Volume 15 Issue 1 / Spring-Summer 2012

# The Renal Pharmacist

Vol 15

Issue 1

Spring-Summer 2012

## In this issue ...



A biannual Insight into the Renal Pharmacist Network

## View from the Chair

"The spring has sprung. So much to do, so little time." Guess we've all heard these before. Well as you can see the RPN Executive has decided to turn the page and got a new look for the Newsletter. Enjoy! Since the last newsletter, your RPN Executive Committee has been actively working at putting together some great and well attended Education Days starting with the Toronto meeting, the highlights of which you will find in this newsletter. The slides of the presentations are now available on the RPN website. Another major endeavor has been to register the RPN as an official non-profit organization, a necessary legal requirement for fiscal obligations. We can definitely say that the RPN has matured to a full grown, mature and responsible organization and I sincerely wish to acknowledge all the fantastic work of the former Executive Committees that have brought the RPN to where it is today.

*"The spring has sprung. So much to do, so little time"*

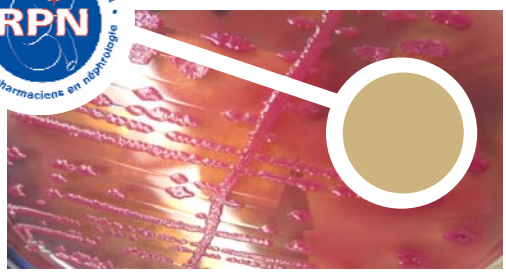
Furthermore, our RPN Executive Committee also had the chance to network with the Canadian Society of Nephrology (CSN) for what we hope will be a long and fruitful partnership. To inaugurate our new alliance, Marisa Battistella, gave an RPN presentation at the CSN Annual Meeting in St. John's, Newfoundland, this past April. I encourage all RPN members to participate either as speaker and/or to present a poster at the next CSN-RPN Annual meeting that will be held in Montreal next year in April, mark your calendars. This will the biggest joint meeting ever held where the CSN, the Quebec Society of Nephrology, the RPN and the Quebec renal pharmacists will have shared and simultaneous sessions. What a great opportunity to network with old colleagues and make new encounters with other pharmacists sharing similar yet different challenges.

We are always on the look-out for colleagues to join the RPN Executive Committee as Chair–Elect for the up coming year (don't be afraid, it's really an easy job, the team is fabulous but the pay is lousy or should I say no pay all !). Please let us know if you are interested in getting more information on the RPN Chair position. Information on the upcoming education evenings in Toronto, Winnipeg and Vancouver will be available for our members as soon as the dates are confirmed. I wish to thank Piera Calissi, for accepting to be Chair-Elect for 2012-2013. Her past experience with the CSHP makes our Executive Committee a real dream team.

Cheers,

*Robert Bell*

Chair, RPN




**Chair:**
Robert Bell, BPharm, DPH
Maisonneuve-Rosemont Hospital
RBell.hmr@ssss.gouv.qc.ca

**External Liaison Officer:**
Marisa Battistella, BScPhm, PharmD
Clinical Pharmacist - Hemodialysis
University Health Network
Marisa.battistella@uhn.on.ca

**Education Coordinators:**
Jenny Ng, BScPhm, ACPR
Clinical Pharmacist - Nephrology
Sunnybrook Health Sciences Centre
Jenny.ng@sunnybrook.ca

Judith Marin, B.Pharm, M.Sc., PharmD
Clinical Pharmacy Specialist - Nephrology
Fraser Health Authority Renal Program
Judith.Marin@fraserhealth.ca

**Communications Coordinator:**
Amy Sood, BScPhm, PharmD
Pharmaceutical Care Coordinator
Manitoba Renal Program
asood@sbgh.mb.ca

**Website Coordinator:**
Elaine Cheng, BScPharm, ACPR, PharmD
Clincial Pharmacotherapeutic Specialist – Nephrology
Vancouver General Hospital
Elaine.Cheng@vch.ca

**Secretary/Treasurer:**
Grace Leung, BScPhm, PharmD
York Region Chronic Kidney Disease Program
GLeung@yorkcentral.on.ca

**Chair Elect:**
Piera Calissi, BSc(Pharm), PharmD, FCSHP
Clinical Pharmacy Specialist-Nephrology
Interior Health Authority
Renal Program, Kelowna, BC
Piera.Calissi@interiorhealth.ca



