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Meet Dr. Cathy Clelland, BC Cancer's Provincial Lead, Primary Care

Long-time Family Practice Oncology Network Council member, Head of Royal Columbian Hospital's Department of Family Practice, and past President and Executive Director of the Society of General Practitioners of BC, Dr. Cathy Clelland, is now Provincial Lead of the BC Cancer's recently established Primary Care Program. She shares insight on the opportunities this new program presents to bring the voice of primary care to BC Cancer and to enhance cancer care resources and education for primary care providers BC and Yukon-wide.

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Dr. Cathy Clelland (seated) took on the leadership of BC Cancer's new Primary Care Program late last year. Accompanied here by Program Manager, Jennifer Wolfe (left), and Medical Education Lead, Dr. Raziya Mia.

Osteoporosis – Sometimes more than just bone loss

By Dr. Simon D. Baxter, Medical Oncologist, BC Cancer – Kelowna

Cancer incidence in British Columbia is on the rise. It is estimated that over 30,000 new cases of cancer will be diagnosed in the year 2020. Family physicians play a crucial role in recognizing and diagnosing cancer, as they are often the first point of contact for our patients.

While some cancers will present with obvious signs and symptoms, for example a breast cancer diagnosis following detection of a breast lump, this is not always the case. More often than not, cancer can present with common or vague symptoms. Unless a cancer diagnosis is in your differential, it can be easily missed. When these patients arrive in the oncology clinic, the diagnosis can seem more evident in retrospect; but in a busy general practice, a cancer diagnosis might not appear so obvious.

In this series, cases will be highlighted to give examples of "hidden" cancers – conditions which may herald an underlying cancer diagnosis, may later develop into cancer, and some unusual presentations of malignancy.

Hidden Cancer Case – Multiple Myeloma:

A 55-year-old construction worker, Mr. X, suffered with chronic back and shoulder pain for many years. Three years prior, he fell from a height of 6-feet, causing a severe L1 compression fracture. He subsequently experienced further vertebral compression fractures, presumed to be related to workplace injury. Over time, he experienced 8-inches of height loss, and X-rays described varying degrees of compression fractures of all lumbar vertebrae. Bone mineral density testing was ordered, revealing a T-score of -3.5 in the lumbar spine. Given this new diagnosis of osteoporosis, the patient commenced bisphosphonate therapy, and was counseled on adequate calcium and vitamin D intake.

Dr. Simon D. Baxter

Osteoporosis is a common diagnosis. It is estimated that over 2 million Canadians are affected by osteoporosis, and that 1 in 3 women, and 1 in 5 men will suffer from an osteoporotic fracture during their lifetime.[1] 2010 clinical practice guidelines for the diagnosis and management of osteoporosis in Canada[2] described significant care gaps, especially for men, where less than 10% of men with fragility fractures received any osteoporosis therapy. To improve the care of patients with osteoporosis, these guidelines recommend assessment for osteoporosis in all individuals over the age of 50 who have experienced a fragility fracture. Assessment should include annual measurement of height, and assessment for presence of vertebral fractures. Due to an estimated prevalence of secondary osteoporosis in nearly 20% in women and up to 50% in men, simple screening tests for secondary causes of osteoporosis should be considered in all patients; this is particularly important, since underlying causes might not be clinically apparent. These tests include complete blood count, creatinine, calcium, alkaline phosphatase, thyroid function, 25-hydroxyvitamin D level, and serum protein electrophoresis (SPEP) – especially for patients with vertebral fractures.

Indeed, Mr. X was found to have mild anemia (Hgb of 114 g/L) and an abnormal SPEP, with

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Colorectal cancer update

By Dr. Barb Melosky, Medical Oncologist, BC Cancer – Vancouver

Colorectal cancer is the 2nd most common cancer in Canada (excluding non-melanoma skin cancers), representing 13% of all new cancer cases last year. Canadian statistics estimate that close to 15,000 men and 12,000 women were diagnosed with colorectal cancer in 2017, and 5,000 men and 4,000 women died from this disease. This represents 12% of all cancer deaths.[1] Statistics like these make it imperative that we strive to find precancerous lesions (screening), kill micro-metastatic disease after curative surgery (adjuvant therapy), and prolong survival in patients with advanced disease. This update will focus on the recent advances in the adjuvant and metastatic setting.

Dr. Barb Melosky

View the full 2017 webcast on this topic at www.fpon.ca – Continuing Medical Education.

Staging in colon cancer has evolved through the last century. Dr. Cuthbert Dukes devised a classification system in 1932, used by and helpful to clinicians for decades. This was later replaced by the TNM staging system, with an upgrade in 2018 leading to the 8th edition.[2] In this most recent edition, more importance is given to the poor prognostic features of depth of invasion (T stage), even if fewer lymph nodes are involved (N stage). This is important as we talk to our patients about the risk of recurrence and the role of adjuvant therapy.

Although the backbone of colorectal cancer adjuvant therapy has not changed for more than a decade,[3] the length of therapy is being evaluated. IDEA, a large global trial, examined 3 vs. 6 months of adjuvant therapy. In an analysis of over 12,800 patients, 3 months of chemotherapy was nearly as effective as 6 months, with relatively similar recurrence risk and fewer side-effects, particularly neurological.[4] IDEA was designed as a non-inferiority trial and the important word is "nearly." A 3-month course of chemotherapy had a less than 1% lower chance of being free of colon cancer at 3 years compared to the standard 6-month course (74.6% vs 75.5%); however, this was not statistically significant. In patients with a low risk of cancer recurrence (low T stage or N1 disease), the difference was even smaller (83.1% vs 83.3%), yet again not meeting the statistical endpoint needed. Should oncologists accept the small difference seen and treat patients with a shorter course? The issue is controversial, as some oncologists argue against the shorter course based on the curative intent of treatment.

Therapies for metastatic colorectal carcinoma have been used in practice for some time and the backbone, be it 5 FU based with irinotecan or with oxaliplatin makes little difference.[5] In the 50% of patients with tumors that are RAS wild type, the combination of chemotherapy with cetuximab, a monoclonal antibody against the epidermal growth factor receptor (EGFR), or bevacizumab, a monoclonal antibody against vascular endothelial growth factor receptor (VEGF) resulted in no winner. The important message is that the overall survival of 30 months in either group gives us new hope and optimism for these patients, as our patients on chemotherapy are living longer and with a good quality of life.

