CANNT|ACITN
Canadian Association of Nephrology Nurses and Technologists
l'Association canadienne des infirmières et infirmiers et des technologues de néphrologie

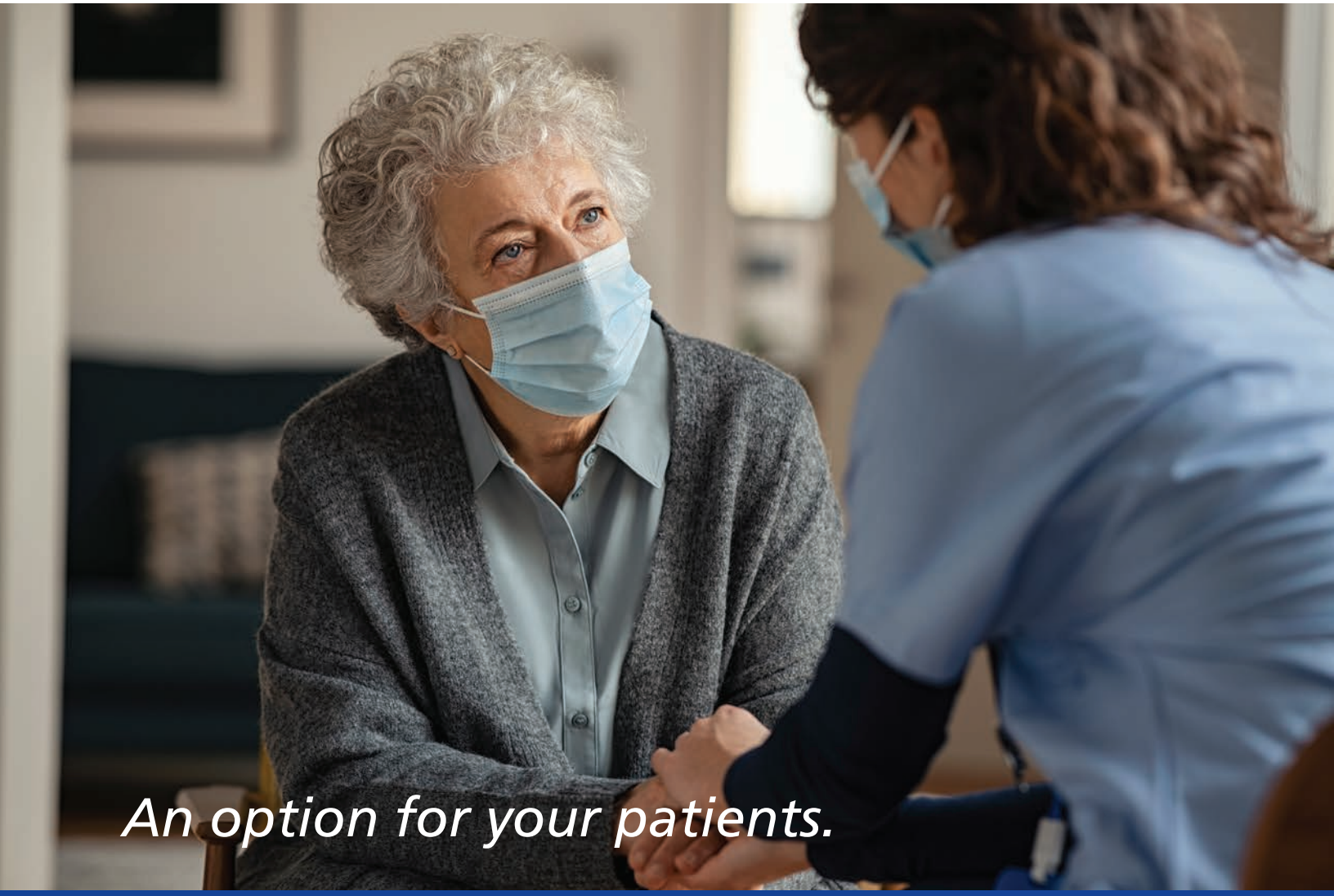
CANNT JOURNAL
JOURNAL ACITN

Volume 31, Issue 1 January–March 2021

CONTENTS

Accel-Sevelamer

(Sevelamer Carbonate 800 mg)



Formulary coverage:

- Ontario (Exceptional Access program: telephone request service)
- Quebec
- Saskatchewan
- Manitoba
- Nova Scotia
- New Brunswick
- Newfoundland
- PEI

www.accelpharma.com

Accel Pharma Inc

CANNT|ACITN
Canadian Association of Nephrology Nurses and Technologists
l'Association canadienne des infirmières et infirmiers et des technologues de néphrologie

JANUARY–MARCH 2021 • VOLUME 31 • ISSUE 1

CANNT JOURNAL
JOURNAL ACITN

CONTENTS

IN EACH ISSUE:

The CANNT Journal is printed on recycled paper.

The CANNT Journal is the official publication of the Canadian Association of Nephrology Nurses and Technologists, 4 Cataraqui St., Suite 310, Kingston, ON K7K 1Z7, telephone: (613) 507-6053, fax: 1-866-303-0626, email: cannt@cannt.ca. Published quarterly, the journal is received by all members of CANNT. Subscriptions are: Canada $80.00 (plus HST), US. $90.00, Outside N. America $115.00. Back issues, when available, are $7.50 (+HST) per issue and are available from the editors. Opinions expressed by writers in the CANNT Journal are not necessarily those held by the editors or CANNT. Contrasting views by our readership and membership are welcome. All letters, comments and articles are to be sent to the CANNT office, 4 Cataraqui St., Suite 310, Kingston, ON K7K 1Z7.

1-877-720-2819
Website: www.cannt.ca

The CANNT Journal accepts articles (manuscripts) on an ongoing basis.

The CANNT Journal is indexed in the Cumulative Index to Nursing and Allied Health Literature (CINAHL), the International Nursing Index (INI), MEDLINE, EBSCO, ProQuest and Thomson Gale.

ISSN 2291-644X (Online)
ISSN 1498-5136 (Print)

The CANNT Journal is produced by Pappin Communications,
www.pappin.com

Letter from the Editors

As of this writing, we remain in the throes of the pandemic that is leaving behind such unmatched and irrevocable destruction in its wake, and it is not quite done yet. This year's World Kidney Day theme, *Living well with kidney disease*, is a timely reminder of how much normality has been taken away from patients (and their families) and healthcare providers alike during these challenging times. This well-timed theme is a clarion call to those of us in the kidney care community at large to ensure that our patients and their families are fully supported such that their quality of life and clinical status are improved, and they can truly state that they are living well with kidney disease. This goal can only be truly achieved by optimal symptom management.

We, at the *CANNT Journal,* are passionate patient advocates through education and increased awareness of issues or interventions that improve the clinical and social outcomes of our patients. In this issue, we lead off with *Online hemodiafiltration: The current state of science and implications for patient-related outcomes* by Yip (2021). HDF has been around for the past 40 years, but it is much more popular in Europe and Japan for reasons that the author has neatly laid out in the article (of course, I will not give the answer that easily). It is indeed a viable renal replacement therapy option to standard dialysis. In *'Phos'ing over phosphorus: A primer on updates in phosphate binders*, Liu and Pemas (2021) also discuss Velphoro (sucroferric hydroxide), a novel iron-based phosphate binder. Both concepts, HDF and Velphoro, represent choices that would help to ameliorate the various symptoms that individuals affected by end-stage kidney disease present before us in our daily practice. As much as dialysis has evolved and improved since George Haas first experimented on humans in the 1920s in Germany, and the survival rates have improved, our patients continue to bear a heavy symptom burden that can so easily weigh them down in life. Cue the dedicated health professionals that we are—let us help motivate our patients to be active agents in their own lives and, thus, feel empowered so that they can thrive and reclaim part of their lives. We start by being more informed, and you have come to the right place.

If you would like to showcase a topic or issue that is relevant to nephrology nursing or technological practice, we encourage you to put pen to paper, and start writing and submit to the *CANNT Journal*. Over the years, we have supported and mentored both novice and seasoned writers. It starts with a healthy dose of a spirit of inquiry peppered with curiosity and determination. We need to publish *your* original research, observational studies, clinical trials, case reports, solutions to clinical bedside problems, and quality improvement projects in order to advance our collective nephrology practice. We have tremendous talent nationwide – we just need to disseminate this wealth of knowledge for the benefit of everyone (patients and their families included) in the nephrology community.

Sincerely,

Jovina Bachynski, MN-NP Adult, RN(EC), CNeph(C), PhD (Student)

Rosa Marticorena, DCE PhD, RN, CNeph(C)

Co-editors, *CANNT Journal*

Message des rédactrices en chef

Au moment d'écrire ces lignes, nous sommes toujours au cœur d'une pandémie qui, dans son sillage, entraîne une destruction inégalée et irrévocable. Ce n'est d'ailleurs pas encore tout à fait terminé. Cette année, le thème de la Journée Mondiale du Rein (11 mars), *Bien vivre avec une maladie rénale*, est un rappel opportun qu'en ces temps difficiles, la normalité s'est vue enlevée aux patients et à leur famille, de même qu'aux professionnels de la santé. Ce thème, qui tombe à point, est un appel à l'ensemble de la communauté des services de soins rénaux. Ensemble, nous pouvons nous assurer que nos patients et leur famille soient pleinement soutenus de manière à ce que leur qualité de vie et leur état clinique soient améliorés et qu'ils puissent réellement affirmer qu'ils vivent bien avec une maladie rénale. Cet objectif ne peut être vraiment accompli que par une prise en charge optimale des symptômes.

À la *Revue de l'ACITN*, nous défendons avec passion nos patients par l'enseignement et par la sensibilisation accrue aux enjeux et aux interventions qui améliorent les résultats cliniques et sociaux de nos patients. Ce numéro commence par l'article *Online hemodiafiltration: The current state of science and implications for patient-related outcomes*, rédigé par Yip (2021). L'hémodiafiltration fait partie du paysage depuis les 40 dernières années, mais elle est encore beaucoup plus populaire en Europe et au Japon, pour des raisons que l'auteur aborde clairement dans son article (évidemment, je ne donnerai pas la réponse aussi facilement). En effet, ce traitement de suppléance rénale serait une option de rechange viable à la dialyse standard. Dans leur article *Phos'ing over phosphorus: A primer on updates in phosphate binders* (2021), Liu et Pemas traitent de Velphoro (oxyhydroxyde sucro-ferrique), un nouveau complexe ferrique agissant comme chélateur de phosphate. Les deux concepts, l'hémodiafiltration et Velphoro, représentent des choix qui aideraient à atténuer les divers symptômes éprouvés par les patients atteints d'une maladie rénale terminale auxquels nous sommes confrontés dans notre pratique quotidienne. Malgré l'évolution de la dialyse et l'augmentation des taux de survie depuis les premières expériences de Georg Haas sur les humains dans les années 1920 en Allemagne, nos patients continuent de souffrir de symptômes qui représentent un lourd fardeau pour eux et peuvent peser sur leur vie quotidienne. En qualité de professionnels de la santé dévoués, nous devons motiver nos patients à être des acteurs de leur propre vie et à se sentir ainsi plus autonomes pour qu'ils puissent s'épanouir et reprendre une partie de leur vie en main. Nous devons commencer par être plus informés, et, pour ce faire, vous êtes au bon endroit.

Si vous souhaitez aborder une problématique ou un sujet relatif aux soins infirmiers en néphrologie ou aux pratiques technologiques, nous vous encourageons à prendre la plume et à soumettre le fruit de votre rédaction à la *Revue de l'ACITN*. Au fil des ans, nous avons soutenu et encadré autant des auteurs novices que chevronnés. Tout commence par une bonne dose d'enthousiasme envers la tâche parsemée de curiosité et de détermination. Nous devons publier *vos* recherches originales, études observationnelles, essais cliniques, études de cas, solutions à des problèmes cliniques, et projets d'amélioration de la qualité, afin de faire avancer notre pratique collective en néphrologie. Nous avons énormément de personnes talentueuses à l'échelle nationale — nous devons simplement disséminer cette richesse de connaissances au bénéfice de tous, y compris les patients et leur famille, dans la communauté néphrologique.

Cordialement,

Jovina Bachynski, M. Sc. inf., IP (adulte), inf. aut. (catégorie avancée), CNéph(C), aspirante au doctorat

Rosa Marticorena, inf. aut., CNéph(C), D.E.S. Épidémiologie clinique, Ph. D.

Corédactrices en chef, *Revue de l'ACITN*

Le *Journal ACITN* est la publication officielle de l'Association canadienne des infirmiers/infirmières et technologues en néphrologie, a/s 4, rue Cataraqui, bureau 310, Kingston (Ontario) K7K 1Z7.

Téléphone : 613-507-6053
Télécopieur : 1-866-303-0626
Courriel : cannt@cannt.ca

Publié quatre fois par année, ce journal est envoyé à tous les membres de l'Association. L'abonnement annuel est: Canada, 80 $ (+TVH), E.-U., 90 $, hors du Canada et E.-U., 115 $. Les publications antérieures, lorsque disponibles, coûtent 7,50 $ (+TVH) chacune. Les opinions émises par les auteurs dans ce journal ne sont pas nécessairement partagées par l'Association ni par le corédactrices en chef. Nous invitons les lecteurs à nous faire part de leurs opinions. Toute correspondance devra être envoyée à l'ACITN, au 4, rue Cataraqui, bureau 310, Kingston (Ontario) K7K 1Z7.

1-877-720-2819
Site Web : www.cannt.ca

Le *Journal ACITN* accepte des articles (manuscrits) de façon continue.

Le *Journal ACITN* est maintenant répertorié dans le *Cumulative Index to Nursing and Allied Health Literature (CINAHL), International Nursing Index (INI), MEDLINE, EBSCO, ProQuest* et *Thomson Gale*.

ISSN 2291-644X (En ligne)
ISSN 1498-5136 (Dans la presse)

Le *Journal ACITN* est préparé par Pappin Communications, www.pappin.com

Rédactrice en chef
Jovina Bachynski, M. Nurs., Inf. aut. (FC), CNéph(C)
Courriel : cannt.journal1@gmail.com

Co-rédactrice
Rosa M. Marticorena, B. Sc. inf., inf. aut., CNéph(C), D.E.S. Épidémiologie clinique, coordonnatrice de recherche clinique III, Ph. D.
Courriel : cannt.journal1@gmail.com

Éditeur
Heather Coughlin, Pembroke (Ontario)

Conception et design
Sherri Keller, Pembroke (Ontario)

Publicité
Heather Coughlin, Pappin Communications,
T : 613-633-1938
Courriel : heather@pappin.com
Publicité : www.pappin.com

Message from the President

Hello, everyone,

I want to start my journal message with Happy 2021!, and whatever the new year has in store, we will be in it together. It is hard not to write about the pandemic, but I will keep it short and focused.

"Pandemic Fatigue" … it is real! Or at least I believe that it is. Over this past pandemic year, we have endured this relentless virus, adapting to revised public health measures, as they are modified to keep us safe, quarantines, isolation, an uncertain economy and its personal challenges, trying to juggle work, home schooling, and childcare, and then continuing to cope with the anxiety we wake up to each morning. Layer on top of this a pervasive uncertainty that makes it difficult to plan for the next day, month or year. When we ask each other how we are "doing" and "managing", we often hear our colleagues tell us they are feeling overwhelmed, tired, burnt out, and unsure of how much longer they can keep positive. You can spend many hours searching the internet for information on the mental health crisis that we are facing in the backdrop of this pandemic—it is quite saturated with details on the subject and, while the news about vaccines sparks a renewed sense of hope, it does not change the reality that we need to find strategies to expand our resilience, nurture our mental health, and reduce our anxiety. So, as you look for ways to care for yourself during this pandemic marathon, please continue to hold each other up and be kind to yourself.