**Graphics Design & Layout:**
Abel Cheng
acabelcheng@gmail.com


**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.

## Biography: Piera Calissi

Piera Calissi is the Clinical Pharmacy Specialist for the Interior Health Authority Renal Program in Kelowna, BC. She graduated with a Bachelor's of Science in Pharmacy from U.B.C. in 1982 and a Pharm.D. from Wayne State University in Detroit, MI in 1994. She completed a residency in hospital pharmacy practice at Royal Inland Hospital in Kamloops, B.C. She is a Fellow of the Canadian Society of Hospital Pharmacists.

Piera's areas of interest include all aspects of chronic kidney disease. She currently provides pharmaceutical care to patients at in the Interior Health Authority Renal Program. She also acts as a preceptor to pharmacy students and residents and is a clinical instructor at the University of British Columbia. She is the author of numerous publications and is a regular presenter in the area of chronic kidney disease.

Piera is an active member of the Canadian Society of Hospital Pharmacists and has served as the Saskatchewan Branch awards chair, treasurer and president. She has been awarded the CSHP Saskatchewan Branch Merit Award and Past- President's Award. She is currently the Interior Chapter Chair for the BC Branch of CSHP.

**Please welcome Piera to the position of RPN Chair-Elect for 2012!.**

## Upcoming Conferences

✦✦✦✦

American Society of Nephrology (ASN), Kidney Week 2012 is scheduled **0ct 30 – Nov 4, 2012** in San Diego, CA.

✦✦✦✦

Canadian Society of Nephrology (CSN) 2013 is scheduled **April 24-28, 2013** in Montreal, Quebec. The RPN will be holding a joint education day prior to meeting so please plan to attend! More information to follow at a later date.

✦✦✦✦

*(Left to Right) Amy Sood, Piera Calissi, Robert Bell, Jenny Ng, Judith Marin, Elaine Cheng, Toronto, Nephrology Education Day.*

# Highlights: Canadian Society of Nephrology 2012, St John's Newfoundland

*Submitted by Amy Sood, BScPhm, PharmD, St. Boniface Hospital, Winnipeg, Manitoba*

The Canadian Society of Nephrology Annual General Meeting was held on April 25-30th, 2012 in St. John's, Newfoundland. The event attracted several renal pharmacists from Newfoundland along with pharmacists from British Columbia, Saskatchewan, Winnipeg, Ontario and Quebec. Over the two and a half days of the Scientific Meeting, there were many presentations of interest to renal pharmacists. Dr J. Bargman reviewed the upcoming KDIGO Glomerulonephritis (GN) Guidelines and also reviewed the principles of drug management of severe lupus nephritis, Dr D. Cattran reviewed current treatment options for Membranous GN, Dr M. Walsh reviewed the evidence for immunosuppressives to treat ANCA-associated vasculitis, Dr Reich discussed new therapeutic strategies in the treatment of FSGS, Dr J. Gill discussed the advantages and disadvantages of immunosuppressive discontinuation after transplant failure and Dr A. Levin discussed the controversies around the SHARP study. The debates focused on great controversial topics. There was a lively debate on the pros and cons of LMWH vs. unfractionated heparin in hemodialysis by Drs. N. Ashman and C. Clase. The other debate was on geriatric dialysis by Drs. R. Carson and V. Jassal.

**Canadian Society of Nephrology**

Our Renal Pharmacist Network presentation focused on drug-induced acute kidney injury (AKI). Our own Marisa Battistella focused on bisphosphonates, providing an overview of the case reports in the literature of bisphosphonate-induced acute kidney injury (mostly pamidronate), risk factors and potential reasons why oral bisphosphonates have not been associated with AKI. She discussed the proposed mechanism, suggesting that the pathways at the cellular level that are responsible for apoptosis of osteoclasts, may also be responsible for apoptosis of podocytes and epithelial tubular cells in the kidney. Dr A. Garg reviewed his recent population-based study linking fibrates to AKI. Intravenous acyclovir-induced AKI was also discussed including a recent population-based study that did not show adverse effects on renal function when comparing new starts on oral acyclovir/valacylovir to oral famciclovir.

