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The Renal Pharmacist

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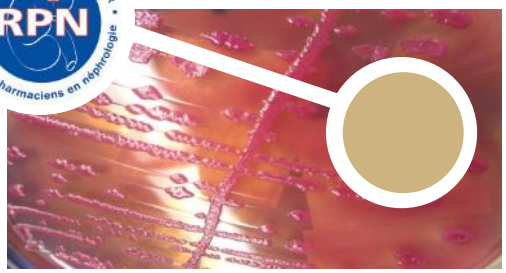
View from the Chair

2018 marked another successful year for the RPN. The 2018 signature education event was held in Vancouver in conjunction with the Canadian Society of Nephrology AGM, which happened to be celebrating its 50th anniversary. Highlights from the RPN education day included presentations on: Nephrology-Oncology, hyperuricemia in chronic kidney disease (CKD), polypharmacy in dialysis as well as updates on vaccination in CKD and many more. In an attempt to reach renal pharmacists from coast to coast, web broadcasting was available for this education event. For those of you interested, the RPN website has a library of many of the presentation slides from past RPN education events.

Joining the RPN executive this year as Chair- Elect is Katie Haubrich, who is a clinical pharmacy specialist for Nephrology and Solid Organ Transplant at the British Columbia Children's Hospital in Vancouver. Looking ahead, I am very excited for our next RPN education event in Montreal as part of CSN in May 2019. Please be sure to check the RPN website for details.

Finally, I would like to thank the RPN executive members, Clifford, Judith, Jenny, Marisa, Katie, Joanne, Elaine and Andrea for their dedication to the network with planning education events, publishing newsletters and maintaining our website. All these activities keeps us connected in our pursuit to provide excellent renal care to our patients.

Jo-Anne Wilson
BscPharm, ACPR, PharmD
Chair, Renal Pharmacist Network 2018



Address/Info Changes:
Please forward any email address / contact information changes to the Website co-ordinator elaine.cheng@vch.ca. We are constantly updating our membership mailing list. Thank you.

www.renalpharmacists.net

Biography: Katie Haubrich

Katie Haubrich is the incoming chair for the Renal Pharmacist Network for 2019. She is currently the Clinical Pharmacy Specialist for Nephrology and Solid Organ Transplant at the British Columbia Children's Hospital in Vancouver. In her role, Katie cares for children in the inpatient and outpatient settings with chronic kidney disease, including those on peritoneal dialysis and hemodialysis, as well those with kidney, liver, heart and lung transplants.

Katie received her PharmD from the University of Alberta in 2014, where she had also previously completed her BScPharm. After obtaining her PharmD, Katie moved to Vancouver to start work at BC Children's Hospital where she first practiced in inpatient general pediatrics and emergency medicine. She moved into her current role in nephrology and solid organ transplant in 2016, where she has since been actively involved with both the BC Renal Agency and BC Transplant, and has focused on developing improved relationships and communication with primary care providers and community pharmacy partners.

Katie regularly precepts University of British Columbia pharmacy students and pharmacy residents, and teaches the CKD module for the University of Alberta PharmD for Practicing Pharmacists program. She has research interests in pharmacokinetic monitoring of immunosuppressant medications in pediatric transplant recipients, and treatment of the unique complications of CKD in pediatrics, such as decreased linear growth.

Katie Haubrich
BScPharm, PharmD

Please enjoy the following articles summarizing presentations from our RPN Education Day (which was held on May 4th 2018 in Vancouver, BC).

Hepatitis B Vaccination Program at Two Tertiary Hemodialysis Centres

Presented by: *Dr. Karen Shalansky, B.Sc.(Pharm), Pharm.D., ACPR, FCSHP. -Pharmacotherapeutic Specialist with Vancouver General Hospital and a Clinical Professor with the Faculty of Pharmaceutical Sciences, The University of British Columbia, Vancouver, British Columbia.*
Author: *Jaclyn Tran, B.Sc.(Pharm), ACPR. -Renal Pharmacist, Central Zone, Nova Scotia Health Authority, Halifax NS.*

At the 2018 RPN Education Day, Dr. Shalansky provided an excellent review of hepatitis B (Hep B) Vaccination. She gave a multidimensional presentation by sharing local research findings from two hemodialysis units in Vancouver.