Your CANNT Board of Directors and office management team are hard at work to provide you with some valuable educational and relevant opportunities. Check out our website for these upcoming events.

Please take some time to share with others the benefits to being a member of CANNT. If you are taking the time out of your busy life to read this message, then please be my champion and tell others that your CANNT membership gives you access to the peer-reviewed quarterly *CANNT Journal*, and to the *Vascular Access Guidelines*, *Standards of Nursing Practice*, and *Standards of Technical Practice*. You get educational opportunities that are eligible for continuous learning hours towards the CNeph(C) certification/ recertification, and connections to the latest information and resources related to nephrology, technology or nursing. Your CANNT association works to represent its membership as affiliates of various organizations and acts as your link to those organizations to help keep you connected and informed. Together, with your help, we can achieve growth in our membership which will yield opportunities to expand our program and services to the members.

The Canadian Nurses Association (CNA) wants certification to be more accessible to nurses while maintaining their history of established high quality and credibility. The CNA certification program has evolved to match changes in nursing curriculums and practice. That is why the eligibility specialty experience hours required for nurses to apply for certification will be reduced. See more at: https://www.cna-aiic.ca/en/certification#st-hash.42OltDcz.dpuf

Just a reminder to those nurses who are considering writing their CNA certification in nephrology—you can receive the voucher code from CANNT to receive a 20% discount on the cost if you are a CANNT member. The discount can be applied to the CNA member rate or the non-member rate of either the initial exam fee or the recertification fee

Warmest wishes to all,
Janice MacKay
CANNT President
2018-2021

Le mot de la présidente

Bonjour à toutes et à tous,

Tout d'abord, je vous souhaite une bonne année 2021! Peu importe ce que la nouvelle année nous réserve, nous serons ensemble dans cette aventure. Il est difficile de ne pas écrire au sujet de la pandémie, mais je serai brève et irai droit au but.

La « fatigue pandémique » est réelle! Du moins, j'y crois. Au cours de la dernière année, nous avons enduré un virus impitoyable. Nous nous sommes adaptés à des mesures sans cesse révisées et modifiées par la Santé publique afin d'assurer notre sécurité. Nous avons fait face à des quarantaines et à des isolements. Nous avons dû composer avec une économie incertaine et des difficultés personnelles, tentant de conjuguer travail, école à la maison et parentalité, tout en continuant d'affronter l'anxiété que l'on vit dès le réveil chaque matin. En plus, nous nous heurtons à une incertitude persistante qui rend difficile la planification de la prochaine journée, du prochain mois et de la prochaine année. Lorsque nous nous demandons comment nous « allons » et comment nous nous « débrouillons », nous entendons souvent nos collègues nous répondre qu'ils se sentent submergés, fatigués, épuisés, ne sachant pas trop combien de temps ils pourront rester positifs. Il est possible de passer de nombreuses heures à chercher sur le Web de l'information sur la crise de santé mentale à laquelle nous faisons face en arrière-plan de cette pandémie. Cette information est saturée de détails sur le sujet et, bien que les nouvelles concernant les vaccins suscitent un espoir renouvelé, ces dernières ne changent pas le fait que nous devons trouver des stratégies pour améliorer notre résilience, prendre soin de notre santé mentale et réduire notre anxiété. Alors que vous cherchez des façons de prendre soin de vous durant ce marathon pandémique, continuez de vous soutenir les uns les autres et d'être indulgents envers vous-mêmes.

Le conseil d'administration et l'équipe de gestion de l'ACITN travaillent d'arrache-pied pour vous offrir de précieuses occasions formatrices et pertinentes. Jetez un coup d'œil à notre site Web pour ces événements à venir.

Prenez un moment pour partager avec les autres les avantages d'être membre de l'ACITN. Si vous prenez le temps de lire ce message malgré votre vie occupée, soyez à mes côtés pour indiquer aux autres que votre adhésion à l'ACITN vous donne accès à la *Revue de l'ACITN*, révisée par les pairs et publiée quatre fois par année, ainsi qu'aux publications *Vascular Access Guidelines, Standards of Nursing Practice* et *Standards of Technical Practice*. Vous profitez aussi d'occasions de formation qui sont admissibles à des heures de formation continue afin d'obtenir votre certification ou votre renouvellement de certification CNéph(C), en plus de liens vers l'information et les ressources les plus récentes en matière de néphrologie, de technologies et de soins infirmiers. L'ACITN représente ses membres dans les diverses organisations auxquelles elle est affiliée et avec lesquelles elle agit comme intermédiaire pour vous tenir au courant et vous informer. Ensemble, avec votre aide, nous arriverons à faire croître notre nombre de membres, qui sera l'occasion d'élargir notre programme et nos services aux membres.

L'Association des infirmières et infirmiers du Canada (AIIC) souhaite que la certification soit plus accessible aux infirmières et aux infirmiers tout en conservant sa réputation bien établie de grande qualité et de crédibilité. Le Programme de certification de l'AIIC a évolué afin de répondre aux changements dans les programmes d'études et la pratique des soins infirmiers. C'est la raison pour laquelle les heures d'expérience requises dans une spécialité pour faire une demande de certification seront réduites. Pour en savoir plus, visitez la page suivante : https://www.cna-aiic.ca/fr/certification.

Je souhaite rappeler aux infirmières et aux infirmiers qui envisagent de passer l'examen de certification de l'AIIC en néphrologie que vous pouvez recevoir un code promotionnel de l'ACITN, qui vous offre un rabais de 20 % sur les frais si vous êtes membres de l'association. Le rabais peut être appliqué au tarif des membres de l'AIIC ou au tarif pour les non-membres, qu'il s'agisse des frais d'examen initial ou des frais de recertification.

Mes vœux les plus chaleureux à toutes et à tous,
Janice MacKay
Présidente de l'ACITN 2018-2021

Your Board in Action

Our one-year mark since the beginning of the pandemic has now passed and, in some respects, it is difficult to remember a time when we could hug each other freely and gather in large numbers. As we still remain in a pandemic crisis, CANNT, once again, has made the responsible decision to deliver our 2021 conference through a virtual platform. Last year's virtual webinar conference series was a resounding success due to your commitment to lifelong professional learning. We are preparing to offer a similar series for our nephrology technologists to meet their need for continuing education with the first virtual webinar *Endotoxin: Control, Analysis and Clinical Relevance* scheduled for March 11, 2021 at 11:00 AM ET. We want to take this opportunity to thank our industry partners for sponsoring this very important educational series.

CANNT continues to acknowledge and applaud your hard work that is vital to providing exemplary nephrology care. We must continue to be diligent as we experience the effects of the variant strains now present in nephrology programs throughout the country. We need to hold fast and continue to adhere to the strict guidelines communicated on our website, as we participate in the rollout of the long-awaited vaccines. On behalf of the executive board of CANNT, I wish to extend a heartfelt thank-you for your dedication.

MEMBERSHIP

We have successfully increased our membership to 314 as of January 31, 2021. The Board of Directors (BOD) continually evolves to provide enduring benefits to all our members. Our latest accomplishment is the partnership with the Ontario Renal Network to provide the Vascular Access Education Program (VAEP) via the CANNT website. Membership is vital to CANNT, as it is an association run by membership.

There are many advantages to becoming a member of CANNT:

- Online access to the peer-reviewed quarterly *CANNT Journal* for all members
- Online access to the *Vascular Access Guidelines*, *Standards of Nursing Practice*, and *Standards of Technical Practice*
- Discount of the annual conference registration fee
- Educational opportunities at a reduced cost or free to members
- Connections to the latest information and resources related to nephrology, technology, or nursing
- Networking opportunities with colleagues practicing in your nephrology specialty on a national level
- Opportunities for collaborative networking and problem solving through participation in a refined clinical practice group
- CANNT awards, bursaries, and research grants offered to individuals in recognition of their excellence in the workplace and/or to further their studies in nephrology
- CANNT represents its membership as affiliates of various organizations and acts as your link to those organizations to help keep you connected and informed.

We are seeking input from our valued membership, and we want to hear from you on ways to increase our association membership. Please share your thoughts with us by contacting your CANNT office team at**:** https://cannt-acitn.ca/

JOURNAL

Guidelines for journal article submission can be found under the "CANNT Journal" section of the CANNT website. We prefer manuscripts that present new clinical information or address issues of special interest to nephrology nurses and technologists. E-mail your manuscript to one of our co-editors Jovina Bachynski or Rosa Marticorena at CANNT.journal1@gmail.com.

Include a cover letter with contact information for the primary author and a one-sentence biographical sketch (credentials, current job title, and location) for each author. The CANNT Journal is published four times per year in electronic versions. The journal is a refereed publication and accepts only original, peer-reviewed articles. Advertising opportunities and corporate sponsored education opportunities are available.

COMMUNICATIONS

CANNT continues to lead the way through offering multiple avenues of communication to respond to the increased needs of our members during the COVID-19 pandemic. We have made every effort to support our members with access to timely information including the provision of updates regarding the pandemic. We acknowledge the importance of members' wellbeing and mental health during this time and have added more resources to our website, as well. We continue to partner with other professional associations, including the Canadian Society of Nephrology, to offer multiple webinars to ensure new knowledge is shared with all nephrology professionals. We promise to support our members in the future with information regarding current evidence-based practices communicated through all our social media platforms. Please visit our website and stay connected through our tweeter feeds and *CANNT Connection* releases. If you have a question, idea, or event to promote, please contact our Director of Communications, Ethan Holtzer.

https://ca.linkedin.com/company/canadian-association-of-nephrology-nurses-and-technologists?trk=-public_profile_experience-item_result-card_subtitle-click

Canadian Association of Nephrology Nurses and Technologists (CANNT) | LinkedIn

Learn about working at the Canadian Association of Nephrology Nurses and Technologists (CANNT). Join LinkedIn today for free. See who you know at CANNT, leverage your professional network, and get hired: ca.linkedin.com

CANNT website (**www.CANNT.ca**)

Facebook: **https://www.facebook.com/Canadian-Association-of-Nephrology-Nurses-and-Technologists-160999717295820/**

LinkedIn: **https://www.linkedin.com/in/cannt-cannt-06910261/**

Twitter: **CANNT (@CANNT1)**

ANNUAL CONFERENCE

CANNT is making plans to offer another Virtual Conference Series this fall to all nephrology nurses and technologists, as well as other healthcare professionals and industry partners. We continue with our promise of making this conference affordable by offering complementary registration to all members and at a very low cost to non-members. We encourage all members to voice their educational needs to their CANNT regional representatives to ensure a more robust agenda that will appeal to the wide range of nephrology professionals and practice settings. Details will be communicated to all members as the webinars are developed.

FINANCES

As a "Not for Profit" professional association, our objective is to provide value to our members that aligns with our mission and vision. CANNT continues to develop innovative financial strategies that will build stability during this unpreceded time. For the second time since the beginning of our organization, our annual conference has been cancelled, and CANNT has responded by using fiscal responsible measures, careful budgeting, and finding alternate financial sources. Our management team continues to work tirelessly to develop new lucrative opportunities with our industry partners and to successfully secure funding to maintain the viability of the CANNT organization. Transparency improves the coherence and cohesion of our association—on this note, you may find the 2020 Annual Report on the CANNT website (https://cannt-acitn.ca/). In closing, the team at CANNT would like to thank you for your efforts and commitment to our association.

Sincerely,
Cathy Cake
CANNT President-Elect/ Treasurer 2020-2021

Votre conseil en action

Un an est maintenant passé depuis le début de la pandémie et, d'une certaine façon, il est difficile de se souvenir du temps où il était possible de se serrer dans nos bras librement et de se rassembler en grand nombre. Alors que nous restons au cœur de cette pandémie, l'ACITN a pris la décision responsable, encore une fois, de tenir son congrès annuel 2021 virtuellement. L'an dernier, notre série de webinaires a connu un succès retentissant en raison de notre engagement permanent envers l'apprentissage professionnel. Nous nous préparons à offrir une série similaire pour nos technologues en néphrologie afin de répondre à leur besoin de formation continue, dont le premier webinaire, Endotoxin : Control, Analysis and Clinical Relevance, est prévu le 11 mars 2021 à 11 h, heure de l'Est. Nous souhaitons profiter de l'occasion pour remercier nos partenaires de l'industrie pour avoir parrainé cette importante série de formations.

L'ACITN continue de reconnaître et de saluer votre travail acharné, qui est vital pour fournir des soins de santé exemplaires en néphrologie. Nous devons continuer d'être rigoureux dans notre pratique alors que nous ressentons les effets des variants, maintenant présents dans les programmes de néphrologie à travers le pays. Nous devons tenir bon et continuer d'adhérer aux directives strictes communiquées sur notre site Web alors que nous participons à la campagne de vaccination longtemps attendue. Au nom du conseil d'administration de l'ACITN, je souhaite vous remercier du fond du cœur pour votre dévouement.

ADHÉSION

En date du 31 janvier 2021, nous avons atteint 314 membres, un succès! Le conseil d'administration évolue continuellement pour offrir des avantages durables à tous nos membres. Notre plus récent accomplissement est notre partenariat avec le Réseau rénal de l'Ontario afin d'offrir le Vascular Access Education Program (VAEP) par le biais du site Web de l'ACITN. Les membres sont la force vive de l'ACITN, puisque ce sont eux qui administrent l'association.

Il y a une foule d'avantages à devenir membre de l'ACITN :

- Accès en ligne pour tous les membres à la revue trimestrielle évaluée par les pairs nommée *Revue de l'ACITN*
- Accès en ligne aux publications *Vascular Access Guidelines*, *Standards of Nursing Practice* et *Standards of Technical Practice*
- Réduction des frais d'inscription au congrès annuel
- Possibilités de formations gratuites ou à prix réduit
- Liens vers l'information et les ressources les plus récentes en matière de néphrologie, de technologies et de soins infirmiers
- Occasions de réseauter à l'échelle nationale avec des collègues évoluant dans votre spécialité néphrologique
- Possibilité de collaborer et de contribuer à la résolution de problèmes grâce à la participation à un groupe de pratique clinique attitré
- Prix, bourses et subventions de recherche de l'ACITN attribués pour souligner l'excellence du travail de certaines personnes ou pour leur permettre de poursuivre leurs études en néphrologie
- L'ACITN représente ses membres dans les diverses organisations auxquelles elle est affiliée et avec lesquelles elle agit comme intermédiaire pour vous tenir au courant et vous informer.

Nous sommes à l'écoute de nos membres, que nous tenons en haute estime, et nous aimerions connaître votre opinion sur la manière d'augmenter notre nombre d'adhérents. Veuillez nous faire part de vos idées en communiquant avec l'équipe administrative de l'ACITN, via le https://cannt-acitn.ca/.

REVUE

Vous trouverez la marche à suivre vous permettant de soumettre un article pour publication dans notre revue sous la section réservée à la Revue de l'ACITN du site Web de l'Association. Nous privilégions les articles qui portent sur de nouvelles données cliniques ou qui traitent de sujets présentant un intérêt particulier pour les infirmières, les infirmiers et les technologues en néphrologie. Envoyez votre article par courriel à l'une des corédactrices en chef, Jovina Bachynski ou Rosa Marticorena, à l'adresse suivante : CANNT.journal1@gmail.com.

Incluez une lettre d'accompagnement avec les coordonnées de l'auteur(e) principal(e) et une notice bibliographique d'une phrase (titres de compétence, titre et lieu du poste actuel) pour chaque auteur. La revue est publiée quatre fois par an dans un format électronique. Elle est soumise à l'examen d'un comité de lecture et seuls les articles originaux, révisés par les pairs, sont acceptés. Des possibilités d'annonces publicitaires et de formations parrainées par des entreprises sont offertes.