Finally, we got a sneak peak of the upcoming KDIGO Anemia Guidelines presented by Dr P. Parfrey. The guidelines will be published in Kidney International in August 2012! Overall, the conference was a success and provided lots of networking opportunities, late into the night on Water Street! Some of us had the opportunity to see the floating iceberg at Quidi Vidi Village (pronounced "Kiddy Viddy"), a small fishing village and the view of the city and the Atlantic Ocean on Signal Hill was magnificent. The next CSN conference will be held in Montreal, Quebec. We hope to see you all there!

# Highlights: RPN Nephrology Education Day 2012, Toronto, ON

*Submitted by Jenny Ng, BScPhm, Sunnybrook Health Sciences Centre, Toronto, ON*

This year the RPN Nephrology Education Day was held once again in Toronto on March 23rd at the Intercontinental Hotel. We had a good representation of pharmacists from across Canada as well as a couple of American pharmacists. It was a great opportunity for renal pharmacists to interact and discuss current issues in our practice.

Presentations included an insightful critique of the PreCLOT study, a practical approach to diabetes management, a review of studies regarding prevention of fungal peritonitis and a few scientific presentations to update all renal pharmacists on upcoming research. Copies of the slides from the presentations are posted on our RPN website to share with those that were unable to attend.

We are already planning for next year's RPN education day and our executive are always open to suggestions for topics and speakers. Please forward any presentation suggestions to jenny.ng@sunnybrook.ca or Judith.marin@frasherhealth.ca.

*Robert Bell, Marisa Batistella, Toronto Nephrology Education Day.*




# Apply for Pharmacist Membership to the Canadian Society of Nephrology!

Pharmacist annual memberships are only $100.00!
CSN Member Pharmacists also get a discounted rate for registration at the CSN conference!
www.csnscn.ca

# Save the Date!
# CSN 2013 is in Montreal, April 24-28!

The ***Renal Pharmacist Network*** will be holding a joint education day prior to the CSN meeting.

The ***Quebec Renal Pharmacist Network*** is also planning joint sessions with the RPN!

The ***Quebec Society of Nephrology Annual Meeting*** will also take place at the CSN meeting with both simultaneous and separate scientific programs!

This unique opportunity in the heart of Montreal promises to provide attendees the opportunity to network with peers and colleagues from across Canada, and stimulate sharing of the latest research on key topics, best clinical practices and case studies.

We hope to see you there!!!
**RPN Executives**




Canadian Society of Nephrology

# Transplant Transitions

*Submitted by Jennifer Dyck BSP, ACPR, Clinical Pharmacist, Transplant Manitoba*

Renal transplantation has many benefits when compared to other forms of renal replacement therapy (RRT) including increased lifespan and decreased health system costs. Compared to hemodialysis in Manitoba, the estimated lifespan years gained for a kidney transplant recipient can be up to 15 years and the annual cost savings are approximately $50,000 per individual.

A variety of immunosuppressant medications are used in combination after solid organ transplantation. The dose and combination depend on the organ type, immunologic match between donor and recipient, antibody level in the recipient, and other patient specific factors. Induction immunosuppression such as Thymoglobulin® or basiliximab (Simulect®) is sometimes administered at the time of transplantation. Maintenance immunosuppression for adult renal transplant recipients in Manitoba typically includes a calcineurin inhibitor (i.e., tacrolimus or cyclosporine), an antiproliferative agent (i.e., mycophenolate or azathioprine) and prednisone. Sirolimus may be used on occasion. This combination is used as the agents target different aspects or stages of T-cell activation. Anti-infective agents such as sulfamethoxazole/trimethoprim, valganciclovir and nystatin may also be used early in the post-transplant course.

Managing immunosuppressant drug levels in a transplant recipient is like balancing a scale – one must weigh potential toxicities with the risk of organ rejection. While there are guidelines for immunosuppressant drug levels, individual patients are likely to have

their own unique range. The individual's appropriate drug level, typically a tighter subset of the laboratory's reference range, is influenced by the time since transplantation, the organ type, the use of any induction agent, other immunosuppression, and the presence of rejection or toxicity.