An exciting area of interest in the world of advanced colorectal disease is in the area of immunotherapy. Microsatellite instability (MSI) occurs when genes coding for proteins to stabilize DNA are missing or mutated; this leads to cancer formation with tumors that have a high mutational load. We now understand that the immune system reacts to neo-antigens being formed when the mechanism to correct them is unstable. By activing the body's own immune system with monoclonal antibodies against a receptor found to enable the immune system, program cell death inhibitors (PD-L1), the cancers may respond favorably.[6] Clinical trials in Canada are ongoing, and there is great hope for this class of drugs for these patients.

Finally, there are differences between tumors of the left and the right side of the colon. This follows the different embryological development of the colon, and the different mutations that develop as one travels down the colon tract. Clinical data has demonstrated that patients with metastatic tumors on the right side of the colon (cecum, ascending, and transverse colon) have a significantly shorter overall survival compared to patients with metastatic tumors on the left side of the colon (descending, sigmoid, and rectum). In a large trial, the overall survival was 19.4 months for patients with right sided tumors versus 33.3 months for patients with left sided tumors.[7] Decisions on which biologic to use may also therefore depend on location. Patients with left-sided tumors who were RAS wild type fared better when treated with an anti-EGFR antibody in the first-line setting, as opposed to those treated with a VEGF inhibitor. At present, this is approved in British Columbia only in patients ineligible for bevacizumab. Therapeutic decisions based on "side" are under discussion in many jurisdictions.

In conclusion, we have made strides in developing better staging criteria to select which patients may benefit from adjuvant therapy and have information to help determine the duration of therapy. The development of new therapeutics in the metastatic setting has been slow but is moving forward, as we now understand that location of the tumor is prognostic, and may predict the efficacy of the biologic used. The role of immunotherapy is finding its niche in advanced colorectal tumors that are MSI high, and we should strive to identify these patients. Median survival in metastatic colorectal cancer is approaching three years, which gives our patients hope for a future that is bright!

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Supporting breast cancer screening retention with physician reminder letters

By Dr. Colin Mar, Medical Director, BC Cancer Breast Screening

BC Cancer Breast Screening encourages family physicians to participate in a patient reminder letter initiative recently introduced in your community. In early 2018, physicians were provided personalized reminder letters that they could sign or stamp for their patients ages 50-69 who are overdue for breast screening. Upon return of these letters to the program, BC Cancer Breast Screening can mail these letters to your patients at no cost to you.

As you may be aware, only 53% of BC women age 50-69 are getting regular mammograms. This provincial participation rate is well below the national target of 70%. Your involvement in encouraging patients to stay up to date with their mammograms will help improve screening participation rates in your health service delivery area. Please note that this initiative is voluntary. This project does not replace the Breast Screening program's direct patient reminder process and the program will continue to recall your patients as per the screening guidelines.

This initiative is based on a 2014 study[1] conducted by our program that found that a signed family physician reminder letter is an effective intervention to improve screening return rates in overdue women. The randomized study showed that adding letters from physicians to standard postcard reminders resulted in 50% more of the recipients coming in for mammograms, compared with the number of women who were only sent reminders directly from the program.

Recent pilot projects based on this initial study support the findings of improved participant response to this intervention. Feedback from physicians participating in the pilot has been mainly positive. On average 45-50% of physicians sign and return the letters to the program for distribution.

The Breast Screening program would like to thank physicians that have already returned letters to us. We kindly ask that physicians contact us at screening@bccancer.bc.ca if they:

- Have questions about whether they have any patients ages 50-69 who are overdue for screening;
- Would like us to resend their package of letters to them;
- Have suggestions for improving this initiative for the future.

Note to physicians:

The Screening Mammography Program recently changed its program name to BC Cancer Breast Screening to support the promotion of cancer screening under a consistent BC Cancer Screening banner (together with BC Cancer Colon Screening and BC Cancer Cervix Screening). BC Cancer Breast Screening's delivery of service is unaffected by the name change. The program's breast cancer screening guidelines and operations have not changed.

Reference

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IgG lambda paraprotein measuring 21.7 g/L. Subsequent bone marrow biopsy confirmed the diagnosis of multiple myeloma, with areas of bone marrow demonstrating complete replacement by an abnormal plasma cell population. The patient was referred to BC Cancer, and treatment was urgently initiated.

The diagnosis of multiple myeloma is important to consider, since it can often present with apparently benign symptoms. This case highlights a very common diagnosis – osteoporosis, with a fairly rare but important underlying cause – multiple myeloma. Traditionally, multiple myeloma is suspected in the presence of CRAB criteria, including hyper**C**alcemia, **R**enal dysfunction, **A**nemia, and **B**one lesions.

Other investigations to aid in diagnosis include measurement of serum and urine protein electrophoresis, serum free light chains, skeletal radiographic survey, and a bone marrow biopsy.[3]

While multiple myeloma remains a serious and incurable diagnosis, there are many excellent treatment options that allow our patients to live with an excellent quality of life for many years.

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Patient Resources

Myeloma Canada.
www.myelomacanada.ca

Urgent need to preserve capacity in BC Cancer pain & symptom management/palliative care clinics

By Dr. Pippa Hawley, Medical Leader, BC Cancer Pain & Symptom Management/ Palliative Care Program

Widespread concern about the epidemic of deaths from illicit opioid use/poisoning has led to a "cooling" in willingness of some family doctors to prescribe opioids. Unfortunately this often extends to patients with advanced cancer, whose circumstances are noted as an exception in the College of Physicians and Surgeons of British Columbia ("College") Safe Prescribing standard. A particular challenge arises following the discharge of patients with difficult pain syndromes requiring methadone therapy for best control. Ongoing prescribing is required as some cancer patients need to continue therapy at home as they approach the end of life, some may live for a long time with slowly progressive disease, and others respond well to effective palliative disease-modifying treatments.

Consider Methadone4pain.ca – one-hour online course to prescribe methadone for analgesic purposes.

There are also patients with pain that justifies opioid therapy in the survivorship context. Nerve injury and peripheral neuropathies are examples where methadone may be the best opioid for long-term pain management.

The current process for obtaining authorization for prescribing methadone for analgesia is separate to that for opioid use disorder. Although Health Canada has announced that effective May 19, 2018, there will no longer be a requirement for federal exemption to prescribe methadone, the College will be working over the next two months to determine what changes will be needed at the provincial level. Therefore, until notice is distributed clarifying the changes, the current provincial authorization process, and the education and approval processes remain in place. In BC, the full analgesia exemption requires completion of a one-hour, free, CME-accredited, online module – Methadone4pain.ca. Temporary authorization for 60-day maintenance of prescribing can be obtained within 24 hours and requires only the completion and submission of a form to the College.

Rationale to pursue

BC Cancer's Pain & Symptom Management/ Palliative Care Clinics have seen a doubling in referrals over the last 5-6 years and are challenged to accommodate new consultations in an appropriate time frame. Inability to discharge patients back to their communities is hampering efforts to maintain capacity to meet demand.