COMMUNICATIONS

L'ACITN continue d'ouvrir la marche par l'intermédiaire de multiples avenues de communication afin de répondre aux besoins accrus de nos membres durant la pandémie de COVID-19. Nous nous sommes efforcés de soutenir nos membres en offrant l'accès à de l'information actuelle, y compris des mises à jour au sujet de la pandémie. Nous reconnaissons l'importance de favoriser le bien-être et la santé mentale de nos membres durant cette période difficile; c'est pourquoi nous avons également ajouté plus de ressources à notre site Web. De plus, nous poursuivons notre association avec d'autres organisations professionnelles, telles que la Société canadienne de néphrologie, afin d'offrir plusieurs webinaires et d'assurer la communication des nouvelles connaissances à tous les professionnels du milieu. Nous continuerons de vous soutenir à l'avenir en vous donnant de l'information au sujet des pratiques fondées sur les données probantes, qui vous sera communiquée sur toutes nos plateformes de médias

sociaux. Visitez notre site Web et restez informés par l'intermédiaire de nos publications sur Twitter et des bulletins *CANNT Connection*. Si vous avez une question, une idée ou un événement à promouvoir, écrivez à Ethan Holtzer, notre directeur des communications.
https://ca.linkedin.com/company/canadian-association-of-nephrology-nurses-and-technologists?trk=-public_profile_experience-item_result-card_subtitle-click

Canadian Association of Nephrology Nurses and Technologists (CANNT) | LinkedIn

Site Web de l'ACITN (**www.CANNT.ca**)
Twitter **CANNT (@CANNT1) | Twitter**

CONGRÈS ANNUEL

L'ACITN prévoit d'offrir une autre série de conférences virtuelles cet automne destinée à tous les infirmiers, infirmières et technologues en néphrologie, ainsi qu'aux autres professionnels de la santé et partenaires de l'industrie. Nous continuons de remplir notre promesse de rendre abordable cette série de conférences en offrant l'inscription gratuitement à tous nos membres et en exigeant des frais minimes pour les non-membres. Nous encourageons tous nos membres à faire part de leurs besoins en matière de formation à leur représentant régional de l'ACITN afin d'assurer un programme substantiel qui saura être attrayant pour un large éventail de milieux de travail et de professionnels en néphrologie. Les détails seront communiqués aux membres lorsque les webinaires seront créés.

FINANCES

En tant qu'association professionnelle sans but lucratif, notre objectif est d'offrir à nos membres une valeur ajoutée en lien avec notre mission et notre vision. L'ACITN continue d'élaborer des stratégies financières innovatrices qui assureront la stabilité durant ces temps sans précédent. Pour la seconde fois depuis la création de notre organisation, le congrès annuel a dû être annulé. L'ACITN a réagi en utilisant des mesures fiscales responsables, un budget prudent et d'autres ressources de financement. Les membres de notre équipe de gestion ont travaillé sans relâche pour imaginer de nouvelles activités lucratives en collaboration avec nos partenaires de l'industrie. Ils ont ainsi réussi à obtenir des fonds pour assurer la viabilité de l'ACITN. Comme la transparence améliore la cohérence et la cohésion de notre association, nos membres peuvent consulter le rapport annuel 2020 de l'Association sur le site Web de l'ACITN (https://cannt-acitn.ca/). Pour terminer, l'équipe de l'ACITN aimerait vous remercier pour vos efforts et votre engagement envers notre organisation.

Cordialement,
Cathy Cake
Présidente désignée et trésorière de l'ACITN 2020-2021

NOTICE BOARD

Canadian Nurses Association (CNA) Exam Timeline.
https://www.nurseone.ca/certification/renewing-your-certification#sthash.IDBqg5i7.dpuf

	Spring 2021	Fall 2021
Initial exam or renewal by exam application window	**January 14 – March 8, 2021**	**June 1-September 1, 2021**
Certification exam window	**May 1-15, 2021**	**November 1-15, 2021**
Renewal by continuous learning application window	**January 14 – November 1, 2021**	

N.B. CNA will provide 20% discount for initial exam writers, renewal exam writers, and renewals by continuous learning in 2021 to active members of CANNT. Contact cannt@cannt.ca for the voucher code in 2021.

- **March 11, 2021.** World Kidney Day—*Living Well with Kidney Disease*. **https://www.worldkidneyday.org/2021-campaign/2021-wkd-theme/**
- **April 6–10, 2021**. National Kidney Foundation (NKF) Virtual Spring Clinical Meetings 2021. **https://www.kidney.org/spring-clinical**
- **April 15–19, 2021**. Virtual World Congress of Nephrology 2021 (WCN'21). **https://www.theisn.org/wcn/**
- **May 2–5, 2021.** American Nephrology Nurses' Association (ANNA) National Virtual Symposium. **https://www.annanurse.org/events/2021-national-symposium**
- **June 5–8, 2021.** 58th European Renal Association – European Dialysis and Transplant Association (ERA-EDTA) Congress, Berlin and Virtual. CityCube Berlin, Berlin, Germany. **https://www.era-edta.org/en/berlin2021/**
- **June 17–19, 2021**. Renal Society of Australasia (RSA) Annual Conference—*Renal care beyond a crisis: Possibilities and future directions*. Melbourne Convention, Melbourne, Australia. **https://www.renalsociety.org/education/2020-annual-conference/**
- **September 4–7, 2021**. 49th Annual European Dialysis and Transplant Nurses Association/European Renal Care Association (EDTNA/ERCA) International Conference: *Knowledge, skills and commitment—core elements to manage care*, Cankarjev dom, Ljubljana, Slovenia. **https://www.edtnaerca.org/conferences/conferences-ljubljana-2020**
- **September 15, 2021**. Nephrology Health Care Professionals' Day (celebrated every third Wednesday of September annually)
- **October 19–December 2, 2021**. Canadian Association Nephrology Nurses and Technologists (CANNT) 52nd Annual Conference 2021, Virtual Conference every Tuesday and Thursday, 2:30 p.m.–3:30 p.m. ET and 6:30 p.m.–7:30 p.m. ET More details coming soon! **www.cannt.ca**
- **November 2–7, 2021**. American Society of Nephrology (ASN) 2021 Kidney Week, San Diego Convention Center, San Diego, CA. **https://www.asn-online.org/education/kidneyweek/archives/future.aspx**

Nephrology Certification Registration Status Report 2020

Initial and Renewal by Exam to Renew in 2020	Renewal by Continuous Learning (CL) Hours	Total of Initials and Renewals	Due
30	116	146	251

Online hemodiafiltration: The current state of science and implications for patient-related outcomes

By Yuk-Chiu Yip

ABSTRACT

This paper aims to identify and critically review available contemporary research regarding online hemodiafiltration, which is used as a modality of renal replacement therapy to promote evidence-based nursing practice for patients. A literature review was conducted using four medical databases (CINAHL, EMBASE, PubMed, and Medline) from 1999 to 2019. Hemodiafiltration removes greater quantities of higher-molecular-weight uremic solutes than standard high-flux hemodialysis. Most contemporary clinical trials using randomized controls indicated that online hemodiafiltration offers a superior survival rate than high-flux hemodialysis if substantial convection volumes are achieved. Hemodiafiltration is associated with a reduced incidence of intradialytic hypotension. Online hemodiafiltration offers many potential improvements to patients' treatment outcomes, particularly regarding better solute clearance. Regarding survival rates, the purported superiority of hemodiafiltration over high-flux hemodialysis should be further tested by verifying the optimal convective dosage for a variety of patient cohorts, organized with reference to specific clinically relevant variables.

Key words: mortality, online hemodiafiltration, patient outcomes, renal replacement therapy, solute removal

In 2017, approximately 89% of patients with end-stage kidney disease (ESKD) worldwide were undergoing hemodialysis (HD); of these, about 10% were on hemodiafiltration (HDF), and 97% patients who were on HDF as their renal replacement therapy (RRT) were using online HDF (Canaud et al., 2020). Hemodiafiltration was first used in the 1980s to address the low levels of middle- and small-molecule clearance achieved by low-flux HD and hemofiltration, respectively.

In HD, solutes are removed across the dialyzer membrane through diffusion, which involves passive movement down a concentration gradient, and/or convection that involves the use of solvent drag (Fischbach et al., 2012). Due to the rapid decrease in diffusion coefficients with increase in molecular size, a relatively low level of larger uremic toxins remains with HD (Farrell & Barb, 1973). The primary mechanism for removing low-molecular-weight molecules that are under 500 Daltons (Da), such as urea (60 Da) and creatinine (113 Da) is by diffusion. Diffusion, however, cannot efficiently remove medium-sized molecules that are between 500 and 60,000 Daltons, such as β2-microglobulin (11,500 Da) (Clark & Winchester, 2003). Furthermore, diffusion is not effective in removing molecules that are above 60,000 Da. These limitations can be overcome by using high-flux dialysis membranes that have a larger pore size.

In contrast, the convection process is used to remove solutes in hemofiltration (HF). It allows solutes of up to 20,000 Da to cross the membrane, thereby removing medium- and large-molecular-weight solutes more efficiently. Although HF clears more of the larger solutes than HD, it is not as effective as conventional HD in removing low-molecular-weight solutes. Convective clearance is determined by both sieving coefficients and ultrafiltration, and the sieving coefficients decrease gradually as the molecular size increases (Wendt et al., 1979).

Hemodiafiltration combines the benefits of diffusion in conventional HD and convection in HF, thus allowing it to offer the high level of small-molecule clearance associated with the former and the better rate of larger-molecule clearance associated with the latter. Online HDF is a common form of HDF. In this process, the dialysis machine generates a substitution fluid that produces a non-pyrogenic, sterile, unlimited, and continuous ultrapure dialysate (Fischbach et al., 2012).

Online HDF has gained approval in recent years in Europe and Asia Pacific (Canaud et al., 2020). Growth in the percentage of patients who undergo HDF has been observed (i.e., an annual average of approximately 12% in Europe and 24% in Asia Pacific). In contrast, this increase far exceeds the 6.6% growth in the overall HD rate globally (Canaud et al., 2020). The Kidney Health Initiatives (KHI), a collaboration between the American Society of Nephrology (ASN) and Food Drug Administration (FDA), spearheaded the implementation of HDF in North America (Ward et al., 2018; Canaud et al., 2018), notwithstanding the lower uptake in HDF utilization in the United States (Blankestijn, 2013). In the United Kingdom, the National Institute for

AUTHOR NOTE

Yuk-Chiu Yip, RN(HK), MNSC, PGCERT, Nurse Educator, School of Health Sciences, Caritas Institute of Higher Education, Hong Kong, China

Correspondence concerning this article should be forwarded to: Yuk-Chiu Yip, School of Health Sciences, Caritas Institute of Higher Education, 2 Chui Ling Lane, Tseung Kwan O, New Territories, Hong Kong, China.

Tel: (+852) 3702-4264; Email: ***jeffreyycyip@gmail.com***

Health and Care Excellence (NICE) has formally recognized the superiority of HDF as a renal replacement modality (National Guideline Centre, 2018).

The considerable variations in HDF utilization rates worldwide may be partly attributable to the differences in the levels of approval from regulators regarding the online production of replacement fluids (Locatelli et al., 2018; Ward et al., 2018). Existing literature has highlighted the various factors that hinder the institution of HDF in dialysis centers (Kim & Park, 2016). HDF incurs additional expenses due to the additional cost of the substitution fluid, machine upgrades, and microbiological tests. More significantly, despite the four decades since its introduction, there is still insufficient evidence suggesting the superior outcomes of HDF over those of HD. Of the four contemporary randomized trials (RCTs) (Convective Transport Study [CONTRAST; Grooteman et al., 2012]; On-Line Hemodiafiltration Survival Study or Estudio de Supervivencia de Hemodiafiltración OnLine [ESHOL; Maduell et al., 2013]; French Convective versus Hemodialysis in Elderly [FRENCHIE; Morena et al., 2017); Turkish online hemodiafiltration [Turkish OL-HDF Study; Ok et al., 2013]), only the ESHOL study (Maduell et al., 2013) demonstrated better survival rates in patients receiving online HDF than those receiving HD. Observational studies provided evidence that high-convective-volume HDF is associated with superior patient outcomes (Canaud et al., 2006; Hazelbag et al., 2017; Imamović et al., 2014), which is contrary to other studies (Locatelli et al., 2018; Siriopol et al., 2015).

Despite these operational challenges, HDF has been shown to be viable as the primary means of managing ESKD patients worldwide. To promote evidence-based nursing care, this review aims to identify and critically assess the best contemporary research on treatment outcomes for patients undergoing online HDF.

METHODS

Four medical databases (CINAHL, EMBASE, Medline, and PubMed) were searched for extant literature from the last 20 years (1999–2019). This search employed the following MeSH terms and keywords:

- Chronic kidney failure (e.g., "chronic renal failure," "end-stage renal disease," "end-stage renal failure," "end-stage kidney disease," or "ESRD")
- Outcomes (e.g., "solute clearance," "solute removal," "survival," "patient-reported outcomes," "advantages," "results," "treatment outcomes," "influences," "mortality")
- Hemodiafiltration (e.g., "convective therapies," "OL-HDF," "olHDF," "online hemodiafiltration," "intermittent renal replacement therapy," or "online HDF")

In addition, notable nephrology journals, including the *American Journal of Kidney Diseases*, *Kidney International*, *Nephrology Dialysis Transplantation*, and *Seminars in Nephrology*, were manually searched for articles. Titles cited in the bibliographies of the retrieved articles and existing review articles were also used to perform a manual search for further relevant studies.

The inclusion criteria were as follows:

- Any prospective or randomized trial that focused on the use of online HDF as a form of RRT;
- Clear descriptions of measurable outcomes of the patients (e.g., solute clearance, all-cause mortality); and
- Research written in English.

Studies that were non-English, non-experimental design, solely qualitative with unclear measures of outcome, commentaries or review articles, cross-sectional, or studies that did not focus on patients with ESKD were excluded in the analysis.

RESULTS AND DISCUSSION

Solute Removal Using Online HDF and Subsequent Clinical Advantages

HDF offers superior clearance of β2-microglobulin than HD (30–40% more using HDF compared to using high-flux HD) (Ward et al., 2000). Employing convective therapy reduces the incidence of β2-microglobulin amyloidosis, and carpal tunnel syndrome and similar problems (Locatelli et al., 1999; Nakai et al., 2001). These advantages are likely attributable to the combined convective transport (enhancing the level of β2-microglobulin removal) and the use of ultrapure fluid and biocompatible materials, thus reducing inflammation.

It is unclear which technique—high-flux HD or HDF—removes greater quantities of phosphate. Contradictory findings have been reported: Lornoy and colleagues (2006) noted no variations between the two methods, whereas Cornelis et al. (2014) demonstrated that post-dilution HDF removed between 15% and 20% more phosphate than high-flux HD. The CONTRAST study demonstrated that the pre-dialysis serum phosphate levels decreased by 6% and the proportion of patients achieving target serum phosphorus levels pre-treatment increased from 64% to 74% (Penne et al., 2010). Alternatively, the Turkish OL-HDF (Ok et al., 2013) and ESHOL (Maduell et al., 2013) studies revealed no variations in serum phosphate levels. The differences between these studies and their inconclusive outcomes may be attributed to the fact that hyperphosphatemia is seldom adequately controlled, although dialysis appears adequate and within the reference values based on urea kinetics (Kt/V). Phosphate removal depends on the levels of residual kidney function and the use of the specific medications for chronic kidney disease–mineral bone disorder, which include calcimimetics, vitamin D analogs, and phosphate binders. Dialysis is merely a single element among the many complex interactions. Therefore, HDF is an inappropriate choice if the only goal is to enhance the clearance of small molecules such as phosphate.