Cyclosporine is either monitored with trough levels (0-30 minutes pre-dose) or 2-hour post dose levels (C2). C2 levels must be drawn 2 hours +/- 10 minutes after the dose is taken and are often difficult to facilitate between the patient and the lab. Pharmacokinetic parameters are not used to estimate C2 levels if the level is drawn outside the 2 hours +/- 10 minute window. Tacrolimus and sirolimus are monitored only by trough level (0-30 minutes pre-dose). Some laboratories may have the capability to determine mycophenolate levels. However, interpretation and dose adjustment of mycophenolate based on blood levels is controversial and is not done routinely.

Mortality appears to be increased during the first three months after transplantation and during the first three months after returning to dialysis following failure of the transplanted kidney. While renal transplantation lowers the mortality risk compared to other methods of RRT, it doesn't eliminate this risk. Mortality is still three to ten times higher than in the general population and there is a higher mortality risk on return to dialysis compared to never receiving a renal transplant.

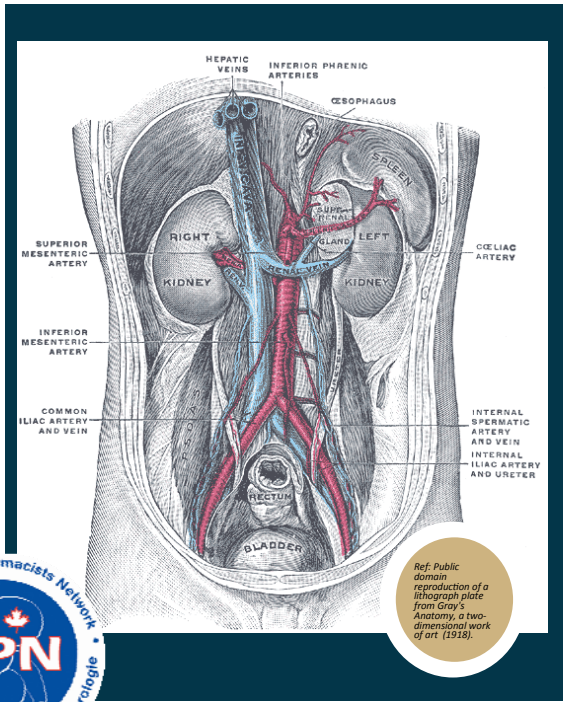
There are similar comorbid disease states between renal transplant recipients and dialysis patients: dyslipidemia, hypertension, anemia, and bone disease. The benefits of HMG-CoA inhibitors ("statins"), ACE-inhibitors (ACEi), angiotensin receptor blockers (ARB), and calcium channel blockers in transplant recipients have been described in several studies.

Anemia often resolves with renal transplantation and the production of endogenous erythropoetin. Several factors can be involved in the persistence of anemia following renal transplantation: azathioprine, mycophenolate, and sirolimus have hematologic adverse effects; frequency of blood draws in the first few months; use of ACEi and ARB; ongoing renal dysfunction, and the use of antiinfective agents (e.g., cotrimoxazole, valganciclovir). Post transplant erythrocytosis ("tertiary hypererythropoietinemia"), or a hematocrit of over 50% (~ hemoglobin 170 g/L), can also occur in about 10% of renal transplant recipients. The proposed mechanism is a lack of normal feedback response by either the native or newly transplanted kidney.

Calcium-phosphate balance and PTH (parathyroid hormone) often normalize within one year after transplant. There is occasional failure of parathyroid gland size to resolve resulting in an elevated PTH in about 25% of recipients after one year. Hypercalcemic hyperparathyroidism bone disease ("tertiary hyperparathyroidism"; elevated serum calcium with elevated PTH) can also develop with the hypercalcemia resistant to most medication therapies.

After a transplanted kidney has failed, and the patient has returned to dialysis, there are several ways that the immunsuppressive agents can be tapered. The typical tapering regimen in Manitoba for renal transplants is: taper mycophenolate/azathioprine over 2-4 weeks; then, taper CSA/TAC over two months; then, taper steroid last. If another donor is available, the immunosuppressive agents may be continued at full doses to limit the development of antibodies which could jeopardize future transplants.

