BC CANCER

Provincial Health Services Authority

Journal of Family Practice Oncology

Issue Number 41, Fall 2023 | www.fpon.ca

Education Update

By Dr. Sian Shuel,
Medical Education Lead, FPON

With the intent to provide cancer care education and resources for primary care providers, several educational events and initiatives have taken place since the last iteration of the FPON Journal, and upon receiving accreditation, the webcast year started with our May webcast on *Things You Can Do In Clinic Today to Prevent Ovarian Cancer*. The goal was to help participants identify individuals at high risk for ovarian cancer, available preventative options for high and average-risk populations, and point-of-care resources. *Management of Treatment-Related Side Effects of*

continued on page 3

BEST PRACTICE CANCER CARE GEMS

Cancer prevention in BC's 10-year cancer action plan: Spotlight on HPV vaccination from a public health lens

By: Dr. Cheryl E. Peters,[1-3]
Dr. Gina Ogilvie,[3-5] *Dr. Monika Naus*[1,6]

1. Population and Public Health, BC Centre for Disease Control
2. Prevention, Screening and Hereditary Cancer, BC Cancer
3. School of Population and Public Health, UBC
4. Cancer Control Research, BC Cancer
5. Women's Health Research Institute, BC Women's Hospital and Health Service
6. Communicable Diseases and Immunization Service, BC Centre for Disease Control

In February 2023, BC's 10-year cancer action plan was released. The action plan has 4 key focus areas for the cancer system, the first of which is "Prevent and Detect". Clear partnership and collaboration across several health system entities are key to the work of all disease prevention initiatives and cancer is no different. Even though execution of the Cancer Plan might seem primarily under the purview of BC Cancer as a unique disease-focused agency, there are a few key areas where this is less so. A great example of this is prevention of cancers caused by HPV, for which public health has a critical role to play in planning, deploying and monitoring the HPV vaccine program in BC. Family practice physicians and other primary care providers both within the Family Practice Oncology Network and more broadly can play a pivotal role in endorsing HPV vaccination for their eligible patients, and can support clear communication on the need and benefits of HPV vaccination, which will play a key role in the eventual eradication of cervical cancer.

Dr. Gina Ogilvie

Dr. Monika Naus

Dr. Cheryl E. Peters

Human Papilloma Virus (HPV) infection is the main cause of cervical cancer, and it also increases the risk of several other cancers including anal and throat cancers. Unlike almost any other cancer, we have an incredible opportunity to stop these cancers from ever developing since HPV infection is preventable with a vaccine. When provided in adolescence, the HPV vaccine is a very effective way to reduce or even eliminate future cases of cervical and other cancers. In response to the World Health Organization's goal to eliminate cervical cancer worldwide this century, the Canadian Partnership Against Cancer also developed an action plan for the elimination of cervical cancer using a combined strategy of HPV vaccination and improving cancer screening, and BC's action plan can help us achieve this important global, national, and provincial goal.

The BC cancer action plan priority is to increase the uptake of HPV vaccine (2 or

continued on page 2

Spotlight on HPV vaccination continued from page 1

more doses) to 90% by age 17 years, and the BCCDC further has a target of having completed an age-appropriate HPV vaccine series by 17 years of age. These goals, coupled with appropriate screening and treatments, will support the eradication of cervical cancer in BC.

HPV vaccine uptake rates vary widely in the province, reflective of the underlying support for vaccination among the resident communities. As a family physician or primary care NP, you play a key role in speaking to adolescents and their parents about the importance of HPV vaccination, dispel any myths about these or other vaccines, and provide information on where to get vaccinated.

The HPV vaccine program began for grade 6 girls in B.C. in September of 2008, with a 3-year program for grade 9 girls. The program has been offered to both sexes since September 2019. While the HPV series completion rate for girls and boys reached 66% and 64%, respectively, for the school year ending June 2019, the COVID-19 pandemic reduced these in 2020 and 2021; in 2022 grade 6 series completion rates were back up at 61 and 59% for girls and boys, respectively, but still not at pre-pandemic rates. In addition, catch-up in older grades such as grade 7 for those who missed being vaccinated during the school closure years resulted in half of the health service delivery areas in BC achieving series completion rates higher than pre-pandemic grade 6 levels, or within a couple of percentage points. However, opportunities for catch-up exist in all parts of BC throughout adolescence for those who have not initiated or completed their series in prior years.