HDF offers greater clearance levels for other solutes, including complement factor D (pro-inflammatory mediator), leptin (satiety hormone), fibroblast growth factor 23 (FGF23) (associated with vascular calcification and metabolic bone disorder), several cytokines, advanced glycation end-product precursors, and circulating advanced glycation end products (Lin et al., 2003; Mandolfo et al., 2006; Patrier et al., 2013; Ward et al., 2018). Prospective studies

demonstrated an association between HDF and depleted levels of C-reactive protein and other forms of sensitive inflammatory biomarkers (e.g., interleukin 6), as well as pro-inflammatory cells (e.g., $CD14^+$ and $CD16^+$ T lymphocytes) (Carracedo et al., 2006; Panichi et al., 2008). There is a correlation between FGF23 and left ventricular hypertrophy/cardiovascular disease events (Scialla & Wolf, 2014), particularly in patients with congestive heart failure concomitant with stages 2 to 4 chronic kidney disease (Seiler et al., 2014). This implies a possible correlation between HDF reduction and decreased mortality rates from coronary disease in ESKD.

It remains unclear whether HDF is beneficial in managing anemia. HDF was shown to be able to reduce the dosage of erythropoiesis-stimulating agents (ESA) (Panichi et al., 2011, 2015). This may be attributable to a combination of the enhanced clearance of middle-sized uremic toxins (erythropoietic inhibitor substances) and the use of better-quality water and dialysate, leading to reduced levels of inflammation (Panichi et al., 2011, 2015). Nonetheless, HDF did not show any effect on ESA resistance based on the results of the CONTRAST study (van der Weerd et al., 2014) and a meta-analysis (Susantitaphong et al., 2013). Three contemporary RCTs (ESHOL, CONTRAST, and Turkish OL-HDF) that compared online HDF and HD reported variations in ESA responsiveness that may be due to differences in anemia management protocols, such as the type of ESA used and the routes of administration rather than the efficiency of online HDF alone (Rosati et al., 2018).

HDF caused a significant decrease in the incidence of intradialytic hypotension compared to conventional HD (Locatelli et al., 2010; Lornoy et al., 2006; Maduell et al., 2013). This may be due to a negative thermal balance (secondary to infusing a relatively cooler substitution fluid), the removal of vasodilation mediators, and/or a mildly positive sodium mass balance caused by the generation of hyponatremic ultrafiltrate (i.e., Gibbs-Donnan effect[1]) (van der Sande et al., 2001).

A recent prospective study found that high-dose HDF increased protein intake, reduced inflammation, and preserved muscle mass compared to high-flux HD (Molina et al., 2018). The authors postulated that HDF plays a beneficial role in preventing protein-energy wastage. In this study, high-dose HDF treatment group consisted of patients who underwent post-dilution online HDF treatment three times a week using a high-flux FX-100 dialyzer (Fresenius Medical Care, Bad Homburg, Germany; Helixone membrane; 2.2 m2 surface area; 73 mL/h/mmHg ultrafiltration coefficient). The treatment approach consisted of a minimum target dialysis dose (Kt/V_{urea}) of greater than or equal to 1.2 over three to six hours (Molina et al.).

Influence of Online HDF on Mortality and Other Outcomes

The Dialysis Outcomes and Practice Patterns Study (DOPPS) found that patients receiving high-volume HDF (15 to 25 L volume of substitution fluid per session) had mortality rates that were 35% below the rate of those who received low-flux HD. In comparison, low-volume HDF (less than 15 L per session) with high-flux HDF provided statistically insignificant results (Canaud et al., 2006). A subsequent examination of the DOPPS data revealed no associations between HDF and lower mortality rates (Locatelli et al., 2018).

The four aforementioned contemporary RCTs (Ok et al., 2013; Grooteman et al., 2012; Maduell et al., 2013; Morena et al., 2017) were influenced by the findings of the DOPPS studies. The primary analysis did not show any improvements in either cardiovascular or overall mortality, but later analyses of both outcomes demonstrated that patients who were administered high convection volumes (greater than 22 L per session) experienced more positive outcomes (Ok et al., 2013; Grooteman et al., 2012]). As much as 50 to 66% of the patient cohort in the CONTRAST study failed to reach the intended convection volume, which may be regarded as a flaw of this study (Penne et al., 2009). Researchers in the CONTRAST study stated that following targeted policy introduction and training for nurses, more than 80% of patients reached the targeted convection volume (greater than or equal to 22 L per session) (Chapdelaine et al., 2014; de Roij van Zuijdewijn et al., 2017), suggesting that below target convection volumes were secondary to inadequacies in clinical practice rather than a limitation of the HDF.

In the third study subjected to primary analysis (ESHOL), with a median convection volume of between 22.9 L and 23.9 L, HDF-treated patients were 30% less likely to have either cardiovascular or all-cause mortality than patients receiving high-flux HD (Maduell et al., 2013). This study also found that patients receiving HDF had a 61% reduction in the risk of mortality from stroke (hazard ratio [HR], 0.39; 95% confidence interval [95% CI], 0.16–0.93) and a 55% reduction in the risk of mortality from infections (HR, 0.45; 95% CI, 0.21–0.96) compared to patients who received HD (Maduell et al., 2013).

Adverse reactions to HDF were analyzed in the FRENCHIE study, which assessed patients aged 65 years or over for self-report outcomes and diabetic tolerance levels (Morena et al., 2017). Primary analysis indicated

1 Hypotension during dialysis has been associated with sodium ion (Na^+) maldistribution. Typically, electrolytes reach equilibrium by diffusion through a dialysis membrane; however, the ion equilibrium collapses if a non-diffusible anion (such as albumin) is located extracellularly. This results in a reduction in the diffusibility of Na^+ as a cation, which leads to a difference in the distribution of Na^+ across the dialysis membranes. This phenomenon is known as the Gibbs-Donnan effect. When online HDF is performed, a significant amount of ultrafiltration takes place through the dialysis membrane, and because of the increase of the albumin concentration on the blood side of the membrane, a decrease in the movement of Na^+ toward the dialysate side occurs. This results in decrease in Na^+ removal and the maintenance of blood pressure (Kawanishi, 2018).

that patients who underwent HDF (84%) and patients receiving high-flux HD (85%) had almost identical risks of experiencing at least one adverse reaction. The secondary analysis found that the patients treated with HDF were significantly less likely to experience muscle cramps or intradialytic symptomatic hypotension. No difference was noted in terms of mortality, morbidity, or patient-reported quality of life (Morena et al., 2017).

There is significant debate regarding the level of convection volume that patients should receive. The CONTRAST study aimed to deliver 24 L of convection volume over a four-hour period (median volume of 19.8 L) (Grooteman et al., 2012). Subsequent analysis revealed that one-third of patients receiving the greatest convection volume (above 21.95 L) had significantly better survival rates. The Turkish OL-HDF study aimed at a minimum substitution fluid volume of 15 L (median volume of 17.2 L) (Ok et al., 2013). Subsequent analysis showed that convection volumes above 19.9 L (2.5 L net ultrafiltration with 17.4 L substitution fluid volume) were associated with improved survival rates. These outcomes were supported by subsequent analysis in the ESHOL study in which patients who received high-flux HD had worse survival rates than those who received HDF over 23.1 L per session (Maduell et al., 2013).

Analyses of all four European RCTs mentioned above supports the theory that positive patient outcomes may depend on convection volume (Davenport et al., 2016; Peters et al., 2016). In this aggregated cohort with a median follow-up of 2.5 years, 769 of 2,793 patients died (28%), of whom 292 (10%) were from cardiovascular causes. Patients receiving HDF were allocated into three groups depending on the convection volume they received; then the mortality rates from all causes, specifically from cardiovascular causes, were compared to those of patients who were treated with HD using hazard ratios derived from Cox proportional hazard regression models (Davenport et al., 2016; Peters et al., 2016). The initial analysis showed that one-third of the patients receiving the highest convection volumes had relatively lower risks of mortality (Davenport et al., 2016). Relative risks for this subset were not as significant when there was no standardized convection volume applied or when the convection volume was normalized to body surface area/total body water (not standardized: hazard ratio, 0.66; 95% confidence interval [CI], 0.52–0.83; standardized to body surface area: hazard ratio, 0.71; 95% CI, 0.57–0.90; and standardized to the total body area: hazard ratio, 0.71; 95% CI, 0.572–0.89). No associated reduction developed when the volume was normalized to body mass index or body weight (Davenport et al., 2016). These findings were confirmed by a secondary analysis that showed that online HDF reduced the relative risks of cardiovascular mortality by 23% and all-cause mortality by 14% when compared to HD (Peters et al., 2016). Differential effects among predetermined subgroups were not found, and the maximum positive outcomes were accrued to patients who were administered the highest convection volumes (greater than 23 L or 26 L/1.73 m^2 body surface area per treatment).

Future Prospects for Clinical Application and Research Recommendations

HDF is widely practiced across Europe and is increasingly accepted in Japan. In the United States, the technique is less commonly used, although this could change soon (Blankestijn, 2013; Ward et al., 2018). This review offers one central question: Why is there no robust evidence to suggest that survival rates for patients receiving HDF are superior to those receiving high-flux HD? Several theories may explain this situation. First, most subjects included in these studies have multiple comorbidities, rendering it problematic to demonstrate the influence of treatment on survival rates. Second, dialyzers have become much more efficient recently. New filter designs provide greater levels of back-filtration, reducing the disparity in convective volumes in comparison to those of HDF. A carefully constructed clinical trial should be undertaken to study the influence of a variety of infusion volumes on patients' outcomes as provided via high-flux HD, and high- and moderate-convection volumes in HDF. Further investigation of the better survival rates for patients receiving HDF in comparison to those receiving high-flux HD could be undertaken through the verification of the ideal convective level for various types of patients, grouped by specific clinically relevant variables. Currently, limited data exist related to the influence of relatively intense online HDF (i.e., more than three times per week) on clinical outcomes.

Vanholder et al. (2014) argued that the more expensive methods of treatment should only be considered if there was clear evidence to support their cost-utility in terms of the treatment cost to treatment outcome ratio. They also proposed that quality of life (QoL) should be considered. Furthermore, following the publication of a study by Canaud et al. (2006), there has been a growing body of evidence to support the view that the effectiveness of HDF treatment is positively correlated with the amount of the convection volume used. This has resulted in a propensity to utilize higher HDF convection volumes than those used in earlier cost analyses. Consequently, future research should assess cost-effectiveness to have a better comprehension of the effect of HDF on QoL and survival rates, and whether these benefits can warrant the potentially higher costs of this procedure justifying the economic feasibility of this treatment modality. Ramponi et al. (2016) found that HDF represented a cost-effective means of treating dialysis patients in comparison to high-flux-HD, more so in patients aged less than 60 years, regardless of diabetes status or gender. Nonetheless, the estimates employed in this study were primarily drawn from a meta-analysis that involved a follow-up period of two to three years. Longer running studies would be preferable. This is particularly true in the treatment of chronic disorders in which the implementation of an intervention to treat middle-aged patients could have significant implications in terms of cost throughout their lifetimes (Kobelt et al., 2003). Furthermore, any potential savings that occur due to a decrease in the cost of hospitalization and ancillary pharmacological therapy were not taken into consideration within the analysis. A more

complete assessment via an RCT is needed to incorporate additional cost dimensions, such as pharmaceuticals, hospitalizations, prevention of long-term dialysis-related complications, and transplantation access.

IMPLICATIONS FOR CLINICAL PRACTICE

As online HDF becomes increasingly common in European practice and has the potential to gain traction in the United States, there is a need for dedicated dialysis nurses who can monitor the outcomes of this form of RRT on patients. To achieve this, clinical evidence regarding patient outcomes must be aggregated and presented to dialysis nurses.

This paper has revealed several issues that are important to the practice of dialysis nurses. Regarding the removal of solutes, online HDF offers a superior level of removal of β2-microglobulin in comparison to HD. Although still controversial, few studies have demonstrated that HDF generally removes 15 to 20% more phosphate levels than high-flux HD. In comparison to high-flux HD, high-dosage online HDF is believed to be superior in terms of preserving muscle mass, increasing protein intake, and reducing inflammation, which suggests that online HDF may be useful in the prevention of protein-energy wastage. Online HDF was associated with a reduction in relative mortality risks (both cardiovascular and all causes) in patients receiving higher convection volumes, regardless of the anthropometric standardizing factor employed. Patients who received the highest delivered convection volume had the greatest benefits (greater than 23 L/session or 25.7 L/1.73 m^2 body surface area). Convection volume in online HDF may be a key contributor to patient survival. This aligns with the current understanding of uremic toxicity and the process through which dialysis therapy is used to detoxify blood.

To assess the efficacy and possible clinical advantages of online HDF, it seems reasonable to employ a quantifying indicator for convective clearance. The overall volume of ultrafiltration attained in one session of HDF, as adjusted to a post-dilution mode, is a simple indicator of convective components that have clinical relevance. A suggested alternative to this is to undertake a more precise assessment of the biological effect by measuring biomarkers to reflect the convective action of HDF. Among uremic toxins, β2-microglobulin appears to be a middle-molecule uremic toxin that is clinically relevant and significantly influences both the mortality and morbidity of patients with ESKD, and thus would be a useful biomarker.

CONCLUSION

Although several advances have been made in both technology and medicine over the past three decades, the morbidity and mortality rates of patients on dialysis remain extremely high. Convective treatment, such as HDF, is now well accepted. HDF produces fresh pure dialysate online that is advantageous clinically and removes more uremic retention solutes compared to standard high-flux HD. Most contemporary RCTs indicate that patients have better survival when treated with online HDF than with high-flux HD, provided that a sufficiently high convection volume is achieved. HDF is also associated with improved clinical outcomes such as a reduction in intradialytic hypotension.

REFERENCES

Blankestijn, P. J. (2013). Has the time now come to more widely accept hemodiafiltration in the United States? *Journal of the American Society of Nephrology*, *24*(3), 332–334. https://doi.org/10.1681/ASN.2013010063

Canaud, B., Bragg-Gresham, J. L., Marshall, M. R., Desmeules, S., Gillespie, B. W., Depner, T., Klassen, P., & Port, F. K. (2006). Mortality risk for patients receiving hemodiafiltration versus hemodialysis: European results from the DOPPS. *Kidney International*, *69*(11), 2087–2093. https://doi.org/10.1038/sj.ki.5000447

Canaud, B., Köhler, K., Sichart, J. M., & Möller, S. (2020). Global prevalent use, trends and practices in haemodiafiltration. *Nephrology Dialysis Transplantation*, *35*(3), 398-407. https://doi.org/10.1093/ndt/gfz005

Canaud, B., Vienken, J., Ash, S., Ward, R. A., & Kidney Health Initiative HDF Workgroup (2018). Hemodiafiltration to address unmet medical needs ESKD patients. *Clinical Journal of the American Society of Nephrology*, *13*(9), 1435–1443. https://doi.org/10.2215/CJN.12631117.