The presentation began with a background on Hep B in hemodialysis patients. Although the prevalence of Hep B infection in Canada is low, hemodialysis patients are at increased risk of transmission due to potential exposure at dialysis (improper disinfection), exposure during other medical procedures (diagnostic procedures, blood transfusions), and compromised immune function. For this reason, national and international guidelines (Canadian Immunization Guide, KDIGO 2012 Guidelines for the Evaluation and Management of Chronic Kidney Disease, CDC 2012 Guidelines for Vaccinating Kidney Dialysis Patients and Patients with Chronic Kidney Disease -summary from ACIP) recommend providing Hep B vaccination to patients with chronic kidney disease. They also recommend that response be confirmed by serological testing.

Dr. Shalansky explained the Hep B serologic markers in detail (see Tables 1 and 2). There is also an excellent video on Viral Hepatitis Serology Training by the Centres for Disease Control and Prevention (CDC) available online: http://www.cdc.gov/hepatitis/resources/professionals/training/serology/training.htm

Table 1: Routine Serology for Hepatitis B

Hepatitis B surface Antigen (HBsAg)	• A protein on the surface of the Hep B virus. • HBsAg indicates an acute or chronic Hep B infection. • Can be detected in the blood approximately 1 month after an acute exposure (range 1-10 weeks).
Hepatitis B surface antibody (anti-HBs)	• Anti-HBs develop after recovery from Hep B infection or after Hep B vaccination. • There is a window period (weeks to months) in between the time when HBs disappears and anti-HBs appears. During that time, anti-HBc is detectable. • The presence of anti-HBs correlates with the level of immunity to Hep B: Anti-HBs titers ≥ 10 mIU/ml indicate an acceptable level of immunity. Titres may decline over time.
Hepatitis B core antibody (anti-HBc)	• Anti-HBc (IgM and IgG) is detected in the serum. Note: you cannot detect the Hep B core antigen in the serum as these antigens are intracellular (expressed in infected hepatocytes). • The presence of anti-HBc indicates past or current Hep B infection. • Anti-HBc (IgM) usually appears ~ 2 months after an acute exposure. Anti-HBc (IgG) persists after recovery of infection.

Table 2: Interpretation of Baseline Serology and Decision to Vaccinate

Serological Markers	Considerations and Interpretation	Decision to Vaccinate
HBsAg = Positive • Irrespective of anti-HBs and anti-HBc.	Patient has an acute or chronic infection.	**Do not vaccinate**
Anti-HBs ≥ 10 mIU/mL • Irrespective of HBsAg and anti-HBc.	Patient has acceptable immunity: recovered from Hep B infection or successful vaccination.	**Do not vaccinate**
All markers = Negative	Patient is susceptible to Hep B	**Vaccinate** (unless non-responder)
Anti-HBc = Positive • HBsAg = Negative, anti-HBs < 10 mIU/mL	There are 4 considerations: • Resolved past infection • False positive • Chronic infection (low level) • Resolving acute infection (window period)	Recheck serology in 1 month: If not an isolated result and Hep B DNA = Negative à **Vaccinate**

Tables 1 and 2: adapted from Dr. Shalansky's presentation and the CDC Professional Resources: Interpretation of Hepatitis B Serologic Test Results (https://www.cdc.gov/hepatitis/hbv/profresourcesb.htm)

There is a brief commentary in the 2012 KDIGO guidelines on rates of seroconversion (approximately 60-80%) in patients with moderate to severe kidney disease, and attribution of this variability in response to different factors, including dosage, number of vaccines, and patient/population characteristics. As patients with chronic kidney disease may experience lower seroconversion rates and waning anti-HBs, the Canadian Immunization Guide specifically recommends revaccination (second vaccine series and/or boosters) in this population. Despite providing higher doses of Hep B vaccines and offering revaccination, seroconversion in dialysis patients remains suboptimal.

Dr. Shalansky reviewed the Hep B Vaccination Schedule for adults and shared the new Hepatitis B Provincial Protocol for Hemodialysis Patients in BC, which is available online (http://www.bcrenalagency.ca/resource-gallery/Documents/Hepatitis%20B%20Guideline.pdf). This protocol is in alignment with the Canadian Immunization Guide for Hep B Vaccination in dialysis patients (see Table 3).

Table 3. Vaccination Schedule for Hemodialysis Patients

Vaccine	Hep B Vaccine Series in Hemodialysis Patients	Revaccination
RECOMBIVAX HB®	40 mcg (1 mL) IM at 0, 1, 6 months (3 doses)	**Failure of series #1:** Give a second vaccine series. **Failure of series #2:** Non responder.
ENGERIX®B	40 mcg (2 mL) IM at 0, 1, 2, 6 months (4 doses)	**If patients seroconvert** (anti-HBs ≥ 10 mIU/mL) **after either series, but titres then fall** (<10 mIU/mL): Give booster.