The vaccine underpinning BC's HPV prevention program is Gardasil9® (HPV9), and provides protection against 7 oncogenic and 2 non-oncogenic strains of HPV. These include HPV types 16 and 18, which cause about 70% of cervical cancers and 80% of anal cancers (source: BCCDC). The HPV9 vaccine also provides protection against five additional HPV strains that cause cancer (HPV 31, 33, 45, 52, 58) which are responsible for an additional 15% of cervical cancers, 11% of anal cancers in females and 4% in males. It also provides protection against 2 types of HPV (6 and 11) that together cause about 90% of genital warts.

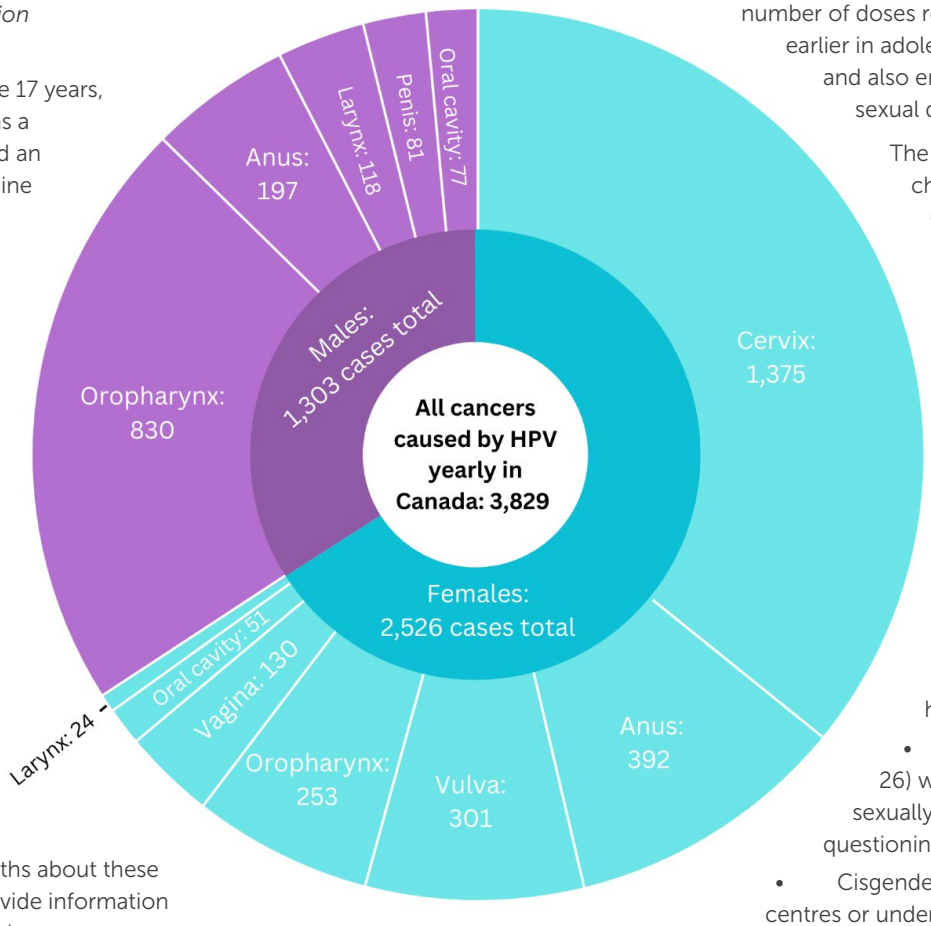


Figure 1: The number of cancers estimated to be caused by HPV every year in Canada, by sex and cancer type (data from ComPARe study, 2015)

The HPV9 vaccine is given as a series over 6 months. Immunocompetent children under 15 years old 2 doses given 6 months apart, but those aged 15 and older and all immunocompromised people require 3 doses, given at 0, 2 and 6 months. The lower dose schedule for younger children is supported by data demonstrating strong immune response on par with older recipients in whom protection against persistent infection was demonstrated. Delay in receipt of subsequent doses does not require restarting a series, and the age at series initiation should guide the total number of doses received. Immunization earlier in adolescence is more efficient, and also ensures protection prior to sexual debut.