Carracedo, J., Merino, A., Nogueras, S., Carretero, D., Berdud, I., Ramírez, R., Tetta, C., Rodríguez, M., Martín-Malo, A., & Aljama, P. (2006). On-line hemodiafiltration reduces the proinflammatory CD14+CD16+ monocyte-derived dendritic cells: A prospective, crossover study. *Journal of the American Society of Nephrology*, *17*(8), 2315–2321. https://doi.org/10.1681/ASN.2006020105

Chapdelaine, I., Mostovaya, I. M., Blankestijn, P. J., Bots, M. L., van den Dorpel, M. A., Lévesque, R., Nubé, M. J., ter Wee, P. M., Grooteman, M. P. C., & CONTRAST Investigators. (2014). Treatment policy rather than patient characteristics determines convection volume in online post-dilution hemodiafiltration. *Blood Purification*, *37*(3), 229–237. https://doi.org/10.1159/000362108

Clark, W. R., & Winchester, J. F. (2003). Middle molecules and small-molecular-weight proteins in ESRD: properties and strategies for their removal. *Advances in Renal Replacement Therapy*, *10*(4), 270–278. https://doi.org/10.1053/j.arrt.2003.11.004

Cornelis, T., van der Sande, F. M., Eloot, S., Cardinaels, E., Bekers, O., Damoiseaux, J., Leunissen, K. M., & Kooman, J. P. (2014). Acute hemodynamic response and uremic toxin removal in conventional and extended hemodialysis and hemodiafiltration: A randomized crossover study. *American Journal of Kidney Diseases*, *64*(2), 247–256. https://doi.org/10.1053/j.ajkd.2014.02.016

Davenport, A., Peters, S. A., Bots, M. L., Canaud, B., Grooteman, M. P. C., Asci, G., Locatelli, F., Maduell, F., Morena, M., Nubé, M. J., Ok, E., Torres, F., Woodward, M., Blankestijn, P. J., & HDF Pooling Project Investigators. (2016). Higher convection volume exchange with online hemodiafiltration is associated with survival advantage for dialysis patients: The effect of adjustment for body size. *Kidney International*, *89*(1), 193–199. https://doi.org/10.1038/ki.2015.264

de Roij van Zuijdewijn, C., Chapdelaine, I., Nubé, M. J., Blankestijn, P. J., Bots, M. L., Konings, C. J., Kremer Hovinga, T. K., Molenaar, F. M., van der Weerd, N. C., & Grooteman,

M. (2017). Achieving high convection volumes in postdilution online hemodiafiltration: A prospective multicenter study. *Clinical Kidney Journal*, *10*(6), 804–812. https://doi.org/10.1093/ckj/sfw140

Farrell, P. C., & Babb, A. L. (1973). Estimation of the permeability of cellulosic membranes from solute dimensions and diffusivities. *Journal of Biomedical Materials Research,* 7(4), 275–300. https://doi.org/10.1002/jbm.820070403

Fischbach, M., Fothergill, H., Zaloszyc, A., & Seuge, L. (2012). Hemodiafiltration: the addition of convective flow to hemodialysis. *Pediatric Nephrology*, *27*(3), 351–356. https://doi.org/10.1007/s00467-011-1779-z

Grooteman, M. P., van den Dorpel, M. A., Bots, M. L., Penne, E. L., van der Weerd, N. C., Mazairac, A. H. A., den Hoedt, C. H., van der Tweel, I., Lévesque, R., Nubé, M. J., ter Wee, P. M., Blankestijn, P. J., & CONTRAST Investigators. (2012). Effect of online hemodiafiltration on all-cause mortality and cardiovascular outcomes. *Journal of the American Society of Nephrology*, *23*(6), 1087–1096. https://doi.org/10.1681/ASN.2011121140

Hazelbag, C. M., Peters, S., Blankestijn, P. J., Bots, M. L., Canaud, B., Davenport, A., Grooteman, M. P. C., Kircelli, F., Locatelli, F., Maduell, F., Morena, M., Nubé, M. J., Ok, E., Torres, F., Hoes, A. W., Groenwold, R. H. H., & HDF Pooling Project Investigators. (2017). The importance of considering competing treatment affecting prognosis in the evaluation of therapy in trials: The example of renal transplantation in hemodialysis trials. *Nephrology Dialysis Transplantation*, *32*, ii31–ii39. https://doi.org/10.1093/ndt/gfw458

Imamović, G., Hrvačević, R., Kapun, S., Marcelli, D., Bayh, I., Grassmann, A., Scatizzi, L., Maslovarić, J., & Canaud, B. (2014). Survival of incident patients on high-volume online hemodiafiltration compared to low-volume online hemodiafiltration and high-flux hemodialysis. *International Urology and Nephrology*, *46*(6), 1191–1200. https://doi.org/10.1007/s11255-013-0526-8

Kawanishi, H. (2018). Is there enough evidence to prove that hemodiafiltrationis superior? *Blood Purification*, *46*(1), 3-6. https://doi.org/10.1159/000487917

Kim, Y. W., & Park, S. (2016). Confronting practical problems for initiation of on-line hemodiafiltration therapy. *Electrolyte & Blood Pressure*, *14*(1), 1–4. https://doi.org/10.5049/EBP.2016.14.1.1

Kobelt, G., Jönsson, L., Young, A., & Eberhardt, K. (2003). The cost-effectiveness of infliximab (Remicade) in the treatment of rheumatoid arthritis in Sweden and the United Kingdom based on the ATTRACT study. *Rheumatology*, *42*(2), 326–335. https://doi.org/10.1093/rheumatology/keg107

Lin, C. L., Huang, C. C., Yu, C. C., Yang, H. Y., Chuang, F. R., & Yang, C. W. (2003). Reduction of advanced glycation end product levels by on-line hemodiafiltration in long-term hemodialysis patients. *American Journal of Kidney Diseases*, *42*(3), 524–531. https://doi.org/10.1016/s0272-6386(03)00747-9

Locatelli, F., Altieri, P., Andrulli, S., Bolasco, P., Sau, G., Pedrini, L. A., Basile, C., David, S., Feriani, M., Montagna, G., Di Iorio, B. R., Memoli, B., Cravero, R., Battaglia, G., & Zoccali, C. (2010). Hemofiltration and hemodiafiltration reduce intradialytic hypotension in ESRD. *Journal of the American Society of Nephrology*, *21*(10), 1798–1807. https://doi.org/10.1681/ASN.2010030280

Locatelli, F., Karaboyas, A., Pisoni, R. L., Robinson, B. M., Fort, J., Vanholder, R., Rayner, H. C., Kleophas, W., Jacobson, S. H., Combe, C., Port, F. K., & Tentori, F. (2018). Mortality risk in patients on hemodiafiltration versus hemodialysis: A 'real-world' comparison from the DOPPS. *Nephrology Dialysis Transplantation*, *33*(4), 683–689. https://doi.org/10.1093/ndt/gfx277

Locatelli, F., Marcelli, D., Conte, F., Limido, A., Malberti, F., & Spotti, D. (1999). Comparison of mortality in ESRD patients on convective and diffusive extracorporeal treatments. The Registro Lombardo Dialisi E Trapianto. *Kidney International*, *55*(1), 286–293. https://doi.org/10.1046/j.1523-1755.1999.00236.x

Lornoy, W., De Meester, J., Becaus, I., Billiouw, J. M., Van Malderen, P. A., & Van Pottelberge, M. (2006). Impact of convective flow on phosphorus removal in maintenance hemodialysis patients. *Journal of Renal Nutrition*, *16*(1), 47–53. https://doi.org/10.1053/j.jrn.2005.10.008

Maduell, F., Moreso, F., Pons, M., Ramos, R., Mora-Macià, J., Carreras, J., Soler, J., Torres, F., Campistol, J. M., Martinez-Castelao, A., & ESHOL Study Group (2013). High-efficiency postdilution online hemodiafiltration reduces all-cause mortality in hemodialysis patients. *Journal of the American Society of Nephrology*, *24*(3), 487–497. https://doi.org/10.1681/ASN.2012080875

Mandolfo, S., Borlandelli, S., & Imbasciati, E. (2006). Leptin and beta2-microglobulin kinetics with three different dialysis modalities. *The International Journal of Artificial Organs*, *29*(10), 949–955. https://doi.org/10.1177/039139880602901005

Masakane, I., Nakai, S., Ogata, S., Kimata, N., Hanafusa, N., Hamano, T., Wakai, K., Wada, A., & Nitta, K. (2017). Annual Dialysis Data Report 2014, JSDT Renal Data Registry (JRDR). *Renal Replacement Therapy*, *3*(1), 1–43. https://doi.org/10.1186/s41100-017-0097-8

Molina, P., Vizcaíno, B., Molina, M. D., Beltrán, S., González-Moya, M., Mora, A., Castro-Alonso, C., Kanter, J., Ávila, A. I., Górriz, J. L., Estañ, N., Pallardó, L. M., Fouque, D., & Carrero, J. J. (2018). The effect of high-volume online haemodiafiltration on nutritional status and body composition: The ProtEin Stores prEservaTion (PESET) study. *Nephrology Dialysis Transplantation*, *33*(7), 1223–1235. https://doi.org/10.1093/ndt/gfx342

Morena, M., Jaussent, A., Chalabi, L., Leray-Moragues, H., Chenine, L., Debure, A., Thibaudin, D., Azzouz, L., Patrier, L., Maurice, F., Nicoud, P., Durand, C., Seigneuric, B., Dupuy, A.-M., Picot, M.-C., Cristol, J.-P., Canaud, B., & FRENCHIE Study Investigators (2017). Treatment tolerance and patient-reported outcomes favor online hemodiafiltration compared to high-flux hemodialysis in the elderly. *Kidney International*, *91*(6), 1495–1509. https://doi.org/10.1016/j.kint.2017.01.013

Nakai, S., Iseki, K., Tabei, K., Kubo, K., Masakane, I., Fushimi, K., Kikuchi, K., Shinzato, T., Sanaka, T., & Akiba, T. (2001). Outcomes of hemodiafiltration based on Japanese dialysis patient registry. *American Journal of Kidney Diseases*, *38*, S212–S216. https://doi.org/10.1053/ajkd.2001.27449

National Guideline Centre (2018). Renal replacement therapy and conservative management. National Institute for Health and Care Excellence (NICE Guideline, No. 107). https://www.ncbi.nlm.nih.gov/books/NBK542264/

Ok, E., Asci, G., Toz, H., Ok, E. S., Kircelli, F., Yilmaz, M., Ozkahya, M., & Turkish Online Haemodiafiltration Study (2013). Mortality and cardiovascular events in online haemodiafiltration (OL-HDF) compared with high-flux dialysis: Results from the Turkish OL-HDF Study. *Nephrology Dialysis Transplantation*, *28*(1), 192–202. https://doi.org/10.1093/ndt/gfs407

Panichi, V., Rizza, G. M., Paoletti, S., Bigazzi, R., Aloisi, M., Barsotti, G., Rindi, P., Donati, G., Antonelli, A., Panicucci, E., Tripepi, G., Tetta, C., Palla, R., & RISCAVID Study Group (2008). Chronic inflammation and mortality in haemodialysis: Effect of different renal replacement therapies.

Results from the RISCAVID study. *Nephrology, Dialysis, Transplantation*, *23*(7), 2337–2343. https://doi.org/10.1093/ndt/gfm951

Panichi, V., Rosati, A., Bigazzi, R., Paoletti, S., Mantuano, E., Beati, S., Marchetti, V., Bernabini, G., Grazi, G., Rizza, G. M., Migliori, M., Giusti, R., Lippi, A., Casani, A., Barsotti, G., Tetta, C., & RISCAVID Study Group (2011). Anaemia and resistance to erythropoiesis-stimulating agents as prognostic factors in haemodialysis patients: Results from the RISCAVID study. *Nephrology Dialysis Transplantation*, *26*(8), 2641–2648. https://doi.org/10.1093/ndt/gfq802

Panichi, V., Scatena, A., Rosati, A., Giusti, R., Ferro, G., Malagnino, E., Capitanini, A., Piluso, A., Conti, P., Bernabini, G., Migliori, M., Caiani, D., Tetta, C., Casani, A., Betti, G., & Pizzarelli, F. (2015). High-volume online haemodiafiltration improves erythropoiesis-stimulating agent (ESA) resistance in comparison with low-flux bicarbonate dialysis: Results of the REDERT study. *Nephrology Dialysis Transplantation*, *30*(4), 682–689. https://doi.org/10.1093/ndt/gfq802

Patrier, L., Dupuy, A. M., Granger Vallée, A., Chalabi, L., Morena, M., Canaud, B., & Cristol, J. P. (2013). FGF-23 removal is improved by on-line high-efficiency hemodiafiltration compared to conventional high flux hemodialysis. *Journal of Nephrology*, *26*(2), 342–349. https://doi.org/10.5301/jn.5000150

Penne, E. L., van der Weerd, N. C., Bots, M. L., van den Dorpel, M. A., Grooteman, M. P. C., Lévesque, R., Nubé, M. J., Ter Wee, P. M., Blankestijn, P. J., &CONTRAST Investigators (2009). Patient- and treatment-related determinants of convective volume in post-dilution haemodiafiltration in clinical practice. *Nephrology Dialysis Transplantation*, *24*(11), 3493–3499. https://doi.org/10.1093/ndt/gfp265

Penne, E. L., van der Weerd, N. C., van den Dorpel, M. A., Grooteman, M. P. C., Lévesque, R., Nubé, M. J., Bots, M. L., Blankestijn, P. J., ter Wee, P. M., & CONTRAST Investigators (2010). Short-term effects of online hemodiafiltration on phosphate control: A result from the randomized controlled Convective Transport Study (CONTRAST). *American Journal of Kidney Diseases*, *55*(1), 77–87. https://doi.org/10.1053/j.ajkd.2009.09.023

Peters, S. A., Bots, M. L., Canaud, B., Davenport, A., Grooteman, M. P. C., Kircelli, F., Locatelli, F., Maduell, F., Morena, M., Nubé, M. J., Ok, E., Torres, F., Woodward, M., Blankestijn, P. J., & HDF Pooling Project Investigators (2016). Haemodiafiltration and mortality in end-stage kidney disease patients: A pooled individual participant data analysis from four randomized controlled trials. *Nephrology Dialysis Transplantation*, *31*(6), 978–984. https://doi.org/10.1093/ndt/gfv349

Ramponi, F., Ronco, C., Mason, G., Rettore, E., Marcelli, D., Martino, F., Neri, M., Martin-Malo, A., Canaud, B., & Locatelli, F. (2016). Cost-effectiveness analysis of online hemodiafiltration versus high-flux hemodialysis. *ClinicoEconomics and Outcomes Research*, *8*, 531–540. https://doi.org/10.2147/CEOR.S109649

Rosati, A., Ravaglia, F., & Panichi, V. (2018). Improving erythropoiesis stimulating agent hyporesponsiveness in hemodialysis patients: The role of hepcidin and hemodiafiltration online. *Blood Purification*, *45*, 139–146. https://doi.org/10.1159/000485314

Scialla, J. J., & Wolf, M. (2014). Roles of phosphate and fibroblast growth factor 23 in cardiovascular disease. *Nature Reviews Nephrology*, *10*(5), 268–278. https://doi.org/10.1038/nrneph.2014.49

Seiler, S., Rogacev, K. S., Roth, H. J., Shafein, P., Emrich, I., Neuhaus, S., Floege, J., Fliser, D., & Heine, G. H. (2014). Associations of FGF-23 and sKlotho with cardiovascular outcomes among patients with CKD stages 2–4. *Clinical Journal of the American Society of Nephrology*, *9*(6), 1049–1058. https://doi.org/10.2215/CJN.07870713

Siriopol, D., Canaud, B., Stuard, S., Mircescu, G., Nistor, I., & Covic, A. (2015). New insights into the effect of haemodiafiltration on mortality: The Romanian experience. *Nephrology Dialysis Transplantation*, *30*(2), 294–301. https://doi.org/10.1093/ndt/gfu347

Susantitaphong, P., Siribamrungwong, M., & Jaber, B. L. (2013). Convective therapies versus low-flux hemodialysis for chronic kidney failure: A meta-analysis of randomized controlled trials. *Nephrology Dialysis Transplantation*, *28*(11), 2859–2874. https://doi.org/10.1093/ndt/gft396

van der Sande, F. M., Kooman, J. P., Konings, C. J., & Leunissen, K. M. L. (2001). Thermal effects and blood pressure response during postdilution hemodiafiltration and hemodialysis: The effect of amount of replacement fluid and dialysate temperature. *Journal of the American Society of Nephrology*, *12*(9), 1916–1920.

van der Weerd, N. C., Den Hoedt, C. H., Blankestijn, P. J., Bots, M. L., van den Dorpel, M. A., Lévesque, R., Mazairac, A. H. A., Nubé, M. J., Penne, E. L., ter Wee, P. M., Grooteman, M. P. C., & CONTRAST Investigators. (2014). Resistance to erythropoiesis stimulating agents in patients treated with online hemodiafiltration and ultrapure low-flux hemodialysis: Results from a randomized controlled trial (CONTRAST). *PloS One*, *9*(4), e94434. https://doi.org/10.1371/journal.pone.0094434

Vanholder, R., Van Biesen, W., & Lameire, N. (2014). Renal replacement therapy: how can we contain the costs? *Lancet*, *383*(9931), 1783–1785. https://doi.org/10.1016/S0140-6736(14)60721-2

Ward, R. A., Schmidt, B., Hullin, J., Hillebrand, G. F., & Samtleben, W. (2000). A comparison of on-line hemodiafiltration and high-flux hemodialysis: A prospective clinical study. *Journal of the American Society of Nephrology*, *11*(12), 2344–2350.

