit of all laws and proceedings for the security of persons and property as is enjoyed by white citizens, and shall be subject to like punishment, pains, penalties, taxes, licenses, and exactions of every kind, and to no other.
(b) “Make and enforce contracts” defined. For purposes of this section, the term “make and enforce contracts” includes the making, performance, modification, and termination of contracts, and the enjoyment of all benefits, privileges, terms, and conditions of the contractual relationship. (c) Protection against impairment. The rights protected by this section are protected against impairment by nongovernmental discrimination and impairment under color of State law

Executive Order 13166
On August 11, 2000, the President signed Executive Order 13166, "Improving Access to Services for Persons with Limited English Proficiency". The Executive Order requires Federal agencies to examine the services they provide, identify any need for services to those with limited English proficiency (LEP), and develop and implement a system to provide those services so LEP persons can have meaningful access to them. It is expected that agency plans will provide for such meaningful access consistent with, and without unduly burdening, the fundamental mission of the agency. The Executive Order also requires that the Federal agencies work to ensure that recipients of Federal financial assistance provide meaningful access to their LEP applicants and beneficiaries.

Dymally-Alatorre Bilingual Services Act of California
The Dymally–Alatorre Bilingual Services Act (California Government Code Section 7290 et. Seq.) was signed into law in 1973, to eliminate language barriers that preclude people of our State, who either because they do not speak or write English or because their primary language is other than English, from having equal access to public services. This Act mandates that State and local agencies directly involved in the furnishing of information or the rendering of services to the public must in specifically prescribed situations employ a sufficient number of qualified bilingual persons in public contact positions to ensure the provision of information and services to the public in the language of the non-English speaking people.
http://www.bsa.ca.gov/pdfs/reports/99110.pdf

Cultural and Linguistic Competence

Center for Effective Collaboration and Practice
It is the mission of the Center for Effective Collaboration and Practice to support and promote a reoriented national preparedness to foster the development and the adjustment of children with or at risk of developing serious emotional disturbance. To achieve that goal, the Center is dedicated to a policy of collaboration at Federal, state, and local levels that contributes to and facilitates the production, exchange, and use of knowledge about effective practices.
http://cecp.air.org/
National Center for Cultural Competence (NCCC)
The mission of the National Center for Cultural Competence (NCCC) is to increase the capacity of health and mental health programs to design, implement, and evaluate culturally and linguistically competent service delivery systems to address growing diversity, persistent disparities, and to promote health and mental health equity. http://nccc.georgetown.edu/index.html

Limited English Proficiency (LEP)
Limited English Proficiency promotes a positive and cooperative understanding of the importance of language access to federally conducted and federally assisted programs. This site acts as a clearinghouse, providing and linking to information, tools, and technical assistance regarding limited English proficiency and language services for federal agencies, recipients of federal funds, users of federal programs and federally assisted programs, and other stakeholders. http://www.lep.gov/

DiversityRx
The purpose of DiversityRx is to improve the accessibility and quality of health care for minority, immigrant, and indigenous communities. We support those who develop and provide health services that are responsive to the cultural and linguistic differences presented by diverse populations. http://www.diversityrx.o

National Alliance for Hispanic Health
Mission is to improve the health and well being of Hispanics. The Alliance informs consumers, supports health and human service providers in the delivery of quality care, improves the science base for accurate decision making by promoting better and more inclusive research, promotes appropriate use of technology, insures accountability, advocates on behalf of Hispanics, and promotes philanthropy. http://www.hispanichealth.org/

National Center on Minority Health and Health Disparities
The mission is to promote minority health and to lead, coordinate, support, and assess the NIH effort to reduce and eliminate health disparities. NCMHD will conduct and support basic, clinical, social, and behavioral research, promote research infrastructure and training, foster emerging programs, disseminate information, and reach out to minority and other health disparity communities. http://www.nih.gov/about/almanac/organization/NCMHD.htm

National Council on Interpreting in Health Care
A multidisciplinary organization based in the United States whose mission is to promote culturally competent professional health care interpreting as a means to support equal access to health care for individuals with limited English proficiency. http://www.ncihc.org/

Think Cultural Health
The goal of Think Cultural Health is to Advance Health Equity at Every Point of Contact through the development and promotion of culturally and linguistically appropriate services. Think Cultural Health provides continuing education programs that are designed to help individuals at all levels and in all disciplines promote health and health equity. https://www.thinkculturalhealth.hhs.gov/content/continuinged.asp

Cultural Guides and Assessment Tools
The Provider’s Guide to Quality & Culture (not a U.S Website)
The quality of the patient-provider interaction has a profound impact on the ability of patients to communicate symptoms to their provider and to adhere to recommended treatment. It also has an impact on the patient’s feelings about being respected (or disrespected) as an
individual, a member of a family, and a member of a cultural group.