*This information was presented by the author at the RPN CE evening in Winnipeg on Nov 3, 2011. For further details, please see the presentation slides posted on [www.renalpharmacists.net](http://www.renalpharmacists.net)*




*Ref: Public domain reproduction of a lithograph plate from Gray's Anatomy, a two-dimensional work of art (1918).*

# When Both Indicated and Contraindicated: Erythropoiesis-Stimulating Agents in Chronic Kidney Disease Patients with Cancer

*Submitted by Bradley Mitchelmore, BSc. (Pharm), ACPR, PharmD Student*
*Leslie Dan Faculty of Pharmacy, University of Toronto*

Erythropoetin-stimulating agents (ESAs) have traditionally been used to treat anemia in both cancer and chronic kidney disease (CKD). However, in light of evidence evaluating their impact on clinical outcomes, their role in both conditions has been re-evaluated. Current guidelines for the management of anemia in CKD and cancer have opposing recommendations, which leaves the clinician to make a difficult decision when a patient presents with both comorbidities.[1,2,3,4]

International guidelines (KDIGO – Kidney Disease: Improving Global Outcomes) for the management of anemia in chronic kidney disease are currently being developed and should be released in 2012. These guidelines should reflect the data published over the past decade that indicate higher hemoglobin targets in patients with chronic kidney disease are associated with worse outcome.[5,6,7,8] None of the four landmark trials published demonstrated an improvement in cardiovascular or mortality outcomes. Impact of ESA treatment on quality of life (QOL) outcomes has been variable, perhaps due to the absence of QOL measures specifically validated in CKD, leaving a reduced risk of red blood cell (RBC) transfusions the only consistently observed benefit of higher hemoglobin targets. Unfortunately, no randomized controlled trial (RCT) is available that addresses the question of whether there is any net benefit to using ESAs, compared to no treatment or transfusions only, when lower hemoglobin targets are used. When considering the use of ESA therapy in a patient with cancer and CKD, one must first consider that in the CKD literature, the only clear goal supported with evidence is a reduction in RBC transfusion rates.

On the other hand, emerging data in the cancer literature consistently shows harm with the use of ESAs in patients with active cancer. A 2009 Cochrane Review using patient-level data of ESA therapy in cancer patients included 53 RCTs of 13 933 patients.[9] Twenty-eight of the trials were placebo-controlled, with the remainder of open-label design. Overall trial quality was generally poor. The majority, 76.6 percent, of patients had solid tumors, and 18.3 percent had hematological malignancies. Epoetin alpha/beta dosing ranged from 21 000 to 61 000 units per week, and darbepoetin dosing ranged from 100 to 157.5 mcg per week for 8 to 52 weeks' duration, generally higher dosing than seen in the CKD population. Dosing regimens were usually fixed, with ceiling hemoglobin concentrations ranging from 130-160 g/L, or hematocrit levels of 0.38 to 0.40. This meta-analysis found an increased risk of on-study mortality [hazard ratio (HR), 1.17, 95% confidence interval (CI), 1.06-1.30), and overall mortality (HR 1.06, 95% CI, 1.00-1.12), with ESA therapy vs. control. Although not always statistically significant, trends of an increased mortality were usually consistent among subgroups analyzed, including tumor type, baseline hemoglobin, background treatment modality (no treatment, chemotherapy, chemotherapy and radiation, radiation, or hemoglobin ceiling).

Another meta-analysis of 52 trials, including 12 006 patients, found a similar increased risk of mortality as the Cochrane Review described above [relative risk (RR) 1.15, 95% CI 1.03-1.29]. In addition, an increased risk of thromboembolic events was identified (RR 1.69, 95% CI, 1.27-2.24). Statistically insignificant trends towards increased risk of cardiovascular events (RR 1.12, 95% CI 0.83-1.50) and hypertension (RR 1.41, 95% CI 0.94-2.12) were also observed. Although significant heterogeneity was observed, there were statistically significant improvements in various quality of life scores. A reduced risk of transfusions was also identified (RR 0.64, 95% CI, 0.56-0.73).