The HPV9 vaccine is free of charge for children in grades 6 through 12, and those starting a series prior to their 19th birthday can complete the series with publicly funded vaccine. It is also recommended for free for some other priority groups, including:

- HIV-positive people up to the age of 26
- Cisgender men (up to age 26) who either have sex with other men
- Cisgender men (up to age 26) who have yet to become sexually active but who are questioning their sexuality
- Cisgender men in youth custody centres or under the care of the Ministry of Children and Family Development
- Two-spirit, transgender, and non-binary people up to the age of 26

And just how important is the HPV vaccination program from a public health perspective? Here are the key messages for your patients and their kids:

1. HPV infections are incredibly common: almost every unvaccinated female who is sexually active will get at least one strain of HPV in their lifetime.
2. HPV vaccines work very well: infection with HPV types that cause most cancers and genital warts have dropped by about 90% among vaccinated girls
3. HPV vaccines prevent cancer: HPV is estimated to cause close to 4,000 cancers in Canada every year, most of which can be prevented with vaccination (Figure 1)

The advice of a trusted health care provider is the key factor in the decision to be vaccinated. Use every health encounter as an opportunity to review your patient's immunization status and recommend vaccination.

Education Update
continued from page 1

Androgen Deprivation Therapy, helping cancer care providers recognize the side effects of androgen deprivation therapy, reviewing prevention and treatment of side effects and citing available point-of-care resources followed. After a two-month summer hiatus, the webcast series resumed with September's *Opioid Prescribing for Cancer Pain in Primary Care* to review the pain assessment approach, opioid prescribing principles, opioid options, including methadone, and clinical advantages of each opioid option.

On October 19, *Prostate Cancer Screening and Early Prostate Cancer Management* will highlight current prostate cancer screening recommendations, the diagnostic process and management options for early prostate cancer. The November 16th webcast on *Female Sexual Health & Cancer Survivorship* will help participants identify common sexual health concerns following breast cancer, apply an approach to managing dyspareunia related to menopause in patients with breast cancer, and describe how to talk about decreased sexual desire in the context of dyspareunia and cancer survivorship.

These accredited complementary webcasts occur on the third Thursday of most months from 8 to 9 AM. The links to previous webcast recordings, slides and resources reviewed during the webcast, and our upcoming webcasts, are posted at fpon.ca. Although the primary target audience for our webcasts is primary care providers, other cancer care providers are welcome to join, so please save the dates!

BC Cancer's Primary Care Program added Lung Cancer to its online learning modules. This Lung Cancer module covers lung cancer screening, diagnosis, treatment, surveillance and practical resources. The online module library also includes Breast Cancer, Colorectal Cancer and Prostate Cancer. To access these modules, go to the Primary Care Learning Session tab at FPON.ca under Continuing Medical Education. The complementary accredited modules are developed by partnering with the UBC Division of Continuing Professional Development.

These modules are the basis for BC Cancer Primary Care small group learning sessions, a platform for engaging participants from a community, including family physicians, a local GPO and Regional Centre oncologist, to connect on module learnings and issues specific to their region. Please let us know if you want to bring this learning and collaborative opportunity to your community.

The Fall 2023 iteration of the 8-week General Practitioner in Oncology (GPO) Education, including the virtual 4-week half-day didactic Clinical Practitioner in Oncology (CPO) Education portion, is underway. Participants in CPO education include newly hired GPOs in BC and Yukon, BC Cancer nurse practitioners, and UBC palliative medicine residents. The Fall 2023 intake also hosts current BC GPOs looking to update their knowledge on topics of their choice. We are happy to be once again hosting GPOs and NPs working in cancer care in Nova Scotia for the second time this year as well as GPOs from Northwest Territories and Ontario. In pursuit of ongoing incorporation of feedback and improvement, scheduling changes this intake include moving most sessions to mornings to maximize information retention, moving foundational talks to the first week of lectures and organizing sessions by tumour groups where possible. FPON is grateful to the 60+ speakers, including medical oncologists, radiation oncologists, GPOs and more, who contribute to the success of GPO education and, in turn, help support the cancer care teams at the Regional Centres and enable GPOs to help provide systemic therapy in the Community Oncology Sites so patients can continue to receive care closer to home.