Cultural competence begins with an honest desire not to allow biases to keep us from treating every individual with respect. It requires an honest assessment of our positive and negative assumptions about others. An organization can help its health care professionals begin to gain cultural competence through formal training, but for most people cultural competence takes consistent individual practice over time.

http://erc.msh.org/mainpage.cfm?file=4.0.htm&module=provider&language=English&ggroup=&mgroup=

Guide to Culturally Competent Health Care

Be prepared for the culturally rich and diverse world of healthcare. This concise, easy-to-read handbook prepares you to relate to individuals from different cultures. This guide explores 34 different cultures and the issues to be sensitive to; including cultural variations regarding personal space, dietary preferences, communication, symptom management, activities of daily living, and religious and health practices.


Assessing Change: Evaluating Cultural Competence Education and Training

The AAMC commissioned an expert panel to review cultural competence studies that measured learner changes in attitudes, knowledge, and skills. This guide, which is based on the panel’s findings, provides these resources for educators and researchers an inventory of the research studies that assess the outcomes of cultural competence education and training, four recommended strategies to advance the research and evaluation, a Cultural Competence Assessment Tool Checklist, along with a guide to using the tool, to help educators and research measure facets of cultural competence in published assessment tools and an overview of three evaluation approaches for curriculum development and evaluation. Assessing Change: Evaluating Cultural Competence Education and Training

AAMC Tool for Assessing Cultural Competence Training

With increasing diversity in the U.S. population and strong evidence of disparities in health care, it is critically important that health care professionals are specifically educated on how their own and their patients' demographic (e.g., gender, income, race and ethnicity, etc.) and cultural (e.g., language, religion, etc.) factors influence health, health care delivery and health behaviors. In 2000, the Liaison Committee on Medical Education (LCME) introduced two standards about cultural competence that inspired medical schools to introduce cultural competence education into the undergraduate curriculum. TACCT will help in that effort. TACCT is a self-administered assessment tool that can be used by medical schools to examine all components of the entire medical school curriculum. TACCT enables schools to identify gaps and redundancies in their curricula, which will enable schools to make the best use of opportunities and resources. The TACCT can be used for both traditional and problem-based curricula.

Tool for Assessing Cultural Competence Training (TACCT) - PDF Version

Health Disparities

AMA Racial/Ethnic Health Care Disparities

Recent studies have shown that despite the steady improvements in the overall health of the United States, racial and ethnic minorities experience a lower quality of health services and are less likely to receive routine medical procedures and have higher rates of morbidity and mortality than non-minorities. Disparities in health care exist even when controlling for gender, condition, age and socio-economic status. The American Medical Association provides links for activities to eliminate health disparities, commission to end health care disparities, and research finding and recommendations. As well as an inspirational program for new generation of physicians called Doctors Back to School. http://www.ama-assn.org/ama/pub/physician-resources/public-health/eliminating-health-disparities.page
Unequal Treatment: Confronting Racial and Ethnic Disparities in Health Care

The Institute of Medicine researched the extent of disparities in the types and quality of health services received by U.S. racial and ethnic minorities and non-minorities; explore factors that may contribute to inequities in care; and recommend policies and practices to eliminate these inequities. The report from that study, Unequal Treatment: Confronting Racial and Ethnic Disparities in Health Care, found that a consistent body of research demonstrates significant variation in the rates of medical procedures by race, even when insurance status, income, age, and severity of conditions are comparable. [IOM Treatment]

OMH Minority Population Health Statistics

The Office of Minority Health is dedicated to improving the health of racial and ethnic minority populations through the development of health policies and programs that will help eliminate health disparities. Supported by the U.S. Department of Health and Human Services, OMH provides detailed demographic, language fluency (where relevant), education, economic, insurance coverage and health status information, as well as full census reports on Black/African American Health, American Indian/Alaskan Native Health, Asian American Health, Hispanic/Latino Health and Native Hawaiian & Pacific Islander Health. [OMH Minority Population Health Statistics]