Some RCTs have suggested there is an increased risk of tumor progression in breast, head and neck, and cervical cancer.[,,,] Potential mechanisms of tumor progression have been identified. ESAs may contribute to anginoegenesis, direct cell proliferation or cytoprotection, and promotion of micrometastasis through activation of

1. NCCN clinical practice guidelines. Cancer-and chemotherapy-induced anemia. V2.2012. Available at http://www.nccn.org/professionals/physician_gls/PDF/anemia.pdf.
2. Rizzo JD, Brouwers M, Hurley P, Seidenfeld J, Arcasoy MO, Spivak JL. American Society of Clinical Oncology/American Society of Hematology Clinical Practice Guideline Update on the Use of Epoetin and Darbepoetin in Adult Patients With Cancer. J ClinOncol 2010;28:4996-5010.
3. Moist LM, Foley RN, Barrett BJ, Madore F, White CT, Klarenbach SW, et al. Clinical Practice Guidelines for evidence-based use of erythropoietic-stimulating agents. Kidney Int 2008;74 (Suppl 110):S12-8.
4. KDOQI. KDOQI Clinical practice guideline and clinical practice recommendations for anemia in chronic kidney disease: 2007 update of hemoglobin target. Am J Kidney Dis 2007;50:471-530.
5. Besarab A, Bolton WK, Browne JK, Egrie JC, Nissenson AR, Okamoto DM. The effects of normal as compared with low hematocrit values in patients with cardiac disease who are receiving hemodialysis and epoetin. N Engl J Med 1998;339:584-90.
6. Drüeke TB, Locatelli F, Clyne N, Eckardt KU, Macdougall IC, Tsakiris D, et al. Normalization of Hemoglobin Level in Patients with Chronic Kidney Disease and Anemia. N Engl J Med 2006;355:2071-84.
7. Singh AK, Szczech L, Tang KL, Barnhart H, Sapp S, Wolfson M, et al. Correction of Anemia with Epoetin Alfa in Chronic Kidney Disease. N Engl J Med 2006;355:2085-98.
8. Pfeffer MA, Burdmann EA, Chen CY, Cooper ME, de Zeeuw D, Eckard KU. A Trial of Darbepoetin Alfa in Type 2 Diabetes and Chronic Kidney Disease. N Engl J Med 2009;361:2019-32.
9. Bohlius J, Schmidlin K, Brillant C, Schwarzer G, Trelle S, Seidenfeld J, et al. Erythropoietin or Darbepoetin for patients with cancer - meta-analysis based on individual patient data. *Cochrane Database of Systematic Reviews* 2009, Issue 3. Art. No.: CD007303.

10. Marcello Tonelli M, Hemmelgarn B, Reiman T, Manns B, Reaume MN, Lloyd A. Benefits and harms of erythropoiesis -stimulating agents for anemia related to cancer: a meta-analysis. *CMAJ* 2009;180:E62-E71.
11. Hoskin PJ, Robnson M, Slevin N, Morgan D, Harrington K, Gaffney C. Effect of Epoetin Alfa on Survival and Cancer Treatment–Related Anemia and Fatigue in Patients Receiving Radical Radiotherapy With Curative Intent for Head and Neck Cancer. *J ClinOncol 2009;27:5751-6.*
12. Henke M, Laszig R, *Rübe* C, *Schäfer* U, Haase KD, Schilcher B, et al. Erythropoietin to treat head and neck cancer patients with anaemia undergoing radiotherapy: randomised, double-blind, placebo-controlled trial. *Lancet* 2003;362:1255–60.
13. Leyland-Jones B, Semiglazov V, Pawlicki M, Pienkowski T, Tjulandin S, Manikhas G. Maintaining Normal Hemoglobin Levels With Epoetin Alfa in Mainly Nonanemic Patients With Metastatic Breast Cancer Receiving First-Line Chemotherapy: A Survival Study. *J ClinOncol 2005;23:5960-5972.*
14. Thomas G,Ali S, Hoebers FJP, Darcy KM, Rodgers WH, Patel M, et al. Phase III trial to evaluate the efficacy of maintaining hemoglobin levels above 12.0 g/dL with erythropoietin vs above 10.0 g/dL without erythropoietin in anemic patients receiving concurrent radiation and cisplatin for cervical cancer. Gyne-Oncol 2008;108:317–25.
15. Hadland BK, Longmore GD. Erythroid-Stimulating Agents in Cancer Therapy: Potential Dangers and Biologic Mechanisms. *J ClinOncol 2009;27:4217-26.*
16. Shander A, Javidroozil M, Ozawa S, Hare GMT. What is really dangerous: anemia or transfusion? Br J Anaesthes 2011;107:i41–i59.
17. U.S. Renal Data System, USRDS 2004 Annual Data Report: Atlas of End-Stage Renal Disease in the United States,National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases, Bethesda, MD, 2004. Chapter 7: Transplantation. Accessed at http://www.usrds.org/atlas04.aspx on April 18, 2012. The 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 author(s) and in no way should be seen as an official policy or interpretation of the U.S. government.
18. Ibrahim HN, Skeans MA, Li Q, Ishani A, Snyder JJ. Blood transfusions in kidney transplant candidates are common and associated with adverse outcomes. Clin Transplant 2011:25: 653–9.
19. Shander A, Goodnough LT. Update on transfusion medicine. Pharmacotherapy 2007;27(9 Pt 2):57S–68S