With the BC Cancer Summit just around the corner, FPON is excited to host its hybrid, accredited GPO Case Study Day at the BC Cancer Summit to help GPOs and BC Cancer NPs stay up to date, meet their privileging requirements and connect with colleagues. At the recommendation of the GPO Case Study Day working group, our speakers will cover *Recently Implemented Systemic Therapies at BC Cancer, Current Management of Chronic Lymphocytic Leukemia, Practical Management of Radiation-Induced Skin Toxicities, Practical Cardio-Oncology for the Systemic and Radiation GPO.* Speakers include a GPO and a cardiologist, radiation oncologist, or medical oncologist teaming up to bring their lens and experience on each topic.

One can find more information on FPON's educational offerings and registration details at fpon.ca We continuously seek feedback from our readers and participants on oncology topics of interest to you. Please email FPON's Medical Education Lead at sian.shuel@bccancer.bc.ca with any suggestions.

BC Cancer provides specialized cancer care services to communities across British Columbia, the territories of many distinct First Nations. We are grateful to all the First Nations who have cared for and nurtured this land for all time, including the xʷməθkwəy̓əm (Musqueam), Sḵwx̱wú7mesh Úxwumixw (Squamish), and səlilw̓ətaɬ (Tsleil-Waututh) First Nations on whose unceded and ancestral territory our head office is located.

Pan-Canadian toolkit spotlights innovative Oncology models of care

By Erika Brown, Manager, Transitions and Care, Canadian Partnership Against Cancer and Logan Broeckaert, Lead, Transitions and Care, Canadian Partnership Against Cancer

As **steward of the Canadian Strategy for Cancer Control**, the Canadian Partnership Against Cancer (the Partnership) works closely with a wide range of partners across the country's health and cancer community and at all levels of government to design and implement initiatives that advance shared pan-Canadian priorities. The Partnership is currently supporting eight provinces and territories to implement 22 projects to introduce new models of care and new ways to care for patients.

Erika Brown

This work is guided by the Partnership's **Models of Care Toolkit**, a digital resource hub that provides information on innovative, evidence-informed models of care for the cancer system.

The toolkit is an important resource for health system planners and program designers seeking to strengthen cancer system equity, quality and efficiency. The toolkit, conceived in collaboration with cancer partners across Canada, was originally designed to respond to an increasing need for person-centred care closer to home, rising cancer incidence, and a desire to achieve equity in care access, delivery and outcomes. The COVID-19 pandemic and deepening health human resource constraints has made access to information on innovative models of care more urgent than ever.

The toolkit supports the uptake of equitable and efficient models of care that

- improve **coordination between the cancer system and primary care** at key points along the patient journey;
- optimize **health professional scope of practice** to enhance cancer care closer home; and
- use **cancer network models** to support collaborative, person-centred care.

A section on how **virtual care and patient navigation** present opportunities to enhance innovative models of care in these three areas and guidance on how cancer programs can understand the **needs and priorities of Indigenous communities** when it comes to organizing cancer services have also been included in the toolkit.

Each section describes how these models of care can improve outcomes and includes examples of how Canadian and international models have been designed.

Connecting Primary Care Providers and the Cancer System

Connected care models — models that enhance coordination between primary care and the cancer system - help primary care providers get their patients timely access to efficient and equitable cancer care and are especially important for patients who must travel significant distances to receive care.

These models demonstrate benefits for both patients and providers, including reduced wait times to diagnosis,[1] more appropriate health care utilization,[2,3] primary care providers who feel more supported to deliver cancer-related services to patients,[4] greater patient and provider satisfaction, and enhanced quality of care.

BC's Ministry of Health recognizes the crucial role primary care providers play across the continuum of care. Primary care is a key enabler of the BC's Cancer Action Plan's goals to reduce the incidence of cancer; improve cancer survival, cure rates and quality of life; and ensure a strong system that delivers modern, evidence-based cancer care to the whole province.