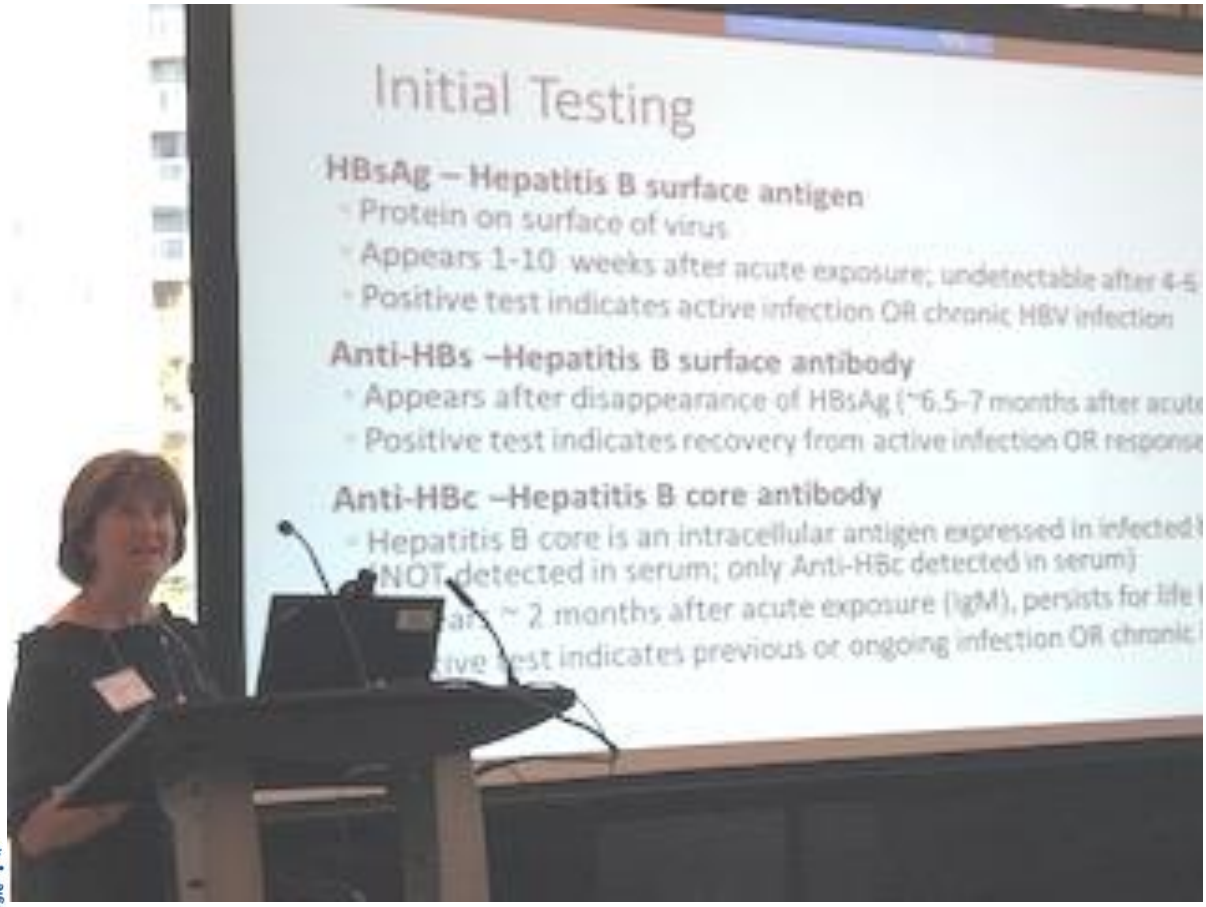
Adapted from Dr. Shalansky's presentation and the Canadian Immunization Guide: Part 4 -Active Vaccines, Hepatitis B

Dr. Shalansky and her research colleagues recently conducted a retrospective chart review to evaluate the new Hepatitis B Vaccination Program in Two Tertiary Hemodialysis Centres. The primary objectives: 1) capture Hep B vaccination response rate after series #1, series #2, and booster doses, and 2) examine factors associated with response to vaccination. Secondary objectives included an evaluation of vaccine uptake, factors associated with vaccine response, and adherence to vaccination protocol, including follow up bloodwork.

The results from this study were shared at the RPN Education Day presentation and Dr. Shalansky's slides have been posted on the RPN website (for granular data). Overall, the research team found that vaccine response rate (defined as anti-HBs ≥ 10 mIU/mL) in these two hemodialysis centres was similar to those described in the literature: approximately 60% after series #1 and series #2, and over 80% after booster doses.