CDC Race & Ethnic Minority Populations and Health Disparities & Inequalities Report 2013

Centers for Disease Control and Prevention’s Office of Minority Health and Health Equity (OMHHHE) mission is to advance health equity and women’s health issues across the nation through CDC’s science and programs, and increase CDC’s capacity to leverage its diverse workforce and engage stakeholders toward this end. Goals are in health equity, women’s health, diversity & inclusion, organizational capacity. Plus visions of a world where all people have the opportunity to attain the best health possible. [http://www.cdc.gov/minorityhealth/populations.html]

[CDC Health Disparities and Inequalities Report – United States, 2013]

HHS Action Plan to Reduce Racial and Ethnic Health Disparities

The [HHS Action Plan to Reduce Racial and Ethnic Health Disparities] outlines goals and actions HHS will take to reduce health disparities among racial and ethnic minorities. With the HHS Disparities Action Plan, the Department commits to continuously assessing the impact of all policies and programs on racial and ethnic health disparities. It will promote integrated approaches, evidence-based programs and best practices to reduce these disparities. The HHS Action Plan builds on the strong foundation of the Affordable Care Act and is aligned with programs and initiatives such as Healthy People 2020, the First Lady’s Let’s Move initiative and the President’s National HIV/AIDS Strategy. [HHS Action Plan to Reduce Racial and Ethnic Health Disparities]

Cultural Knowledge/ Language – Specific Sites

Ethnomed

EthnoMed contains information about cultural beliefs, medical issues and related topics pertinent to the health care of immigrants to Seattle or the US, many of whom are refugees fleeing war-torn parts of the world. [http://ethnomed.org/ethnomed]

The Cross Cultural Health Care Program

The mission of The Cross Cultural Health Care Program is to serve as a bridge between communities and health care institutions to advance access to quality health care that is culturally and linguistically appropriate. We provide resources and training for individuals and institutions with the goal of systems change and a vision that Healthcare in every Community, every Community in Healthcare. [http://xculture.org/]

[67]
**Black/African American Health**
Traditional Beliefs: Cultural Competency
[http://etl2.library.musc.edu/cultural/traditional/traditional_2.php](http://etl2.library.musc.edu/cultural/traditional/traditional_2.php)

**OMH Minority Populations: African American Profile**

**American Indian/Alaska Native/Native Hawaii**
Alaska Native Knowledge Network
ANKN is a resource for compiling and exchanging information related to Alaska Native knowledge systems and ways of knowing. ANKN creates and distributes a variety of publications that assist Native people, government agencies, educators and the general public in gaining access to the knowledge base that Alaska Natives have acquired through cumulative experience over millennia. [http://www.ankn.uaf.edu/Publications/Knowledge.html](http://www.ankn.uaf.edu/Publications/Knowledge.html)

**OMH Minority Populations: American Indian/Alaska Native Profile**

**Asian American/Pacific Islander**

**OMH Minority Populations: Asian American Profile**

**OMH Minority Populations: Native Hawaiians and Pacific Islanders**

**Hispanic/Latino/Spanish**

The Provider's Guide to Quality and Culture
Designed to assist healthcare organizations throughout the United States in providing high quality, culturally competent services to multi-ethnic populations.
Sponsoring organization: Health Resources and Services Administration.
[http://erc.msh.org/mainpage.cfm?file=1.0.htm&module=provider&language=English](http://erc.msh.org/mainpage.cfm?file=1.0.htm&module=provider&language=English)

**Traditional Beliefs: Cultural Competency**

**Hablamos Juntos: Basic Building Blocks of Translation**

**Hablamos Juntos: Interpreter Services**
[http://www.hablamosjuntos.org/is/default.index.asp](http://www.hablamosjuntos.org/is/default.index.asp)

**Quality & Culture Topic: Working with an Interpreter**
[http://erc.msh.org/mainpage.cfm?file=4.5.0.htm&module=provider&language=English](http://erc.msh.org/mainpage.cfm?file=4.5.0.htm&module=provider&language=English)

**Quality & Culture Topic: Non-Verbal Communication**

**Legal Mandates for Interpreter Services**
[http://etl2.library.musc.edu/cultural/interpreters/interpreters_3.php](http://etl2.library.musc.edu/cultural/interpreters/interpreters_3.php)