platelets and endothelial cells in blood vessels through the activation of increased mortality were usually consistent among subgroups analyzed, including tumor type, baseline hemoglobin, background treatment modality (no treatment, chemotherapy, chemotherapy and radiation, radiation, or hemoglobin ceiling).

Another meta-analysis of 52 trials, including 12 006 patients, found a similar increased risk of mortality as the Cochrane Review described above [relative risk (RR) 1.15, 95% CI 1.03-1.29].[10] In addition, an increased risk of thromboembolic events was identified (RR 1.69, 95% CI, 1.27-2.24). Statistically insignificant trends towards increased risk of cardiovascular events (RR 1.12, 95% CI 0.83-1.50) and hypertension (RR 1.41, 95% CI 0.94-2.12) were also observed. Although significant heterogeneity was observed, there were statistically significant improvements in various quality of life scores. A reduced risk of transfusions was also identified (RR 0.64, 95% CI, 0.56-0.73).

Some RCTs have suggested there is an increased risk of tumor progression in breast, head and neck, and cervical cancer.[11,12,13,14] Potential mechanisms of tumor progression have been identified.[15] ESAs may contribute to anginoegenesis, direct cell proliferation or cytoprotection, and promotion of micrometastasis through activation of platelets and endothelial cells in blood vessels through the activation of EPO receptors in tumor cells, endothelial cells, and platelets.

Based on the above data, clinical practice guidelines in cancer do not routinely recommend the use of ESAs. The US National Comprehensive Cancer Network (NCCN) guidelines do state that ESA therapy can be considered in patients with underlying chronic kidney disease as per the Food and Drug Administration (FDA) approved guidelines.[1] However, the risks versus benefits of therapy should be weighed. The harms that have been identified with the use of any amount of ESAs in those with active cancer needs to be balanced with the role ESAs have to reduce the need for RBC transfusions in CKD. Transfusions generally have a low complication rate. In one observational study, reported serious adverse events occurred in 500 per million transfusions.[16] Alternatively, the risk of transfusions may be higher in patients who are candidates for kidney transplant. The development of panel reactive antibody (PRA) can occur with exposure to red blood cell transfusions.[17] The risk of high PRA increases with the number of transfusions. However, available observational cohort data, while finding an increased risk of reduced graft survival and mortality after transplant in patients with high PRA, 1 year patient survival at 1 year post-transplant in patients with a positive PRA remain high (96.6% vs. 100% in patients with a sensitizing event and positive PRA vs. unsensitized patients with a negative PRA).[17,18] Risks evolve over time with transfusions. Increased cumulative use of transfusions is associated with a higher risk of complications, including iron overload.[19] This must be considered if patients are receiving multiple transfusions in place of ESA therapy, and in these cases therapy selection should be individualized.

Additional considerations in this population also include the goals of therapy for their cancer treatments. Patients in which the goal of therapy is no longer cure should still be considered at risk of increased mortality and complications from ESA therapy, as the majority of patients in the Cochrane Review had advanced or metastatic disease.[9] While the goal of therapy for chemotherapy in the palliative setting is no longer cure, it may include extending progression-free survival and prolonging life, which can be adversely affected by ESA therapy. Alternatively, patients who have been cured or are in remission may also be at increased risk of complications. A subgroup analysis of the TREAT trial, a trial of darbepoetin versus placebo in diabetic patients with CKD, suggests that patients with a history of cancer may be at increased risk of cancer related death with darbepoetin.[8] These data must be interpreted with caution, as it is a subgroup analysis and includes a small number of patients.