One of the key findings from this retrospective chart review was the significant impact of adherence to the vaccination protocol on vaccine response. Although none of the patient specific factors investigated in this study were found to significantly impact Hep B vaccine seroconversion, several factors have been associated with rates of seroconversion in the literature. A recent Review Article on Vaccination Practices in Dialysis Patients summarized and referenced some of these factors (*Seminars in Dialysis* 2018;1-12), including but not limited to age, stage of kidney disease, obesity, dialysis vintage, type of dialysis, malnutrition (and vitamin D deficiency), and comorbidities (diabetes). Dr. Shalansky also discussed a study published in the International Journal of General Medicine (Ayub 2014;7:109-113), which found that patients with weaker anti-HBs responses (titres 10-100 mIU/mL) were more likely to have titres drop (<10 mIU/mL) after 1 year compared to patients with stronger anti-HBs responses (titres > 100 mIU/mL). Ultimately, predicting vaccine response and also the duration seroconversion in dialysis patients is complicated and multifactorial!

I left this presentation wondering: How many of the patients in our local hemodialysis unit currently have protective anti-HBs (≥ 10 mIU/mL)? How many of these hemodialysis patients received Hep B vaccination before they start on dialysis? Should we evaluate the impact of different factors on rates of seroconversion in our patients? For example, timing of vaccination, adherence to our local protocol, strength of anti-HBs response (10-100 mIU/mL versus > 100 mIU/mL), patient characteristics, etc. Dr. Shalansky's presentation has provoked us to gather this information locally and has inspired preliminary discussions about potential quality initiatives on Hep B vaccination. I cannot help but think, this is exactly the impact that we all strive for in a successful presentation: motivate an audience to ask themselves these questions and then to go out into their practice in pursuit of the answers.



Hyperuricemia in Chronic Kidney Disease

Presented by: *Joanne M. Bargman MD FRCPC, University Health Network and University of Toronto*
Author: *Ashten Langevin, BSc, BScPharm, PharmD – Clinical Pharmacist, Foothills Medical Centre*

With this shift in thinking, researchers wanted to determine if elevated uric acid levels were associated in a faster decline in function and death in patients with CKD. The observational Chronic Renal Insufficiency Cohort Study found that the association of serum uric acid and kidney failure depends on CKD stage and ultimately a J-shaped relationship between baseline uric acid and all-cause mortality was found. Further research into the treatment of the elevated levels was prompted. The post-hoc analysis of the RENAAL trial found that losartan lowered serum uric acid as compared to placebo. This was associated with a decreased risk of renal events. An RCT evaluating allopurinol 100mg/day compared to usual therapy found that the treatment group had less significant deterioration in kidney function or dialysis. All of these findings were promising but Dr. Bargman reminded the audience to be cautious of any CKD study where the GFR improves. She further reviewed systematic reviews and meta-analyses that concluded study numbers are too small, heterogeneous, and limited to make any conclusions at this point whether or not uric acid lowering therapy should be recommended.

In the end, an important learning point was that hyperuricemia as a risk factor for cardiovascular events or renal decline is confounded by kidney impairment, even though studies suggest uric acid may be pro-inflammatory and toxic. At this point the treatment of asymptomatic at-risk patients is not yet recommended as the evidence is not robust. This may be addressed in the future as numerous relevant trials are not yet reported or in progress. Perhaps there will be a presentation at a future RPN Education Day with an answer to the question of whether asymptomatic elevated uric acid levels in chronic kidney disease should be treated and the related clinical significance.

Review of Nephro-Oncology

***Presented by**: Dr. Abhijat Kitchlu MD FRCPC, University Health Network*
***Author:** Carlee Balint, BSP, ACPR -– Clinical Pharmacist, Sheldon M. Chumir Health Centre*

Dr. Kitchlu began the Renal Pharmacists Network education day with a very informative talk on Nephro Oncology. Dr. Kitchlu has himself been involved in a number of patients and case reports that reported kidney injury, following therapies for cancer. He started off discussing how immunotherapies such as checkpoint inhibitors such as Ipilimumab, and Nivolumab, and Pembrolizumab that have in some case reports been shown to cause minimal change disease. He reviewed two specific patients that he was involved with in his Onco-Nephrology clinic and described their course. Patients displayed distinct drops in GFR as well as nephrotic syndrome and hypoalbuminuria following initiation of these medications. These agents seemed to cause production of a "permeability factor" that then caused podocyte injury that may be linked to T cell cytokines. This agents also have been implicated in acute kidney injury, with some reviews siting incidence as high as 29% with some cancer regimens, although this is difficult to tease out in the literature given the number of risk factors and comorbidities in this patient population.