Family physicians are encouraged to support their colleagues and patients by assuming ongoing prescribing responsibility for opioids including methadone. Cancer patients whose symptoms have stabilized will benefit receiving care closer to home, with continuity, and improved coordination of care.

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Long-term management of TSH suppression in differentiated thyroid cancers

By Karen Mason, Pharmacist, BC Cancer – Surrey

Karen Mason

Well-differentiated papillary and follicular thyroid cancers account for more than 90% of thyroid cancers. Patients treated with thyroidectomy, with or without remnant ablation, and thyrotropin (TSH, thyroid stimulating hormone) suppression using levothyroxine (LT4) have a very good prognosis with a 5 year survival of 98%. An individualized approach is needed to answer the following questions:

1. What are the indications for TSH suppression?

TSH suppression with thyroid hormones is needed to suppress thyroid cancer growth, while maintaining normal physiological functions.[1]

2. How should hormone levels be monitored?

Long-term management of resected differentiated thyroid cancers involves monitoring for possible recurrence with serum TSH and thyroglobulin (Tg). [2] The level of TSH suppression is based on the individual extent of disease and risk of recurrence.[2-4] TSH suppression should be:

- below 0.1 mU/L in high-risk patients as it may improve outcomes;[2-4]
- between 0.1 and 0.5 mU/L for intermediate-risk disease;
- and below 2 mU/L for low-risk disease.[2-5]

The benefit of aggressive TSH suppression needs to be balanced with the potential for subclinical thyrotoxicosis. Supraphysiologic doses of LT4 may lead to risk of angina in patients with ischemic heart disease, atrial fibrillation in older patients, and osteoporosis in postmenopausal women.[2]

For individual patients, guidance documents by major endocrine societies are not meant to replace clinical judgment or the recommendation of their consultants.

Consideration for detectable serum Tg may influence target serum TSH.[2] Serum Tg levels have a high degree of specificity and sensitivity to detect recurrent disease after thyroidectomy. Serum Tg levels up to 0.2 - 0.3 mcg/L while on LT4 are considered acceptable for all risk groups.[2] Beware as interference of Tg levels by anti-Tg antibodies may confound results. Rising Tg or anti-TgAb titre suggests the possibility of disease recurrence and should be investigated accordingly.[2]

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Meet Dr. Cathy Clelland
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What's the rationale for a Provincial Primary Care Program at BC Cancer?

The need for this new program correlates to the predicted ~40% increase in cancer diagnoses expected in Canada by 2030. If we are to manage this dramatic rise in BC and the Yukon, primary care providers will need to play a more important role than ever before counselling patients on prevention and screening for cancer, striving for early diagnoses, supporting patients through the cancer care system, and providing follow-up, survivorship and palliative care. BC Cancer's Primary Care Program recognizes this pivotal role, aiming to ensure primary care is a valued partner throughout the cancer care continuum and that effective resources and education are available.

The idea for this program is based on the success of the Family Practice Oncology Network established in 2002. The Network, which will continue in name, initiated several highly regarded education programs and developed resources to build the cancer care skills and confidence of family physicians. These efforts will continue with the new Primary Care Program building on these achievements, advocating for the role of primary care, and facilitating communication throughout the cancer care system.

Describe your vision for the program over the next 2 years.

We just concluded a major primary care needs assessment whereby we sought input from family physicians, primary care providers, and oncologists from throughout BC and the Yukon to guide the program's development and build the role that primary care will play throughout the cancer care system. We expect to turn strategy into action starting this fall.

I'll know we are reaching our goals when BC Cancer routinely considers the impact of all new programs and changes on primary care, and views the Primary Care Program as the conduit to ensure useful input and representation. We will also have ongoing, effective relationships within BC Cancer and with primary care focussed organizations such as the General Practice Services Committee, and the Divisions of Family Practice, plus with the Ministry of Health and all Health Authorities.

How do you see the role of the family physician changing with regard to cancer care?

Currently the family physician's responsibilities focus on diagnosis and referral of patients without a significant role during acute treatment for cancer. We often receive patients back without a clear path for ongoing management.

I'd like to see family physicians involved throughout each cancer patient's journey, having a better understanding of the issues, and feeling confident in managing that patient's care afterward. We will have an appropriate care plan for every patient and be truly part of their cancer care team. Shared care as such is not an easy shift, but we will develop the relationships to facilitate this and expect noticeable change within 3-5 years.

What appeals to you about the role of Provincial Lead?

The opportunity to improve the impact of family physicians on cancer patients' lives throughout their journey excites me. Often patients lose connection with their family physician during acute treatment which can effect management of their other conditions and lead to poorer outcomes. I want to see patients treated holistically regardless of their underlying condition – and that's the role of a family physician. It's about the relationship all the way through.

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Long-term management of TSH suppression
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3. How should thyroid hormone replacement products be optimally used?

Controversy exists regarding the use of monotherapy with LT4 (levothyroxine, SYNTHROID ELTROXIN®) or LT3 (L-triiodithyronine, CYTOMEL®) or combination therapy with LT4/LT3 (levothyroxine/liothyronine, THYROLAR®) in totally thyroidectomized patients.[6-9] There is insufficient evidence to switch from LT4 monotherapy to LT3 monotherapy in long-term management.[6,9] Extensive studies conclude there is no clinical advantage to add LT3 to LT4 treatment.[6,8-11] Instead, when symptoms of hypothyroidism persist despite adequate LT4 therapy and serum TSH is optimal for the particular risk group, investigation is warranted to detect contributing lifestyle factors or comorbidities, such as endocrine and autoimmune disorders, hematological conditions, end-organ damage, nutritional deficiencies, metabolic syndromes, and concomitant medications.[6,12]

LT4 products may vary in potency;[13] therefore, LT4 products from different manufacturers should not to be used interchangeably.[14] For a product switch, re-titration of the dose, and retesting serum levels in 4 to 6 weeks is necessary.[14,15]

Desiccated natural thyroid contains LT4 and LT3 of porcine/bovine origin.[16,17] There are no controlled trials to support using desiccated thyroid hormone over synthetic LT4 in the treatment of hypothyroidism or any other thyroid disorder.[6,9] The quantity of thyroid hormones vary in natural thyroid supplements and may increase the risk of thyrotoxicosis.[6,18] Although Health Canada and the USA FDA approve numerous natural thyroid products,[19,20] their ability to monitor the content or ratios of LT4 and LT3 in these thyroid hormone products may be limited.[11]

No data supports using natural supplements including iodine, nutraceuticals, or thyroid-enhancing preparations in the treatment of hypothyroidism.[9] In addition, thyroid hormones should not be used as an adjunct for weight loss or well-being in patients with or without hypothyroidism.[4,9,14,16,17]

Conclusion: Well-differentiated thyroid cancer has excellent clinical outcomes. The majority of patients are cured with a combination of surgery, radioactive iodine, and external beam radiotherapy depending on their initial risk. Long-term management involves suppression of TSH using exogenous thyroid supplementation, and monitoring for recurrence with intermittent thyroglobulin testing.