Ward, R. A., Vienken, J., Silverstein, D. M., Ash, S., Canaud, B., & Kidney Health Initiative HDF Workgroup (2018). Regulatory considerations for hemodiafiltration in the United States. *Clinical Journal of the American Society of Nephrology*, *13*(9), 1444–1449. https://doi.org/10.2215/CJN.12641117

Wendt, R. P., Klein, E., Bresler, E. H., Holland, F. F., Serino, R. M., & Villa, H. (1979). Sieving properties of hemodialysis membranes. *Journal of Membrane Science, 5,* 23–49. https://doi.org/10.1016/S0376-7388(00)80436-6

CONTINUING EDUCATION SERIES

CONTACT HOUR: 2.0 HRS

'Phos'ing over phosphorus: A primer on updates in phosphate binders

By Franky Liu and Maeghan Pemas

ABSTRACT

Addressing serum phosphorous in patients with ESRD remains a challenging balancing act of appropriate pharmacological treatment. Multiple agents are available for binding dietary phosphates in attempts to maintain a harmony of serum phosphorous and other important factors in CKD-MBD, such as calcium and parathyroid hormone. In this brief primer, we aim to compare, discuss, and share clinical experience of different phosphate binders, old and new, and to discuss what research has yet to address in current clinical practice. Guidelines and best practices in CKD-MBD are also briefly reviewed. This primer concludes with reviewing a novel iron-based phosphate binder, succroferic oxyhydroxide (SO), and its perceived current place in therapy.

"Serum phosphorus" or "serum phosphate"—regardless of which clinical synonym one uses, practitioners arguably spend countless hours educating patients on the clinical significance and management of chronic kidney disease-associated mineral and bone disorders (CKD-MBD). Perhaps this is rightfully so – renal osteodystrophy is associated with increased bone fracture rates, with hip fractures in particular leading to significant morbidity and mortality (Kidney Disease: Improving Global Outcomes (KDIGO) CKD-MBD Update Work Group (2017). In fact, one study suggests that every 0.33 mmol/L increase in serum phosphorus is correlated with an 18% increase in mortality (Palmer et al., 2011). Experts have also suggested correlations with cardiovascular disease, possibly due to increased vascular and valvular calcification, although evidence of these associations is still uncertain (Adeney et al., 2009).

AUTHOR NOTE

Franky Liu, BScPhm, MSc, RPh, Clinical Pharmacist – Nephrology, Halton Healthcare Services, Oakville, ON; Maeghan Pemas, BScPhm, RPh, Clinical Pharmacist – Nephrology, Halton Healthcare Services, Oakville, ON

Correspondence concerning this article should be forwarded to: Franky Liu, Halton Healthcare Services, 3001 Hospital Gate, Oakville, ON L6M 0L8.
Tel: (905) 845-2571 ext 6521. Fax: (905) 338-4498.
*Email: **fliu@haltonhealthcare.com***

At its core, osteocytes undergo a homeostatic cycle of bone resorption and ossification, collectively referred to as bone turnover. Disharmony of this cycle occurs with elevated serum phosphorous, which causes nodular hyperplasia secondarily from cacophonic phosphorus stimulation of the parathyroid. This results in increased serum PTH, which cascades to abnormal bone formation, and ultimately to osteoporosis or osteopenia (Hruska et al., 2008).

The management of CKD-MBD, while at times laborious, is a crucial puzzle piece in the comprehensive care of patients with end-stage renal disease (ESRD). Its complexities usually call for "all hands on deck", often requiring the patient and their care team to make complex and drastic lifestyle changes, along with meticulous handling of dialysate bath concentrations.

WHAT ARE OUR NEPHROLOGY COLLEAGUES DOING NOW?

Nephrology health workers may look to the Kidney Disease Improving Global Outcomes (KDIGO) organization to guide treatment and management of the complexities that come with ESRD. In their 2017 update, KDIGO had recommended steering treatment based on serial assessments of phosphorus, calcium and PTH in concert, specifically lowering high serum phosphorous while maintaining calcium levels with an age-appropriate normal range (KDIGO Working Group, 2017). In particular, a retrospective observational study found an increased mortality risk with either hypocalcemia (less than 2.10 mmol/L) or hypercalcemia (greater than 2.75 mmol/L) over time. Contrarily, although there is an increased time-dependent mortality risk with low phosphorus (less than 1.13 mmol/L), mortality risk with high phosphorus (greater than 1.78 mmol/L) remains unclear (Floege et al., 2011).

Diligent case management therefore necessitates a multidisciplinary, multifactorial approach. Congruent with the KDIGO guidelines, dietary modifications, with particular consideration of dietary source of phosphates, act as one facet of care (Liu et al., 2013). That is, since not all phosphate sources are equal (i.e., inorganic phosphate sources from animal products and additives are generally more

bioavailable than vegetable sources), careful dietary assessments could supplant many hyperphosphatemia woes (Hruska et al., 2008). Current evidence on its efficacy is still uncertain, and it is believed that, over time, dietary modifications will unlikely serve as the sole treatment regimen for hyperphosphatemia. Pharmacotherapy is often required.

Calcium-Salt Phosphate Binders

Patients are often started on calcium-salt binders, such as calcium carbonate in flavoured chewable (such as Tums™) or regular tablets, as an inexpensive and readily accessible choice of therapy. These binders are activated by gastric acid, which then precipitates dietary phosphate into the gastrointestinal tract. Although ubiquitous and generally safe at low doses, calcium-based binder tablets are usually numerous and/or bulky, often perceived as "difficult pills to swallow" both literally and figuratively. Furthermore, these binders are not ideal in patients at risk of hypercalcemia; in fact, doses surpassing 2 g in a day have been associated with vascular calcification (Hutchison, 2009; KDIGO Working Group, 2017). Alternative non-calcium-based binders may be preferred in patients with high-normal to high serum calcium levels.

Polymeric Non-Calcium Phosphate Binders

Binders such as sevelamer hydrochloride (Renagel™) or sevelamer carbonate (Renvela™) tablets/lightly citrus-flavoured powders for oral suspension are calcium-free, evading hypercalcemia while offering a means of reducing dietary phosphate absorption. Sevelamer is a non-absorbable and fat-soluble synthetic polymer that, when activated by gastric acid, weakly complexes with dietary phosphate (Hutchison, 2009). This weaker interaction makes sevelamer less potent than calcium-salt binders, translating to a higher pill or liquid volume burden (Daugirdas et al., 2011); this, combined with its exorbitant cost, may be less accessible to patients without full drug insurance coverage. Other considerations include binding of fat-soluble vitamins when taken together, and risk of metabolic acidosis. Interestingly, because of its fat solubility, some studies have suggested that sevelamer may decrease LDL-C and total cholesterol, with some studies reporting up to 36% reduction; this may be congruent with associations with decreased risk of coronary and aortic calcification (Nikolov et al., 2006). Given the potential complexities in drug administration and potential high pill/volume burden, other solutions may be available to overcome these hurdles.

Other Metallic-Salt Phosphate Binders

Historically and perhaps more acutely, practitioners have used aluminum hydroxide as a phosphate binder. With approximately double the potency of calcium salts and non-reliance on gastric acidity, these could be effective in very short-term therapy in patients also with hypercalcemia (Daugirdas et al., 2011; Hutchison, 2009). However, there is no official safe dose or level of aluminum, with potential risk of fecal impaction and encephalopathy (KDIGO Working Group, 2017).

In contrast, lanthanum, which is similarly trivalent cationic as aluminum, seems to have an acceptable safety profile while binding dietary phosphate at the same potency. Because of this, patients usually require fewer tablets for a greater decrease in serum phosphorus than calcium-salt or polymeric binders (Daugirdas et al., 2011). Formulated as a carbonate in a tasteless chewable tablet (Fosrenol™), lanthanum readily forms insoluble salts with phosphate without acid, leading to less variability caused by gastric acidity. A near-infinitesimal amount does get absorbed, which seems to bind plasma proteins and eventually get excreted through bile; some long-term studies have suggested low levels associated with treatment in ESRD are not associated with any long-term toxicity (Hutchison, 2009). However, because it forms very insoluble salts when bound to phosphate, patients may experience constipation. This may rarely lead to bowel obstruction and colonic perforation, reinforcing its relative contraindication in history of bowel obstruction and decreased bowel peristalsis (Hutchison, 2009). Moreover, lanthanum, being a rare earth metal, is generally expensive, which may be inaccessible to patients not covered by an insurance plan, ineligible for product coverage, or both.

WHAT WERE THE GAPS IN RESEARCH AND THERAPY?

So far, research has suggested that there is some decrease in mortality with use of any phosphate binder, although at the time of this primer, no binder has demonstrated superiority over others. There is also clinical uncertainty if there is any benefit to combining non-calcium binders. One study suggests that combining lanthanum and sevelamer leads to serum phosphorus reductions similar to monotherapy with either agent. These findings raise questions about possible antagonistic pharmacodynamic interactions between binders (Senatore et al., 2011).

In clinical treatment, each therapy mentioned so far appears to have their own mix of pros and cons; practitioners may encounter patients with specific combinations of contraindications with compromises that become difficult to balance. To illustrate, a patient with diverticular disease and gastroparesis, simultaneously with swallowing issues (for which high pill burden or large liquid volumes are intolerable), hypercalcemia, and hyperphosphatemia absent of other confounders may be left without any good option. One would need to consider the risk of obstruction if deciding on lanthanum; risk of non-adherence or choking on sevelamer; risk of aluminum toxicity with aluminum hydroxide; or risk of fatal hypercalcemia with calcium carbonate. Therapies with a different mix of efficacy and safety considerations are needed to relieve this therapeutic "deadlock".

WHAT ABOUT IRON-BASED PHOSPHATE BINDERS?

As of recent, sucroferric oxyhydroxide (SO, Velphoro™) was the first iron-based phosphate binder officially approved for hyperphosphatemia in Canada. Supplied as flavoured chewable tablets containing 500 mg of elemental iron equivalent (or 2,500 mg of drug; dosages are usually expressed based on equivalent iron content), SO is an insoluble complex of sucrose and iron stabilized with starch that strongly binds with dietary phosphate (Vifor Fresenius Medical Care Renal, 2019).

Because this entire chemical complex is virtually insoluble in water, very little of its constituents (particularly iron) get absorbed. More specifically, pharmacokinetic studies

found only a median of 0.04% w/w of iron was actually absorbed after chronic dosing after 21 days; interestingly, however, healthy volunteers did absorb approximately 10 times more iron than the CKD group, possibly owing to the lower serum ferritin and/or compensatory hepcidin release that would otherwise impair oral iron absorption in patients with ESRD (Canadian Agency for Drugs and Technologies in Health [CADTH], 2019).

HOW DOES SUCROFERRIC OXYHYDROXIDE (SO) COMPARE TO OTHER BINDERS?

One extension of an open-label, multi-centred, active-controlled study showed non-inferiority to sevelamer at all points of its study for patients on hemodialysis(treatment difference in change from baseline phosphorus –0.04 [-0.12, 0.04], p = .293) (Floege et al., 2015; Vifor Fresenius Medical Care Renal, 2013). Patients were titrated from a similar baseline hyperphosphatemia over eight weeks, with either SO 1,000-3,000mg (two to six tablets daily) or sevelamer 2,400-14,400mg (three to 18 tablets daily). Participants were then monitored, with minor adjustments in dose based on tolerability over four weeks. The study was extended for 12 additional weeks with dose fine-tuning (CADTH, 2019; Vifor Fresenius Medical Care Renal, 2013, 2019). Another one-year open-label study showed similar results in patients on peritoneal dialysis (-0.6 mmol/L change from baseline phosphorous for both groups, p = .53) (Floege et al., 2017).

At a glance, it might appear that SO may require fewer tablets than sevelamer to elicit a similar response, although the translatable difference in average and median number of tablets from either group is unclear. Furthermore, formal quantitative dose conversions between SO and other binders has not yet been studied. Patients with disorders that affect gastric acid may respond differently by the binder chosen. SO and lanthanum, for instance, are unaffected by gastric acidity. However, patients with hypochlorhydria may respond inadequately to sevelamer or calcium-based binders (CADTH, 2019). Importantly, patient preference in therapy may also be a matter of taste. SO is strongly woodberry-flavoured and sweetened with neohesperidin to mask its metallic taste; despite this, some patients may still notice an unpleasant aftertaste (Vifor Fresenius Medical Care Renal, 2019). This contrasts to lanthanum carbonate and film-coated sevelamer tablets, both of which are virtually flavourless.

WHEN MIGHT SO BE AN ALTERNATIVE FOR PATIENTS?

SO is officially indicated for treating hyperphosphatemia in patients 18 years or older with ESRD on either peritoneal dialysis or hemodialysis. This iron-based binder might serve as an alternative when other binders are inadequate or intolerable, or when a patient also has hypercalcemia. Patients with hypochlorhydria that are refractory to other binders may respond better to SO (Vifor Fresenius Medical Care Renal, 2019); causes of hypochlorhydria could include specific pathologies, or concomitant therapy with high-dose proton-pump inhibitors or other acid reducers. In addition, SO may be preferred over lanthanum in patients with other gastrointestinal issues, such as history of bowel obstruction or chronic constipation (Hutchison, 2009).

WHEN SHOULD I *NOT* CONSIDER SO?

Although studies suggest that absorption is insignificant, monographs still list haemochromatosis or other iron accumulation disorders as contraindications. Patients with evidence of iron overload (e.g., excessively elevated serum ferritin or a transferrin saturation greater than 50%) should not be started on SO, and caution should be exercised if deciding to continue pre-existing therapy. Also, though no allergic reactions have yet been reported, patients allergic to any component of its formulation, such as maize or potato starch, or the drug itself should not take SO (Vifor Fresenius Medical Care Renal, 2019).

Practitioners should note that SO has not yet been studied in hepatic disease or patients with peritonitis (for which any iron treatment should be avoided). Clinical decisions to continue therapy require careful balance of risk and benefit (Vifor Fresenius Medical Care Renal, 2019).