He then went on to discuss other agents used in chemotherapy regimens including anti-angiogenesis agents, or anti VEG-F agents and their effects on the renal system. There are a number of emerging therapies that continue to be developed and affect a number of areas of the kidney. From Anti VEG-F agents having effects on the podocytes, to BRAF inhibitors causing tubular toxicity and EGFR monoclonal antibodies affecting the distal convoluted tubule and causing hypomagnesemia, Dr. Kitchlu highlighted some of the potential complications that these medications can cause. He also highlighted the lack of information in regards to renal dosing of this wide range of medications.

To finish his talk, Dr. Kitchlu highlighted the work he has done in the area of Cancer in the Chronic Kidney disease population. He noted the high incidence of cancer related deaths in this group and discussed the risks of cancer in this population and how they may be higher than in the general population. There was some discussion in regards to the utility of screening in the dialysis population, given their high mortality rates and how evidence has shown that regular cancer screening in CKD patients are much lower than those in the general population. He also reviewed the complications of treating cancer in those with chronic

kidney disease as dosing regimens and adjustments needed for those with kidney dysfunction is very limited. This is exacerbated by the fact that a high number of cancer trial exclude those patients with CKD.

Overall, Dr. Kitchlu provided a new wealth of knowledge in a very innovative type of clinic and research that will continue to progress in the future. As more cancer therapies and medications emerge, there will be a number of lessons to be learned in regards to their renal effects especially in those with chronic kidney disease. We look forward to following his continued work in this field.

Please send any articles of interest to
renalpharmacistsnetwork@gmail.com

Recent Publications

Non–Vitamin K–Dependent Oral Anticoagulants for Nonvalvular Atrial Fibrillation in Patients With CKD: Pragmatic Considerations for the Clinician

Gautam R. Shroff, Rachel Stoecker, Allyson Hart.

AJKD. 2018; 72 (5) 717-727

Proton Pump Inhibitors, Histamine-2 Receptor Antagonists, and Hip Fracture Risk among Patients on Hemodialysis

Chandan Vangala, Jingbo Niu, Colin R. Lenihan, William E. Mitch, Sankar D. Navaneethan and Wolfgang C. Winkelmayer.

CJASN. 2018; 13 (10) 1534-1541

High-Dose Seasonal Influenza Vaccine in Patients Undergoing Dialysis

Dana C. Miskulin, Daniel E. Weiner, Hocine Tighiouart, Eduardo K. Lacson, Klemens B. Meyer, Taimur Dad and Harold J. Manley.

CJASN. 2018; 13 (11) 1703-1711

An Adjustable Dalteparin Sodium Dose Regimen for the Prevention of Clotting in the Extracorporeal Circuit in Hemodialysis: A Clinical Trial of Safety and Efficacy (the PARROT Study)

Steven Soroka, Mohsen Agharazii, Sandra Donnelly, Louise Roy, Norman Muirhead, Serge Cournoyer, Martin MacKinnon, Neesh Pannu, Brendan Barrett, François Madore, Karthik Tennankore, Jo-Anne Wilson, Fiona Hilton, Nancy Sherman, Kevin Wolter, John Orazem, Guillaume Feugère.

Canadian Journal of Kidney Health and Disease. November 4, 2018

Intravenous Iron in Patients Undergoing Maintenance Hemodialysis

Iain C. Macdougall, M.D., Claire White, B.Sc., Stefan D. Anker, M.D., Sunil Bhandari, Ph.D., F.R.C.P., Kenneth Farrington, M.D., Philip A. Kalra, M.D., John J.V. McMurray, M.D., Heather Murray, M.Sc., Charles R.V. Tomson, D.M., David C. Wheeler, M.D., Christopher G. Winearls, D.Phil., F.R.C.P., and Ian Ford, Ph.D. for the PIVOTAL Investigators and Committees.

NEJM. October 26, 2018

Future Meetings & Events

The Canadian Society of Nephrology
Annual General Meeting (CSN AGM)

May 2019

Montreal, QC

SAVE THE DATE

Thursday May 2nd, 2019

RPN at the CSN

Come join us for an afternoon education session and an opportunity to network with your fellow renal pharmacists.

More details to come shortly.
https://renalpharmacists.net/events/

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