Thank you to Dr. Cheryl Ho, BC Cancer Head and Neck Systemic Therapy Tumour Group, Dr. Mario de Lemos, BC Cancer Professional Practice Leader, Drug Information, and Nadine Badry BC Cancer Editor, Cancer Drug Manual, for their expert review.

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Corridor Consults – Oncology Q&A

Q What is the most effective manner to administer opioid analgesics to patients with cancer pain while managing associated side-effects such as nausea and vomiting? Is there an alternative to opioid analgesics for patients who are intolerant to this class of drugs?

Answer from Drs. Cindy Lou, Emily Harrison, and Charlie Chen, University of British Columbia, Department of Medicine, Division of Palliative Care

Opioids are the mainstay of pain management in palliative care due to their rapid onset of action, available routes of administration, as well as their efficacy in treating cancer pain of mixed etiology. Effective analgesia requires careful consideration of the etiology of pain. While opioids are often useful in cancer related pain, agents for neuropathic pain (such as gabapentin, pregabalin, other anti-convulsants, or tricyclic antidepressants) and other adjuvants (such as bisphosphonates, acetaminophen, NSAIDs, or steroids) may reduce the dosage of opioids required and can work synergistically to improve overall pain control. Patients may also benefit from interventional procedures such as nerve blocks, vertebroplasties, and radiation therapy.

Approximately 70% of patients develop nausea with opioid therapy, more commonly upon initiation. Persistent nausea and vomiting are rare, especially with gentle titration. Opioids induce nausea and vomiting through stimulation of dopaminergic receptors in the chemoreceptor trigger zone, contribute to stasis in the GI tract, and increase sensitivity of the vestibular apparatus. Antiemetics that bind to dopaminergic receptors such as haloperidol and metoclopramide, both of which can be administered subcutaneously, are effective in managing opioid induced nausea.

It is important to recognize that the cause of nausea in cancer is often multifactorial. Most of the evidence around the efficacy of antiemetics comes from studies on chemotherapy and radiation therapy induced nausea. There are very few randomized controlled trials looking at the efficacy of anti-emetics for cancer related nausea. Case studies and consensus, however, show that haloperidol and metoclopramide are often effective.

Vigilant management of constipation is also very important. A regular stimulant laxative should be prescribed with regular opioid use, and an osmotic laxative should be added when required.

Palliative care consultation is strongly encouraged in cases where achieving effective analgesia, with or without concomitant nausea and vomiting or other side-effects, proves complex or challenging.

The BC Centre for Palliative Care and the BC Guidelines and Protocols Advisory Committee (GPAC) Palliative Care Guidelines are helpful resources for physicians caring for palliative care patients.

http://www.bc-cpc.ca/cpc/symptom-management-guidelines/

https://www2.gov.bc.ca/assets/gov/health/practitioner-pro/bc-guidelines/palliative2.pdf

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Q Can I prescribe a direct oral anticoagulant (DOAC) to my cancer patient with a diagnosed venous thromboembolism (VTE)?

Answer from Dr. Erica Peterson, Clinical Hematologist, Vancouver General Hospital, Division of Hematology, and Clinical Assistant Professor, University of British Columbia

DOACs targeting thrombin (dabigatran) or Factor Xa (rivaroxaban, apixaban, edoxaban) are currently recommended as first-line treatment of acute VTE in non-cancer patients.[1] These agents are an attractive option for cancer patients due to their oral administration, few drug interactions, and no requirement for laboratory monitoring.

Currently, only two randomized controlled trials comparing a DOAC (edoxaban and rivaroxaban) to the current standard of care (low molecular weight heparin [LMWH]) have been completed in a cancer patient population.[2,3] In the recently published Hokusai VTE Cancer study, patients with acute symptomatic or incidentally-detected VTE were randomized to 5 days of LMWH followed by edoxaban (60 mg daily) or dalteparin (200 IU/kg daily for the first month, then 150 IU/Kg daily) for 6-12 months.[2] Over the twelve-month study, edoxaban was non-inferior to dalteparin for the composite primary endpoint of recurrent VTE or major bleeding (12.8% edoxaban vs. 13.5% dalteparin, p=0.006 for non-inferiority). Edoxaban was associated with a non-significant decrease in the risk of recurrent VTE (7.9% edoxaban vs. 11.3% dalteparin, p=0.09) at the expense of a significant increase in major bleeding (6.9% edoxaban vs. 4.0% dalteparin, p=0.04). The SELECT-D trial, a smaller pilot study comparing rivaroxaban monotherapy to dalteparin for treatment of acute cancer-associated VTE, has not been formally published.[3] Preliminary results presented in abstract form demonstrated similar rates of major bleeding, while clinically relevant non-major bleeding was increased with rivaroxaban (2% vs. 13%). In both studies, the majority of bleeding events occurred in patients with upper gastrointestinal malignancies.

Several issues must be considered when determining whether a DOAC is a suitable option for an individual patient. Patient-specific factors which prohibit DOAC use include DOAC-chemotherapy drug interactions or severe renal and/or hepatic impairment (creatinine clearance <30mL/min). In addition, DOACs should also be avoided in patients with significant nausea, vomiting, or mucosal erosion due to the potential for unreliable administration and absorption. Compared to LMWH, edoxaban and rivaroxaban are associated with an increased risk of bleeding; hence, LWMH would be the agent of choice in patients with a high bleeding risk and in patients with gastrointestinal malignancies.

Finally, studies comparing DOACs to LWMH in a cancer-specific patient population have only been completed with edoxaban or rivaroxaban, thus the use of other DOACs (apixaban, dabigatran) is not supported at this time.

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Endometrial cancer: the understated malignancy

By Dr. Janice Kwon, Gynecologic Oncologist, BC Cancer – Vancouver

Endometrial cancer is the most common gynecologic cancer in Canada, with an estimated 7,300 new cases diagnosed in 2017, including 970 in British Columbia. In the same year, there were 350 ovarian cancer cases and 180 cervical cancer cases in BC; hence, endometrial cancer cases exceed the total number of ovarian and cervical cancer cases combined. In fact, endometrial cancer is the 4th most common cancer in women, yet it receives little attention. Furthermore, according to Canadian Cancer Statistics, the incidence of endometrial cancer is increasing by 2-3% every year. The average age at diagnosis is 62, and the 5-year survival is approximately 70%.