Practitioners should also note that, particularly for patients who recover from dialysis or receive a transplant, SO has not been studied in CKD patients not on dialysis; continuing therapy would therefore be off-label.

WHAT SHOULD I MONITOR IF SO THERAPY IS INITIATED?

Similar to the usual management of CKD-MBD, serum calcium, phosphorous, and PTH should be monitored at least every one to three months, or more frequently if deemed necessary. Iron studies, ferritin, and transferrin saturation could be added if a patient has been historically responsive to oral iron therapy and/or is at imminent risk of iron overload (KDIGO Working Group, 2017). Of interesting note, although increased serum calcium from treatment seems unlikely, patients with hyper- or hypocalcemia were excluded from major studies with SO; response from these patients is uncertain at this time.

Patients will sometimes experience side effects upon starting, most of which are GI-related like diarrhea. These are usually self-limiting, and will resolve with time, and are minimal if SO is titrated weekly in 500 mg increments. Doses generally start at 500 mg three times daily with meals for most patients. Dark stools are also common since SO is not absorbed, although this will not interfere with fecal occult blood testing (FOBT) if a patient is due to repeat a test while on therapy (Vifor Fresenius Medical Care Renal, 2019).

In addition to its metallic aftertaste as mentioned, SO may also discolour teeth and mucous membranes to an orange-brown colour: this should be rinseable with water. Patients may hold the medication if the colour remains despite rinsing. So far it is uncertain if progressive use leads to irreversible staining, although literature from the manufacturer suggests this is likely benign (Vifor Fresenius Medical Care Renal, 2019).

Patients concomitantly on oral bisphosphonates, tetracyclines (including doxycycline), and levothyroxine/thyroid hormones, whether pre-existing or added in the future, should space administration away by at least one hour. These drug classes are potentially inactivated in the presence of divalent cations such as iron. However, these

interactions have not yet been proven outside of in vitro testing. Interestingly, however, in vitro testing showed no interaction with ciprofloxacin, although other fluroquinolones were not tested (Vifor Fresenius Medical Care Renal, 2019).

WHAT SHOULD WE KNOW ABOUT ACCESSIBILITY AND COVERAGE?

Based on recommendations by CADTH (2019), SO appears on provincial formularies as an exceptional access benefit. Clinical criteria indicated for coverage are similar to sevelamer and lanthanum, and will require case-by-case approval through specific provincial health ministries. Patients with private insurances should also have coverage for SO, but some may require prior authorization paperwork before reimbursement; pharmacists and social workers can facilitate arranging additional paperwork if required.

In the event that patients must pay out-of-pocket, SO averages approximately $416 monthly. This contrasts to sevelamer hydrochloride ($450), sevelamer carbonate ($286), lanthanum carbonate ($214), or calcium carbonate ($54) (CADTH, 2019). Practitioners should also be aware that sevelamer carbonate powder for oral suspension formulations may not be listed in some provincial exceptional access benefits.

WHAT ARE SOME QUESTIONS STILL LEFT UNANSWERED?

Although SO adds yet another tool to our arsenal for treating hyperphosphatemia, the relative potency of SO from other binders is not yet clear. Literature seems to suggest that SO has at least equal or less pill burden compared to sevelamer. Also unclear is the effect of SO and other non-calcium-based binders on all-cause mortality, and/or risk of vascular calcification. Some small-scale studies suggest that sevelamer exacerbates aortic calcification less frequently than calcium-based binders; further larger-scaled studies are needed (Block et al., 2005).

As we obtain more experience with the use of these various phosphate binders with time, we may learn more about post-marketing effects of SO, in addition to any ancillary benefits or risks not yet studied prior to approval. Nonetheless, SO may find further niche uses as we share more clinical experiences within our network of nephrology professionals. After all, we all collectively have a "bone to pick" with persistently elevated serum phosphorous levels; new and developing solutions will hopefully ease some common discussion points in patient care and bloodwork rounds.

REFERENCES

Adeney, K. L., Siscovick, D. S., Ix, J. H., Seliger, S. L., Shlipak, M. G., Jenny, N. S., & Kestenbaum, B. R. (2009). Association of serum phosphate with vascular and valvular calcification in moderate CKD. *Journal of the American Society of Nephrology*. https://doi.org/10.1681/ASN.2008040349

Block, G. A., Spiegel, D. M., Ehrlich, J., Mehta, R., Lindbergh, J., Dreisbach, A., & Raggi, P. (2005). Effects of sevelamer and calcium on coronary artery calcification in patients new to hemodialysis. *Kidney International*. https://doi.org/10.1111/j.1523-1755.2005.00600.x

Canadian Agency for Drugs and Technologies in Health. (2019). *Clinical review report: Velphoro*. CADTH. https://cadth.ca/sites/default/files/cdr/clinical/sr0571-velphoro-clinical-report.pdf

Daugirdas, J. T., Finn, W. F., Emmett, M., & Chertow, G. M. (2011). The Phosphate Binder Equivalent Dose. *Seminars in Dialysis*. https://doi.org/10.1111/j.1525-139X.2011.00849.x

Floege, J., Covic, A. C., Ketteler, M., Mann, J. F. E., Rastogi, A., Spinowitz, B., Chong, E. M. F., Gaillard, S., Lisk, L. J., & Sprague, S. M. (2015). Long-term effects of the iron-based phosphate binder, sucroferric oxyhydroxide, in dialysis patients. *Nephrology Dialysis Transplantation*. https://doi.org/10.1093/ndt/gfv006

Floege, J., Covic, A. C., Ketteler, M., Mann, J., Rastogi, A., Spinowitz, B., Rakov, V., Lisk, L. J., & Sprague, S. M. (2017). One-year efficacy and safety of the iron-based phosphate binder sucroferric oxyhydroxide in patients on peritoneal dialysis. *Nephrology Dialysis Transplantation*. https://doi.org/10.1093/ndt/gfw460

Floege, J., Kim, J., Ireland, E., Chazot, C., Drueke, T., De Francisco, A., Kronenberg, F., Marcelli, D., Passlick-Deetjen, J., Schernthaner, G., Fouqueray, B., & Wheeler, D. C. (2011). Serum iPTH, calcium and phosphate, and the risk of mortality in a European haemodialysis population. *Nephrology Dialysis Transplantation*. https://doi.org/10.1093/ndt/gfq219

Hruska, K. A., Mathew, S., Lund, R., Qiu, P., & Pratt, R. (2008). Hyperphosphatemia of chronic kidney disease. *Kidney International*, *74*(2), 148–157. https://doi.org/10.1038/ki.2008.130

Hutchison, A. J. (2009). Oral phosphate binders. *Kidney International*. https://doi.org/10.1038/ki.2009.60

Kidney Disease: Improving Global Outcomes (KDIGO) CKD-MBD Update Work Group. (2017). KDIGO 2017 Clinical practice guideline update for the diagnosis, evaluation, prevention, and treatment of chronic kidney disease–mineral and bone disorder (CKD-MBD). *Kidney International Supplements,* 7(3), e1. https://doi.org/10.1016/j.kisu.2017.10.001

Liu, Z., Su, G., Guo, X. F., Wu, Y., Liu, X., Zou, C., Zhang, L., Yang, Q., Xu, Y., & Ma, W. (2013). Dietary interventions for mineral and bone disorder in people with chronic kidney disease. *Cochrane Database of Systematic Reviews*, *2013*(2). https://doi.org/10.1002/14651858.CD010350

Nikolov, I. G., Joki, N., Maizel, J., Lacour, B., Drüeke, T. B., & Massy, Z. A. (2006). Pleiotropic effects of the non-calcium phosphate binder sevelamer. *Kidney International*, *70*(SUPPL. 105). https://doi.org/10.1038/sj.ki.5001994

Palmer, S. C., Hayen, A., Macaskill, P., Pellegrini, F., Craig, J. C., Elder, G. J., & Strippoli, G. F. M. (2011). Serum levels of phosphorus, parathyroid hormone, and calcium and risks of death and cardiovascular disease in individuals with chronic kidney disease a systematic review and meta-analysis. In *JAMA - Journal of the American Medical Association*. https://doi.org/10.1001/jama.2011.308

Senatore, M., Coppolino, G., Papalia, T., Greco, R., Lofaro, D., & Bonofiglio, R. (2011). Does concomitant administration of sevelamer hydrochloride and lanthanum carbonate modify the control of phosphatemia? In *European Review for Medical and Pharmacological Sciences*.

Vifor Fresenius Medical Care Renal. (2013). *Clinical Study Report: Integrated PA-CL-05A and Extension study PA-CL-5B. Open-label, randomised, active-controlled, parallel group, multicentre Phase 3 studies to investigate the long-term safety, tolerability and efficacy of PA21 compared with sevelamer*.

Vifor Fresenius Medical Care Renal. (2019). *Product Monograph Including Patient Medication Information for Velphoro*.

CONTINUING EDUCATION STUDY QUESTIONS

CONTACT HOUR: 2.0 HRS

'Phos'ing over phosphorus: A primer on updates in phosphate binders

By Franky Liu and Maeghan Pemas

1. Patients should have phosphorous targeted to appropriate levels based on degree of renal impairment for the following reasons:
   a) Increased mortality risk with hypophosphatemia
   b) Decrease bone fracture rate by avoiding hyperphosphatemia
   c) Increased mortality risk with hyperphosphatemia
   d) A and B
   e) All of above

2. 63-year-old female (dialysis vintage 3 years) with normocalcemia; hyperphosphatemia. Renal dietitian has assessed and would prefer not to restrict diet d/t limited intake. Currently on lanthanum 500 mg tid. Patient unable to increase d/t constipation at higher doses. PMHx does not reveal any significant GI disorders. Patient pays for meds out-of-pocket. Most appropriate course of action for treating CKD-MBD includes:
   a) Titrate lanthanum (Fosrenol™) to higher dose with scheduled Senokot 17.2 mg qhs
   b) Switch to sucroferric oxyhydroxide (Velphoro™)
   c) Switch to CaCarb 500 mg tid cc (or Tums™ product if patient prefers chewable)
   d) Switch to aluminum hydroxide
   e) Switch to sevelamer hydrochloride (Renagel™)

3. 55-year-old male (dialysis vintage 1 year) with Hx failed renal transplant 10 years ago on mycophenolate mofetil 500 mg bid. Mildly low calcium; hyperphosphatemia. Other blood work of note includes Hgb 94. TSAT 15%. Ferritin 250. Patient has private drug coverage. BEST option for treatment:
   a) Lanthanum (Fosrenol™)
   b) Sevelamer hydrochloride (Renagel™) (with separation from Cellcept™ doses by 2 hours)
   c) Calcium (with separation from Cellcept™ doses by 2 hours)
   d) Succoferric oxyhydroxide (Velphoro™) (help with iron levels as well) with separation from Cellcept™ doses by 2 hours
   e) Switch to aluminum hydroxide

4. 70-year-old female (dialysis vintage 3 years) on pantoprazole 40 mg bid (Zollinger-Ellison syndrome) with hypercalcemia; hyperphosphatemia. Also has PMHx bowel perforation. BEST option for treatment:
   a) Calcium
   b) Sucroferric oxyhydroxide (Velphoro™)
   c) Lanthanum (Fosrenol™)
   d) Sevelamer hydrochloride (Renagel™)
   e) Sevelamer carbonate (Renvela™)

5. 85-year-old male (dialysis vintage 10 years) with hyperphosphatemia; normocalcemia. Patient is unable to swallow tablets whole. Relevant PMHx includes calciphylaxis (approx. 14 mos ago; now in remission) and chronic constipation.
   a) Calcium
   b) Sucroferric oxyhydroxide (Velphoro™)
   c) Lanthanum (Fosrenol™)
   d) Sevelamer carbonate (Renvela™) (as powder for suspension)
   e) B or C

6. In comparing sucroferric oxyhydroxide to sevelamer hydrochloride (Renagel™) in clinical trials, Velphoro™:
   a) Showed superior phosphate control
   b) Had more favorable side effect profile
   c) Shown to be non-inferior to sevelamer hydrochloride (Renagel™)
   d) Showed inferior phosphate control with increased side effects
   e) Showed inferior phosphate control with improved side effect profile

7. Which phosphate binder(s) are indicated in treatment of hyperphosphatemia in pre-dialysis patients?
   a) Calcium
   b) Sevelamer (Renvela™ and Renagel™)
   c) Lanthanum (Fosrenol™)
   d) Sucroferric oxyhydroxide (Velphoro™)
   e) A, B and C

8. Appropriate counselling point(s) for Velphoro™ include:
   a) GI side effects (diarrhea)
   b) Black stool
   c) Can discolour teeth – rinse with water
   d) Metallic aftertaste
   e) All of the above

9. Which of the following statements is TRUE:
   a) Calcium and lanthanum should not be used first-line in patients with acid hypersecretory disorders
   b) Calcium and sucroferric oxyhydroxide administration should be separated from levothyroxine
   c) Aluminum hydroxide fell out of common usage d/t decreased effectiveness in comparison with calcium
   d) Elemental calcium in doses greater than 3 g / day have been associated with vascular calcification
   e) Combining sevelamer hydrochloride (Renagel™) and lanthanum (Fosrenol™) has shown superior efficacy compared with combining sevelamer hydrochloride (Renagel™) and calcium

10. 49-year-old male (dialysis vintage 8 years) with hyperphosphatemia requiring treatment. Patient also has GI disease, metabolic acidosis, and hypercalcemia. Most appropriate treatment option:
    a) Calcium tid cc (less absorption with meals)
    b) Lanthanum (Fosrenol™)
    c) Sucroferric oxyhydroxide (Velphoro™)
    d) Sevelamer hydrochloride (Renagel™)
    e) Diet restrictions only

CONTINUING EDUCATION STUDY ANSWER FORM

CE: 2.0 HRS CONTINUING EDUCATION

‘Phos’ing over phosphorus: A primer on updates in phosphate binders

Volume 31, Number 1

By Franky Liu and Maeghan Pemas

Post-test instructions:

- Select the best answer and circle the appropriate letter on the answer grid below.
- Complete the evaluation.
- Send only this answer form (or a photocopy) to:
  CANNT National Office
  4 Cataraqui Street, Suite 310
  Kingston, ON K7K 1Z7
  or submit online to www.cannt.ca
- Enclose a cheque or money order payable to CANNT.
- Post-tests must be postmarked by March 31, 2022.
- If you receive a passing score of 80% or better, a certificate for 2.0 contact hours will be awarded by CANNT.
- Please allow six to eight weeks for processing. You may submit multiple answer forms in one mailing, however, you may not receive all certificates at one time.

CANNT member – $12 + HST ($13.56); Non-member – $15 + HST ($16.95)

POST-TEST ANSWER GRID

Please circle your answer choice:

1.	a	b	c	d	e
2.	a	b	c	d	e
3.	a	b	c	d	e
4.	a	b	c	d	e
5.	a	b	c	d	e
6.	a	b	c	d	e
7.	a	b	c	d	e
8.	a	b	c	d	e
9.	a	b	c	d	e
10.	a	b	c	d	e

EVALUATION

	Strongly disagree				Strongly agree
1. The offering met the stated objectives.	1	2	3	4	5
2. The content was related to the objectives.	1	2	3	4	5
3. This study format was effective for the content.	1	2	3	4	5
4. Minutes required to read and complete:	50	75	100	125	150

Comments: _____

_____

_____

_____

COMPLETE THE FOLLOWING:

Name: _____

Address: _____

_____

CANNT member? ❑ Yes ❑ No Expiration date of card _____

CANNT Awards

There are several awards and grants that CANNT members can apply for yearly. Members can also nominate a fellow CANNT member for their outstanding work in nephrology.