Given that the risk to the patient of ESA therapy in cancer, and marginal benefit of ESA therapy in CKD in general, there is no well established indication for ESA therapy in CKD patients with active cancer. No safe dose of ESA therapy in cancer has been established. Until more information is known on the benefit of ESA therapy in CKD patients, it is prudent to avoid their use in CKD patients with active cancer.

# What's New in the Nephrology Literature? A Focus on Renal Pharmacotherapeutics...

*Click on the title to go to the PubMed link*


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

### Clinical pharmacists and patients with chronic kidney disease.

*Wazny LD, Raymond CB, Verrelli M. Kidney Int. 2012;81:597-8.*

This Letter to the Editor nicely points out the lack of mention of the role of a renal pharmacist in the care of patients with chronic kidney disease in the recently published article by KDIGO on drug dosing in patients with acute and chronic kidney disease (Kidney Int. 2011;80:1122-37).

### Comparative evaluation of the Cockcroft-Gault Equation and the Modification of Diet in Renal Disease (MDRD) study equation for drug dosing: an opinion of the Nephrology Practice and Research Network of the American College of Clinical Pharmacy.

*Nyman HA et al. Pharmacotherapy. 2011;31:1130-44.*

This opinion article reviews the controversial debate of using MDRD versus CG for drug dosing. The authors propose an algorithm for using serum creatinine-based kidney function assessments for drug dosing.

### Impact of Pharmacist-Managed Erythropoiesis-Stimulating Agents Clinics for Patients With Non-Dialysis-Dependent CKD.

*Aspinall SL, et al; ESA Clinic Study Group. Am J Kidney Dis 2012 May 25. [Epub ahead of print]*

In this historical cohort study involving 10 veterans Affairs Medical Centers, pharmacist-managed ESA clinics provided improved quality of ESA management compared to physician-directed usual care in patients with non-dialysis CKD.

### Hypoglycemics for the treatment of type 2 diabetes in patients with chronic kidney disease: a focus on new agents.

*Fang V, Wazny LD, Raymond CB. CANNT J. 2012;22:30-6; quiz 37-8.*

This review discusses the newer agents available for diabetes management in CKD. A great resource for students on nephrology rotations.

### Iron replacement and supplementation in patients with chronic kidney disease.

*Wazny LD, Raymond CB. CANNT J. 2011;21:26-30; quiz 31-2.*

A review of iron therapy including the new agent, ferumoxytol (Feraheme®), which received a Notice of Compliance from Health Canada on Feb 1, 2012.

### Bedtime dosing of antihypertensive medications reduces cardiovascular risk in CKD.

*Hermida RC et al. J Am Soc Nephrol. 2011;22:2313-21.*

According to this open-label study of 661 CKD patients, bedtime dosing of antihypertensives was associated with a reduction of cardiovascular events.

### Catheter Dysfunction: The Role of Lock Solutions.

*Niyyar VD. Semin Dial. 2011 Dec 16. doi: 10.1111/j.1525-139X.2011.00991.x. [Epub ahead of print]*

A review of catheter locking solutions. A great resource for students on nephrology rotations.

### Fat-Soluble Vitamins in Advanced CKD/ESKD: A Review.

*Holden RM et al. Semin Dial. 2012 May;25(3):334-43.*

A review of the vitamins A, D, E & K in CKD. Another great resource!

*The Renal Pharmacists Network would like to thank the following sponsors for their continued support and generous contributions.*

# SPONSORS

## Platinum (> $9,999)

AMGEN PARTNERSHIP PROGRAM in it for life™

Takeda

## Gold ($5,000 - $9,999)

SANOFI

Otsuka

LEO Pharma Inc.

## Silver ($2,500 - $4,999)

Janssen Pharmaceutical Companies of Johnson & Johnson

Roche

AstraZeneca Canada

Shire

## Bronze (< $2,500)

SERVIER