Dr. Janice Kwon

There are 2 types of endometrial cancer. Type 1 makes up 85% of all cases and is associated with an excess of estrogen, which can be endogenous (obesity, polycystic ovarian syndrome) or exogenous (unopposed estrogen, tamoxifen). Obesity is a risk factor because of conversion of androstenedione in adipose tissue to estrone. Polycystic ovarian syndrome (PCOS) yields a relative excess of estrogen, because these women do not ovulate and produce a corpus luteum, which secretes progesterone and regulates growth of the endometrium. An easy analogy to remember is the lawn, lawnmower, and fertilizer, where the lawn is the endometrium, the lawnmower is progesterone, and estrogen is fertilizer. In the absence of the lawnmower, with excess fertilizer, there is unregulated growth of the endometrium, which can ultimately lead to hyperplasia (pre-cancer), or cancer. As obesity rates continue to increase in our population, so will the incidence of endometrial cancer.

Type 2 endometrial cancer is characterized by high-grade serous, clear cell carcinoma, and carcinosarcoma. These are not associated with the same risk factors as Type 1 cancers. Any woman with a diagnosis of Type 2 endometrial cancer should be referred to a gynecologic oncologist.

Treatment for endometrial cancer is surgery (hysterectomy and bilateral salpingo-oophorectomy). Adjuvant therapy (radiotherapy and/or chemotherapy) is based on stage and presence of high-risk factors, such as a high grade tumor and deep myometrial invasion, even when the tumour is confined to the uterus.

After treatment, patients enter a surveillance program for 5 years. In general this includes a speculum and bimanual pelvic examination. There is no role for pap smears during follow-up of endometrial cancer, as this is a screening test for cervical cancer. Women with endometrial cancer are also at increased risk for breast and colorectal cancer, and should be counseled about the importance of screening for these cancers.

Women at highest risk for endometrial cancer are those with Lynch Syndrome, which is characterized by an inherited mutation in one of the DNA mismatch repair genes. The lifetime risk of endometrial cancer in women with Lynch syndrome is about 60% (same as colorectal cancer risk). Their lifetime risk of ovarian cancer is also increased at 10% (about 10 times higher than general population risk). Women known to have Lynch Syndrome are advised to have prophylactic surgery (hysterectomy and bilateral salpingo-oophorectomy) upon completion of childbearing. There is no evidence that screening with ultrasound or endometrial biopsy will improve their survival, although many guidelines still suggest discussion of these interventions with patients.

Identifying Lynch Syndrome can be done through family history, and tumour testing for mismatch repair deficiency. If there is a significant family history of Lynch-associated cancers, individuals can be referred to the Hereditary Cancer Program (HCP) for genetic testing. However, relying on family history alone will miss a significant number of those with Lynch Syndrome. If there is a personal diagnosis of colorectal or endometrial cancer, the tumour tissue can be tested for mismatch repair (MMR) deficiency, which is the hallmark feature of Lynch Syndrome. If the tumour has MMR deficiency, patients can be referred to the HCP for genetic testing, irrespective of family history. Genetic testing is important, even if there is already a diagnosis of cancer because:

1) their family members can benefit from more intense surveillance or cancer-preventing surgery;
2) women with endometrial cancer are still at high risk for colorectal cancer, and should undergo frequent colonoscopy; and
3) patients with colorectal cancer will have different treatment if they are known to have Lynch Syndrome.

There are some notable scenarios, including young women diagnosed with endometrial cancer who wish to preserve fertility. This may be possible with high-dose progestin therapy, however, the response rate is only about 60-70%. If patients still have persistent endometrial cancer on biopsy by 1 year, they are advised to have surgery.

Bilateral salpingo-oophorectomy is recommended concurrently with hysterectomy. Although the likelihood of ovarian metastases is low, there is a risk of synchronous ovarian cancer, particularly in young women. If premenopausal women have their ovaries removed at hysterectomy, they can go on hormone replacement therapy (HRT), as there is no evidence that it has an adverse effect on outcome. Without HRT, they are at increased risk for long-term health consequences such as osteoporosis and coronary heart disease.

Tamoxifen is a selective estrogen receptor modulator (SERM) that decreases breast cancer recurrence risk, but increases endometrial cancer risk. However, the absolute risk of endometrial cancer is still low (1-2% if used for 5 years). Women using tamoxifen are more likely to develop benign endometrial pathology (asymptomatic endometrial thickening, polyps). In the absence of bleeding, annual screening with ultrasound or endometrial biopsy is not recommended.

In summary, endometrial cancer is a common cancer in women, although understated as there is little publicity about this cancer. The incidence is rising because of increasing obesity rates. Women at highest risk of endometrial cancer are those with Lynch syndrome. Identifying Lynch syndrome can be done through family history, but also by testing colorectal and endometrial cancers for mismatch repair deficiency. Ultimately this testing can help family members to avoid being diagnosed with cancer.

Contact Dr. Janice Kwon at janice.kwon@vch.ca

Supporting cancer patients in the north – a family physician/GPO perspective

There are 114 GPOs practising in 35 different BC/Yukon communities – family physicians with enhanced oncology education who can deliver systemic therapy and provide all aspects of supportive care. BC Cancer's Family Practice Oncology Network initiated the GPO Education Program in 2004 to ensure all cancer patients receive the best quality care as close to home as possible.

Team Vanderhoof: (left to right) Dr. Suzanne Campbell – GPO, Jennifer Pelto, Dr. Shannon Douglas – GPO, Tina Auchstaetter, Dr. Davy Dhillon – GPO, and Leila van der Giessen. Missing but equally important: Louise Betker

Dr. Shannon Douglas is a full service family physician born, raised and practising in Northern BC. She is also one of the first graduates of the Family Practice Oncology Network's General Practitioner in Oncology (GPO) Education Program – class of 2004. Dr. Douglas has much to share on the powerful role a family physician can play in supporting patients through a cancer diagnosis especially in rural and remote locations. Dr. Douglas' practice covers Fraser Lake with regular outreach to Burns Lake and two First Nations communities.

What's the role of a family physician in breaking news of a cancer diagnosis to a patient?

When there is an established relationship with the patient, a family physician is the best person to deliver this tough news. As primary care providers, we can provide reassurance and comfort during this transition, supporting them through the shock and throughout the journey to come. I always take ownership of this responsibility with my patients.

It is important to prepare oneself for these conversations – to research and develop a plan going forward. When you walk into that appointment, it helps to know the options available to the patient, and the recommendations you would make provided the patient is agreeable. The appointment can then be a more positive experience reassuring the patient and their family that "We've done this before. This is where we are going, and we will help you through."