For more information on eligibility and forms for award applications, see **www.cannt-acitn.ca** under **Resources – CANNT Awards/ Bursaries**.

IMPORTANT: Members may apply for more than one bursary per year but will only be able to be the recipient of one award per year.

Deadline to apply: May 1, 2021 or June 30, 2021 (varies for different awards)

CANNT Board of Directors Nominations

Call for nominations 2021

The CANNT Nominating Committee is looking for CANNT/ACITN members to apply for the following positions on the CANNT/ACITN Board of Directors. Positions will commence October 2021.
Deadline for nominations is June 1, 2021.

The positions open are:
President-Elect/Treasurer
(Two-year term followed by two-year term as President)
Director of Communications
(Two-year term)

Eligibility for office: Member in good standing.

GENERAL REQUIREMENTS:

Each candidate must:

- Understand the responsibilities of each position.
- Be willing to commit the required amount of time to fulfil the duties of office.
- Be willing to work within parliamentary procedure, which is used to ensure an efficient and fair voting procedure by self-governing organizations.
- Will submit a National Officer Candidate Information Form available online at **www.cannt.ca**.

BENEFITS TO BOARD MEMBERSHIP

- Having a direct voice in how your Association is run.
- Complimentary registration for the CANNT annual conference.
- CNA recognition of a professional committee membership/participation (executive of a specialty association) and 25 hours can be claimed annually toward certification hours.

POSITION DESCRIPTIONS

1. **President-Elect/Treasurer:** Elected by the membership for a period of two years prior to becoming President for two years. Assists the President in the overall administration, including the financial affairs of the Association while becoming familiar with the operation of CANNT in preparation to assume the Presidency.

2. **Director of Communications:** Elected by the membership for a period of two years. Maintains external communications on behalf of CANNT.

For more information and forms for candidates and nominations,
see **www.cannt.ca**
under Member Resources — Call for Nominations for
the CANNT Board of Directors.

CANNT Membership

First Name _____

Last Name _____

Home Address _____

City _____

Province _____ Postal Code _____

Telephone (H) (_____) _____ - _____

(W) (_____) _____ - _____

Email _____

Employer _____

Employer Address _____

City _____

Province _____ Postal Code _____

Do you consent to the use of your name and address on mailing lists that CANNT has considered pertinent and appropriate?
❏ Yes ❏ No

Do you consent to the use of your email for all correspondence with CANNT?
❏ Yes ❏ No

❏ New Member or ❏ Renewal

Membership Fee (HST #100759869)
Membership fee is tax deductible.
❏ One Year: $80.00 + HST/GST
❏ Two Years: $150.00 + HST/GST
❏ Student Rate: $40.00 + HST/GST*
**Proof of full-time enrolment must accompany application*
AB/BC/SK/MB/NT/NU/QC/YT: 5% GST; ON: 13% HST; NB/NL/NS/PEI: 15% HST

I enclose $ _____
made payable to Canadian Association of Nephrology Nurses and Technologists.

Method of payment:
❏ Cheque ❏ Money order ❏ Visa ❏ Mastercard

Cardholder Name: _____

Credit Card Number: _____

Expiry Date: _____ 3-digit CVV code: _____

Signature: _____

Return to **CANNT**
Mailing Address:

CANNT,
4 Cataraqui Street, Suite 310
Kingston, ON K7K 1Z7

❏ I have attained CNeph(C)/cdt designation

❏ I am a member of CNA

Ontario applicants only
Do you belong to RNAO?
❏ Yes ❏ No

Professional Status
❏ Registered Nurse
❏ Registered Practical Nurse/Registered Nursing Assistant/ Licensed Practical Nurse
❏ Technician
❏ Technologist
❏ Other (Specify) _____

Number of years in nephrology _____

Area of responsibility
❏ Direct Patient Care
❏ Administration
❏ Technical
❏ Teaching
❏ Research
❏ Other (Specify)

_____

Work environment
❏ Acute Care
❏ Self-Care Unit
❏ Independent Health Care
❏ Private Sector

Highest level of education

Nursing	*Non-Nursing*
❏ Diploma	❏ Diploma
❏ Baccalaureate	❏ Baccalaureate
❏ Master's	❏ Master's
❏ Doctorate	❏ Doctorate

I am at present studying toward

Nursing	*Non-Nursing*
❏ Specialty Certificate	❏ Specialty Certificate
❏ Baccalaureate	❏ Baccalaureate
❏ Master's	❏ Master's
❏ Doctorate	❏ Doctorate

Primary area of practice
Choose one
❏ Adults
❏ Combined Adult/Pediatrics
❏ Pediatrics
❏ Other

Select all that apply
❏ Full-Care Hemo
❏ Self-Care Hemo
❏ Home/Independent Hemo
❏ In-Patient Nephrology
❏ In-Patient Peritoneal Dialysis
❏ In-Patient Transplantation
❏ Home/Independent PD
❏ Out-Patient Transplantation
❏ Clinical Educator
❏ Academic Educator
❏ Corporate Education
❏ Vascular/Body Access
❏ Nurse Navigator
❏ Research
❏ Administration
❏ Corporate Sales

Guidelines for Authors

The Canadian Association of Nephrology Nurses and Technologists (CANNT) Journal invites letters to the editor and original manuscripts for publication in its quarterly journal. We are pleased to accept submissions in either official language—English or French.

Which topics are appropriate for letters to the editor?
We welcome letters to the editor concerning recently published manuscripts, association activities, or other matters you think may be of interest to the CANNT membership.

What types of manuscripts are suitable for publication?
We prefer manuscripts that present new clinical information or address issues of special interest to nephrology nurses and technologists. In particular, we are looking for:

- Original research papers
- Relevant clinical articles
- Innovative quality improvement reports
- Narratives that describe the nursing experience
- Interdisciplinary practice questions and answers
- Reviews of current articles, books and videotapes
- Continuing education articles

How should the manuscript be prepared?
Form: The manuscript should be typed double-spaced, one-inch margins should be used throughout, and the pages should be numbered consecutively in the upper right-hand corner. More formal research or clinical articles should be between five and 15 pages. Less formal narratives, question-and-answer columns, or reviews should be fewer than five pages.

Style: The style of the manuscript should be based on the *Publication Manual of the American Psychological Association (APA),* Seventh Edition (2020).

Title page: The title page should contain the manuscript title, each author's name (including full first name), professional qualifications [e.g., RN, BScN, CNeph(C)], position, place of employment, address, telephone, fax numbers, and email address. The preferred address for correspondence should be indicated.

Abstract: On a separate page, formal research or clinical articles should have an abstract of 100 to 150 words. The abstract should summarize the main points in the manuscript.

Text/Reference List: Proper names should be spelled out the first time they are used with the abbreviation following in brackets, for example, the Canadian Association of Nephrology Nurses and Technologists (CANNT). Generic drug names should be used. Measurements are to be in Standards International (SI) units. References should be cited in the text using APA format. A reference list containing the full citation of all references used in the manuscript must follow the text.

Tables/Figures: Manuscripts should only include those tables or figures that serve to clarify details. Authors using previously published tables and figures must include written permission from the original publisher. Such permission must be attached to the submitted manuscript. Table/figure formatting should comply with APA style.

How should the manuscript be submitted?
Email your manuscript to: **cannt.journal1@gmail.com**. Include a covering letter with contact information for the primary author and a one-sentence biographical sketch (credentials, current job title and location) for each author.

How are manuscripts selected for the CANNT Journal?
Each manuscript will be acknowledged following receipt. Research and clinical articles are sent out to two members of the *CANNT Journal* manuscript review panel to be reviewed in a double-blind review process. All manuscripts may be returned for revision and resubmission. Those manuscripts accepted for publication are subject to copy editing; however, the author will have an opportunity to approve editorial changes to the manuscript. The editor reserves the right to accept or reject manuscripts. The criteria for acceptance for all articles include originality of ideas, timeliness of the topic, quality of the material, and appeal to the readership. Manuscripts that do not comply with APA formatting and style will be returned to the author(s).

What are the implications for copyright ownership?
Authors should note that manuscripts will be considered for publication on the condition that they are submitted solely to the *CANNT Journal*. Upon acceptance of submitted material, the author(s) transfer(s) copyright ownership to CANNT. Statements and opinions contained within the work remain the responsibility of the author(s). Authors retain the right to include their respective published work in a thesis or dissertation provided that it is not published commercially. Although no permission is required in this instance, it is expected that you reference *CANNT Journal* as the original source. All other material may not be reproduced without the written permission of CANNT.

Checklist for authors

✓ Cover letter
✓ Article
- Title page to include the following:
  - Title of article
  - Each author's name (including full first name)
  - Professional qualifications
  - Position
  - Place of employment
  - Author to whom correspondence is to be sent, including address, phone, fax number, and email address
- Text of article, with abstract if applicable, **double-spaced, pages numbered**
- References (on a separate sheet)
- Tables (one per page)
- Illustrations (one per page)
- Letters of permission to reproduce previously published material

Revised March 2018

Lignes directrices à l'intention des auteurs

Le *Journal* de l'Association canadienne des infirmières et infirmiers et des technologues de néphrologie (ACITN) vous invite à faire parvenir articles, textes et manuscrits originaux pour publication dans son journal trimestriel. Nous sommes heureux d'accepter vos documents soumis dans l'une ou l'autre des langues officielles, anglais ou français.

Quels sont les sujets d'article appropriés?
Nous acceptons les articles portant sur des manuscrits récemment publiés, des activités de l'Association ou tout sujet d'intérêt pour les membres de l'ACITN.

Quels types de manuscrits conviennent à la publication?
Nous préférons des manuscrits qui présentent de nouveaux renseignements cliniques ou qui traitent des enjeux propres aux champs d'intérêt des infirmières et infirmiers et des technologues en néphrologie. Nous recherchons plus particulièrement des :

- Exposés de recherche originaux;
- Articles cliniques pertinents;
- Rapports sur des approches innovatrices en matière d'amélioration de la qualité;
- Textes narratifs relatant une expérience de pratique infirmière ou technologique;
- Textes sous forme de questions et de réponses sur la pratique interdisciplinaire;
- Revues d'articles courants, de livres et de films;
- Articles en formation continue.

Comment les manuscrits doivent-ils être présentés?
Forme : Le manuscrit doit être présenté à double interligne avec une marge de 1 po et une numérotation consécutive des pages dans le coin supérieur droit de la page. Les articles plus formels de recherche ou d'études cliniques doivent compter de 5 à 15 pages. Les articles moins formels, tels que textes narratifs, questions-réponses ou revues, doivent compter moins de 5 pages.

Style : Le style du manuscrit doit être conforme au manuel de publication de l'Association américaine de psychologie (AAP), 7e édition (2020).

Page titre : La page titre doit inclure le titre du manuscrit ainsi que les renseignements suivants : nom de chacun des auteurs (y compris les prénoms au complet), titres professionnels (c.-à-d. inf., B.Sc. Inf., CNéph[C]), titre du poste occupé, nom de l'employeur, adresse, numéros de téléphone et de télécopieur et adresses courriel. L'adresse privilégiée de correspondance doit aussi être indiquée.

Résumé : Sur une page distincte, les articles formels de recherche ou d'études cliniques doivent être accompagnés d'un résumé de 100 à 150 mots, reprenant brièvement les principaux points du manuscrit.

Texte/Liste de références : Les sigles, abréviations ou acronymes doivent être écrits au long la première fois qu'ils apparaissent dans le texte, suivis de l'abréviation entre parenthèses : p. ex., Association canadienne des infirmières et infirmiers et des technologues de néphrologie (ACITN). Les noms génériques des médicaments doivent être employés. Les unités de mesure doivent être indiquées selon le Système international d'unités (SI). Les références doivent être citées dans le texte en utilisant le format de l'AAP. Une liste de références comprenant la bibliographie complète de toutes les références utilisées doit suivre le texte.

Tableaux/Figures : Les manuscrits ne doivent inclure que les tableaux et figures (incluant schémas, illustrations, croquis, etc.) visant à clarifier certains détails. Les auteurs qui utilisent des tableaux et des figures qui ont déjà fait l'objet d'une publication doivent fournir l'autorisation écrite de l'éditeur d'origine et la joindre au manuscrit soumis. La mise en forme des tableaux et des figures doit être conforme au style de l'AAP.

De quelle manière doit-on soumettre les manuscrits?
Veuillez envoyer par courriel votre manuscrit à : **cannt.journal1@gmail.com**.

Veuillez inclure une lettre de présentation en précisant les coordonnées de l'auteur principal ainsi qu'une notice biographique d'une phrase (incluant titres de compétences, titre du poste actuel et lieu de travail) pour chaque auteur.

Quel est le processus de sélection des manuscrits pour publication dans le *Journal ACITN*?
À la réception de chaque manuscrit, un accusé de réception est envoyé. Les articles de recherche et d'études cliniques sont envoyés à deux membres du comité de révision du *Journal ACITN* afin d'être révisés suivant un processus à double insu. Tous les articles peuvent être retournés aux auteurs pour révision et nouvelle soumission par la suite. Les manuscrits acceptés pour publication peuvent subir des changements éditoriaux; toutefois, les auteurs pourront approuver ces changements. La rédactrice en chef se réserve le droit d'accepter ou de refuser tout manuscrit. Les critères d'acceptation pour tous les manuscrits comprennent l'originalité des idées, l'actualité du sujet, la qualité du matériel et l'attrait des lecteurs. Les manuscrits qui ne sont pas conformes à la mise en forme et au style de l'AAP seront renvoyés à l'auteur ou aux auteurs.

Quelles sont les conséquences du transfert des droits d'auteur?
Les auteurs doivent prendre note que les manuscrits seront considérés pour publication à la condition qu'ils ne soient soumis qu'au *Journal ACITN*. Sur acceptation du matériel soumis, les auteurs transfèrent leur droit d'auteur à l'ACITN. Les déclarations et opinions émises par les auteurs dans leurs articles, textes ou manuscrits demeurent leur responsabilité. Les auteurs conservent le droit d'insérer leurs travaux publiés respectifs dans une thèse ou un mémoire, pour autant que ces derniers ne soient pas publiés à des fins commerciales. Bien qu'aucune permission ne soit requise en pareil cas, il est attendu que les auteurs indiquent en référence le *Journal ACITN* comme source originale. Tous les autres documents ne peuvent être reproduits sans l'autorisation écrite de l'ACITN.

Aide-mémoire à l'intention des auteurs

✓ Lettre de présentation
✓ Article
- Page titre incluant les renseignements suivants :
  - Titre de l'article
  - Nom de chaque auteur (incluant prénoms au complet)
  - Titres de compétence
  - Titre du poste actuel
  - Nom et adresse de l'employeur
  - Nom de l'auteur à qui la correspondance doit être envoyée (y compris adresse, numéros de téléphone et de télécopieur et adresse courriel)
  - Texte de l'article avec résumé, s'il y a lieu à **double interligne et pages numérotées**
- Références (sur une feuille distincte)
- Tableaux (un par page)
- Figures (une par page)
- Lettre d'autorisation pour tout matériel ayant déjà fait l'objet d'une publication

THANK YOU TO OUR SPONSORS!

PLATINUM

AMGEN®

Otsuka

FRESENIUS MEDICAL CARE

janssen
PHARMACEUTICAL COMPANIES OF
Johnson & Johnson

GOLD

AstraZeneca

BD

SILVER

Baxter

CardioMed
LIFE-SUSTAINING SOLUTIONS


World Kidney Day™
11 March 2021
LIVING WELL
WITH
KIDNEY DISEASE
World Kidney Day is a joint initiative of
ISN
IFKF-WKA
© World Kidney Day 2006 - 2021