It's when family physicians don't know the next steps that challenges can arise. For example, I took a call recently from a physician whose patient showed a strong suspicion of lung cancer on CT. With the closest respirologist hours away, this physician was unsure whether to refer or even to pursue a diagnosis. Another call came from a physician who needed to decide whether to refer a patient with metastatic breast cancer or to focus on symptom management alone. These two cases illustrate that not every family physician has the knowledge or experience to understand the options available for patients with malignant disease including some of the excellent treatments available. This is where a local GPO, internist or surgeon can be helpful. Supporting family physicians in being better prepared for these conversations is one of the more satisfying elements of my GPO role. Cancer diagnoses can be very complex, and it is useful to have someone to problem solve with.

BC Cancer's Website (www.bccancer.bc.ca) also provides excellent information regarding staging and how to make referrals.

What are the challenges faced by rural practitioners in Northern BC?

Accessing diagnostics and medical oncology consultation can be big challenges. Some weeks there are no medical oncologists available in the North and frequent changes in personnel make it difficult to develop relationships. Another barrier results from the lack of familiarity with the geographic challenges and the 'work-arounds' needed to coordinate care and avoid excessive travel for our patients. *continued on page 9*

Next GPO education course begins September 10, 2018

The GPO Education Program is an eight-week course offering rural family physicians and newly hired BC Cancer GPOs the opportunity to strengthen their oncology skills and knowledge, and provide enhanced cancer care. The program covers BC and the Yukon and includes a two-week Introductory Module held twice yearly at BC Cancer – Vancouver followed by 30 days of flexibly scheduled clinical rotation.
Full details at www.fpon.ca

Managing symptoms in palliative cancer patients

By Dr. Julia Ridley, Pain and Symptom Management/Palliative Care Physician, BC Cancer – Vancouver

Symptom management leads to improved tolerance of cancer therapies and quality of life. While symptom management is not targeted at disease control, increased evidence as well as anecdotal experience supports that symptom management can increase length of life, putatively by maintaining patients' functional levels and ability to continue with cancer-directed interventions.

Dr. Julia Ridley

New symptom management guidelines have been published by the BC Centre of Excellence for Palliative Care and are freely accessible online (http://www.bc-cpc.ca/cpc/symptom-management-guidelines/). They summarize an approach to the assessment and management of 15 symptoms including constipation, nausea/vomiting, dyspnea, delirium and fatigue, the 5 symptoms covered in the Family Practice Oncology Network's February 2018 Webcast, Managing Symptoms in Palliative Cancer Patients.

Spending time and effort on symptom assessment is worthwhile, as it usually yields more appropriate and specific investigations and management plans. Assessment of pain is more frequently taught and practiced than assessment of other symptoms. Common mnemonics used for pain assessment, such as "OPQRSTUV" (**O**nset, **P**rovoking/**P**alliating, **Q**uality, **R**egion/**R**adiation, **S**everity, **T**reatment, **U**nderstanding, **V**alues) can be used to assess other symptoms, with modification to the problem at hand. Incorporating understanding of the patient's severity and trajectory of illness is also important in management of symptoms, as some investigations and interventions may be more or less tolerable, appropriate, or acceptable to patients in the later stages of disease.

Helpful tips:

- Consider the etiology of nausea, and correlating mechanisms of action for any pharmacological treatment chosen;
- Metoclopramide is the most specific medication for opioid induced nausea/vomiting;
- Rotation to methadone may be beneficial for opioid-induced side effects – http://www.methadone4pain.ca is a useful module for those wishing to improve their knowledge;
- Senna is the most specific laxative for opioid induced constipation;
- Use routine and rescue, rather than only 'reactive' laxatives for those with ongoing constipation (from opioids, or other causes);

View the full 2018 webcast on this topic at www.fpon.ca – Continuing Medical Education.

- Cancer related fatigue is multifactorial, but often primarily disease-related, and difficult to improve;
- Education of patient/family and modification of activity is usually the best option for treatment of fatigue, although corticosteroids and stimulants can be tried if not contraindicated;
- Differentiate dyspnea and hypoxia; if patients are dyspneic and NOT hypoxic, low dose opioids are safe and appropriate if underlying causes cannot be eliminated/reduced in severity;
- Hypoactive delirium is underdiagnosed and difficult to treat; and
- Primary treatment of delirium, whether hyperactive or hypoactive, should be non-pharmacological, focused on care, company and environment.

Contact Dr. Julia Ridley at jridley@bccancer.bc.ca

Supporting cancer patients in the north continued from page 8

Recommendations to improve the process for patients?

There is much uncertainty after a cancer diagnosis which is challenging for patients. It is difficult, for example, when patients are not informed of the timelines of their diagnostics, consultations or treatments. It would be a great help if they could navigate aspects of their care including confirming receipt of referrals and accessing estimates regarding the timelines for processing. We could then better support them in managing expectations. I'd like to see our processes evolve towards a more patient centred system.

What impresses you most about the acute cancer care system?

When everything comes together, the system is fantastic and the staff provide tremendous support for patients. The challenges are in the logistics, in making the initial connection, and in knowing how to navigate the system based on resources.

Contact Dr. Shannon Douglas at shannon.douglas@northernhealth.ca.

Oncology scholarships for family physicians: July 15 deadline

THE CANADIAN ASSOCIATION OF GENERAL PRACTITIONERS IN ONCOLOGY

The Canadian Association of General Practitioners in Oncology (CAGPO) offers a scholarship program to support family physicians in enhancing their knowledge and skills in oncology. The learning activity supported generally takes the form of a clinical traineeship from one to four weeks' duration and consists of an active, individualized, practical experience related to clearly defined educational objectives. (The Family Practice Oncology Network's GPO Education Program is a perfect fit!)

CAGPO scholarships are available to community-based family physicians/general practitioners as well as those currently employed full or part time by cancer agencies or programs. The value of each scholarship is up to $4,500 per full-time week of training with a maximum of four weeks per recipient. This year's application deadline is July 15, 2018. Full details at cagpo.ca/scholarships

A Cancer Plan for BC

BC CANCER

Our **Vision** is "A world free from cancer."

Our **Mission** is "To reduce the burden of cancer in British Columbia"

BC CANCER plans, coordinates and evaluates cancer care in collaboration with the health authorities and primary care providers across BC to provide high-quality, accessible and cost-effective care for people living with or affected by cancer.

THE PROVINCIAL CANCER PLAN FOR BC 2018-2021

BC CANCER is committed to this three-year Provincial Cancer Plan, which takes a person-centred approach to serve patients and families who are affected by cancer. The Plan has three strategic priority areas:

1. **Cancer System Governance.** BC CANCER will improve the way that the cancer care system is governed by incorporating input from patients, families and the public and by strengthening relationships with our many partners across BC.
2. **Service Delivery Excellence.** BC CANCER will continue to develop innovative cancer prevention, screening, diagnostic and treatment strategies, and will improve care delivery with a more person-centred approach.
3. **Building Capacity.** BC CANCER will ensure that we have the right people to deliver care, that they have the education and support that they need, and that we have the facilities, equipment, programs and technology to provide the best care possible.

This Plan lays the foundation for an integrated cancer system that provides access to high quality cancer services for all British Columbians, that is easy for patients to navigate and understand, and delivers world-leading outcomes and performance.

Each strategic priority area has two themes. Our work with Family Practice is highlighted in the Partnership theme under Cancer System Governance.

Most cancer patients begin and end their cancer journeys through the offices of primary care providers – a key part of the system. A robust partnership with primary care is required to enhance prevention and screening efforts, and to support patients through all aspects of their cancer journey, including end-of-life care and survivorship.

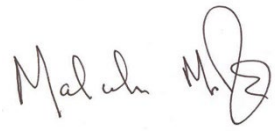
After consultation with primary caregivers, BC Cancer will commit to 4 key goals:

1. **Development and dissemination of comprehensive primary care guidelines for cancer.** We will focus on guidelines for the management of patients who have completed cancer treatment and are returning to your care.
2. **Better communication with Primary Care.** We will ensure you are updated on your patients' progress and that each patient has a personalized care plan to assist you in providing ongoing care. We will also develop easier methods for you to access the cancer system when facing challenges with an individual patient. Further on, we will work with the Health Authorities on diagnostic assessment programs so that your patients with a suspected cancer can be triaged and managed efficiently.
3. **We will continue and expand our educational efforts for both CME and GPO education led by the Family Practice Oncology Network.**
4. **We will work with you to increase the rates of screening for patients with cervical, breast and colon cancer.**

Dr. Malcolm Moore

This work will align not just with the BC Cancer Plan, but also with Primary Care initiatives within the Ministry of Health and with Primary Care providers.

There are great opportunities to improve cancer outcomes and the cancer patient experience. We look forward to working with Cathy Clelland and the BC Primary Care Program, as well as with all of you who work in Family Practice, to deliver a safe, high quality and accessible cancer control program for everyone in BC.



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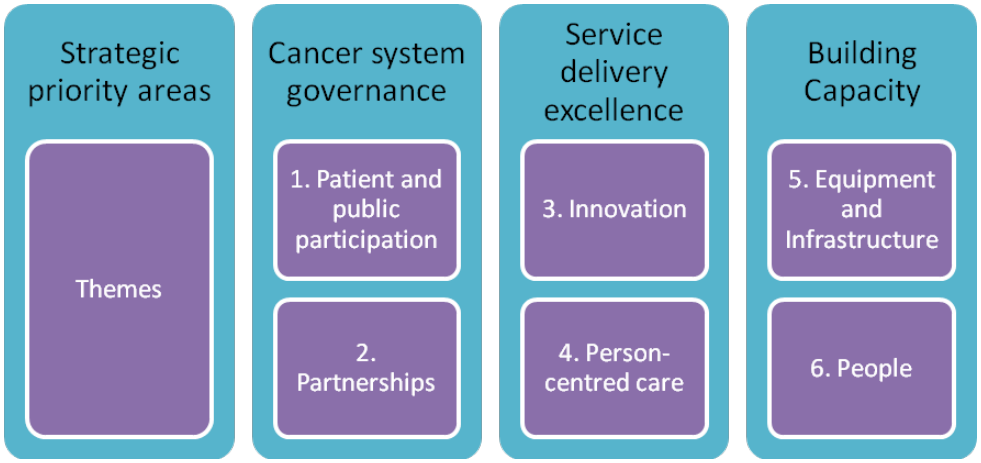


Endometriosis and cancer association

By Dr. Paul Yong, Staff Gynecologist, BC Women's Hospital and Vancouver General Hospital, Research Director, BC Women's Centre for Pelvic Pain and Endometriosis and UBC Endometriosis and Pelvic Pain Laboratory, Assistant Professor, UBC Department of Obstetrics and Gynaecology, http://yonglab.med.ubc.ca

Dr. Paul Yong

Endometriosis affects 10% of reproductive-aged women, or 1 million women in Canada. It is an estrogen-dependent condition defined as uterine endometrium growing in extra-uterine locations, such as on the ovaries, other visceral organs, or on the abdominal-pelvic peritoneum. There are three anatomic sub-types of endometriosis: superficial peritoneal endometriosis, deep infiltrating endometriosis, and ovarian endometriosis cysts (also known as endometriomas).

Endometriosis is a common cause of pelvic pain and infertility, and recent evidence suggests associations with pregnancy complications, autoimmune diseases, and coronary heart disease. Treatment includes progestin-based hormonal therapy, and surgical removal of lesions or more radical surgery including hysterectomy with or without bilateral salpingoophorectomy.

Endometriosis is also associated with an approximately 2-fold increased risk of ovarian cancer. This increase risk is primarily for the clear cell or endometrioid ovarian cancer histotypes (rather than the more common high-grade serous histotype). Supplementing these epidemiologic findings, work by the OVCARE team has shown genomic evidence that ovarian endometriosis is indeed the precursor lesion for these ovarian cancer histotypes.

While these ovarian cancer subtypes are relatively uncommon, endometriosis is common. We need to better understand why a subset of endometriosis becomes capable of undergoing malignant transformation, and whether there is a window for intervention to prevent transformation. Better understanding of this area is important because there is a trend towards more conservative management of endometriosis, including observation, hormonal therapy, and less radical surgery. For example, research has shown that surgical removal of ovarian endometriosis can negatively impact fertility, which has contributed to clinician and patient preference for more conservative management.

View the full 2017 webcast on this topic at www.fpon.ca – Continuing Medical Education.

Possible future avenues for prevention of malignant transformation may include longer-term use of progestin-based hormonal therapy, patient stratification through identification of genetic risk factors, and the possibility that some aspects of endometriosis surgery may further reduce risk. Ongoing research and collaboration between OVCARE and the BC Women's Centre for Pelvic Pain and Endometriosis is shedding light into these potential opportunities for prevention. Tertiary-level clinical referrals can be made to the Centre at http://www.womenspelvicpainendo.com.

Contact Dr. Paul Yong at paul.yong@vch.ca

Pap awareness month – May 2018

BC Cancer Cervix Screening encourages primary care providers to join the program in working to raise awareness of the importance of cervix cancer screening during Pap Awareness Month in May. Please consider recalling your patients who are overdue for their Pap test, or setting aside some drop-in times to accept women for Pap tests who are not necessarily your patients. The Cervix Screening Program has developed some tools to support these activities:

- An online clinic locator tool that lists clinics accepting patients for Pap tests on a drop-in basis. Simply visit the program website (www.screeningbc.ca/cervix) and click on "Add Your Clinic". The online clinic locator will be supported by a social media based campaign aimed at clarifying misconceptions about cervix screening and driving visits to the BC Cancer Cervix Screening website.
- Promotional posters and materials for your waiting areas promoting the importance of cervix cancer screening. A package of these promotional materials will be mailed to physician offices in early May.

BC's overall cervix cancer screening participation rate is 66.5 per cent. This rate is below the national target of 70 per cent and has been declining over the past several years.

Primary care providers are a significant influence on a woman's decision to participate in screening. It is important that your eligible patients are aware that a Pap test is an excellent way to prevent cervix cancer, and the only way to detect abnormal cells in the cervix which, if left untreated, could develop into cancer.

Quick Facts

- 52 per cent of those diagnosed with cervix cancer in 2015 were five years or more overdue for screening or had never been screened.
- 78 per cent of cervix cancer cases occurred in women between the ages of 30-69.
- BC's overall cervix cancer screening participation rate is 66.5 per cent. Participation rates are less than the BC average for some regions in BC, particularly urban areas like Richmond, Vancouver and the Fraser Valley.
- Since the launch of organized cervix cancer screening in BC, the province has successfully reduced cervix cancer rates by 70 per cent. *continued on page 12*

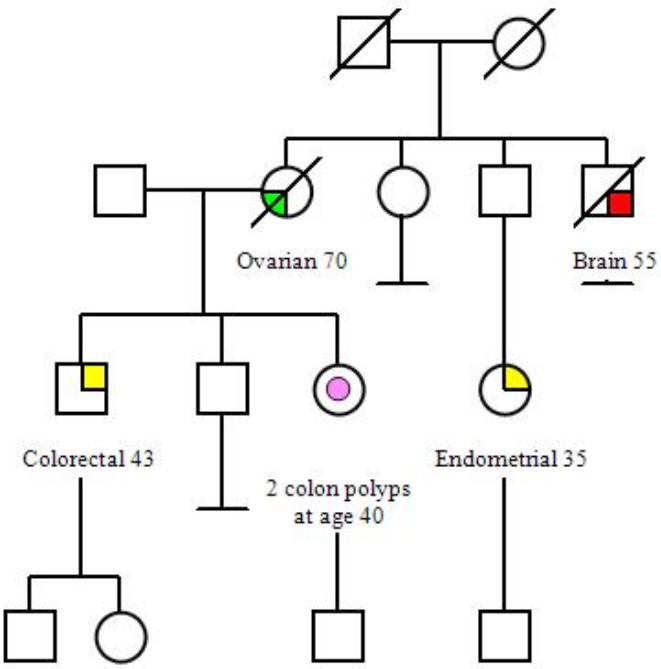
Lynch Syndrome – Improving cancer prevention for the next generation

By Genetic Counsellors, Mary-Jill Asrat and Zoe Lohn, BC Cancer Hereditary Cancer Program

Lynch syndrome (LS; formerly HNPCC) is the most common hereditary colorectal and endometrial cancer syndrome. 3-4% of all cases of colorectal cancer and 2-3% of all cases of endometrial cancer are related to LS. In addition to colorectal and endometrial cancers, LS is also associated with gastric, ovarian, small bowel, hepatobillary, urinary tract, brain and skin (sebaceous neoplasms) cancer. Together with your help in identifying families suspicious for LS, BC CAN improve cancer prevention for the next generation.

Family history is a key tool in assessing for LS. Family history features suggestive of LS include: LS cancers diagnosed at young ages (one case before age 50), multiple individuals affected with a LS cancer, more than one generation affected with LS cancer, individuals with a personal history of two or more LS cancers. When asking a patient about their family history, remember that a history of colon polyps is important to assess as well; specifically, adenomatous polyps diagnosed before age 40 and individuals with multiple polyps.

Today in BC, many colorectal and endometrial cancers are being universally screened for LS at the time of diagnosis by MLH1, MSH2, MSH6 and PMS2 immunohistochemistry, and in some cases secondary testing (ie *BRAF* or methylation) to rule out a somatic cause. Tumors that have been screened for LS will include a comment on the pathology report (often as an addendum). If your patient's tumor is suggestive of LS, or if their family history remains suggestive despite normal tumour testing, refer them to the BC Cancer Hereditary Cancer Program (HCP). HCP is the provincial service offering hereditary cancer risk assessment in BC/Yukon.



Example of a family suspicious for LS

Patients that are approved for a HCP appointment will meet with a genetic counsellor either in-person, by video conference, or by telephone. The genetic counsellor will assess the family history to determine the best approach to genetic testing in the family. In families diagnosed with LS, we can then offer carrier genetic testing to family members. Increased cancer screening and risk reduction (ie, colonoscopy, prophylactic gynecological surgery) is recommended for individuals with LS and has been proven to reduce associated morbidity and mortality.

UPDATE: New research has identified *POLE* and *POLD1* gene mutations in families previously thought to be suggestive of LS. Mutations confer an increased risk of colorectal and colorectal/endometrial cancer, respectively. Please contact HCP directly if you have questions about these genes.

The HCP Referral form and referral criteria can be found on our updated website: http://www.bccancer.bc.ca/health-professionals/clinical-resources/hereditary-cancer.

Contact Mary-Jill Asrat at MJAsrat@bccancer.bc.ca and Zoe Lohn at Zlohn@bccancer.bc.ca

FOR MORE INFORMATION

To learn more about the Family Practice Oncology Network or become involved please contact:
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Visit the Network website: www.fpon.ca

The content of articles in this Journal represent the views of the named authors and do not necessarily represent the position of BC Cancer, PHSA or any other organization.

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Pap awareness month – May 2018
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- BC updated its cervix cancer screening policy in 2016. The new policy recommends that women between the ages of 25 to 69 get tested every three years. This new evidence-based policy ensures that women continue to benefit from screening while avoiding unnecessary tests and follow-up treatment.

Note to physicians:

The Cervical Cancer Screening Program recently changed its program name to BC Cancer Cervix Screening to support the promotion of cancer screening under a consistent BC Cancer Screening banner (together with BC Cancer Breast Screening and BC Cancer Colon Screening). The program's screening guidelines and operations have not changed.

Long-term management of TSH suppression continued from page 5

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