The toolkit spotlights a number of models of care that help connect primary care with the cancer system across the continuum of care from **rapid referral services** to **post-treatment care** to **palliation**.

Models of Care for Unattached Patients

Connected care only works if a patient is attached to a primary care provider. One of the biggest challenges facing Canada's health systems is a shortage of primary care providers. Our partners have noted that the shortage is impacting their ability to deliver efficient, equitable care.

Although BC is in the midst of significant transformation in how its primary care services are delivered and funded, about 900,000 British Columbians remain unattached. Patients attached to a primary care provider often receive better care, including more timely diagnosis of new cancers and improved surveillance for the late effects of treatment and recurrence.

Like BC, jurisdictions across Canada are implementing solutions to close the attachment gap but tackling the issue will take time. The Partnership has heard from partners across the country that models of care are needed that support unattached patients to transition into and out of the cancer system. As a first step, we are looking to understand more about existing promising approaches and to work with partners to identify ways to strengthen care for unattached patients.

Models of care like these are already in place. In BC, a **nurse practitioner-led model of care** supports cancer patients who do not have a family physician. Email us if you know of other promising models of care for unattached patients or other types of models of care that you think should be included in future toolkit updates.

Production of this article has been made possible through financial support from Health Canada. The views expressed herein do not necessarily represent the views of Health Canada.

CANADIAN PARTNERSHIP AGAINST CANCER

To learn more about the Canadian Partnership Against Cancer visit www.partnershipagainstcancer.ca

continued on page 11

A primer on Anal Cancer screening

By Dr. Troy Grennan, Provincial HIV/STI Program, BC Centre for Disease Control, and Infectious Diseases, University of British Columbia

Dr. Troy Grennan

Despite effective HIV treatment,[1,2] certain malignancies continue to disproportionately impact people living with HIV.[3] Key amongst these is anal squamous cell carcinoma (SCC). HIV-positive men who have sex with men (MSM) have anal SCC rates up to 100-times those of the general population.[4] Increasingly, other populations (e.g. those with prior vulvar cancer and pre-cancer; individuals with solid organ transplant) are being recognized as having an elevated anal SCC risk as well.[5] Similar to cervical cancer, nearly all anal SCC are caused by the human papillomavirus (HPV).[6] Anal SCC shares a common pathogenesis with cervical cancer.[7,8,9,10] As a result, analogous approaches to screening and treatment of cervical SCC precursor lesions are being used for anal SCC.

Population-based cervical cytology screening has resulted in dramatic declines in cervical cancer incidence.[11,12] In contrast, the incidence of anal cancer in Canada and in other countries continues to increase.[13] Despite this, there are no evidence-based anal SCC screening programs or guidelines in existence, though age- and key population-based guidelines are expected in late 2023 from the International Anal Neoplasia Society.

How to screen for anal cancer?

Like cervical cancer, one way to screen for anal SCC is via cytology (i.e. anal Pap), which is graded using the Bethesda system[14] (see Table 1). The interchangeable use of high-grade squamous intraepithelial lesion (HSIL) for cytology and histology is based on recommendations of the Lower Anogenital Squamous Terminology (LAST) project,[15] whose work has attempted to standardize the terminology used for anogenital squamous cell lesions. Currently, cytology is our only screening tool for anal cancer.

Table 1: Bethesda system for cytology interpretation*

Negative for intraepithelial lesion or malignancy (NILM)

- Normal or negative

Squamous cell abnormalities

- Squamous cell carcinoma
- High-grade squamous intraepithelial lesion (HSIL)
  - With features suspicious for invasion (if invasion suspected)
- Low-grade squamous intraepithelial lesion (LSIL)
- Atypical squamous cells
  - Atypical squamous cells of undetermined significance (ASCUS)
  - Atypical squamous cells; cannot exclude HSIL (ASC-H)

*This table is not an exhaustive list of findings according to the Bethesda system, but rather highlights the most common and/or relevant cytologic abnormalities seen on anal cytology.

Anal SCC can occur anywhere from the perianus to the distal rectum. The gold standard for anal HSIL and SCC assessment is high-resolution anoscopy (HRA),[16] which is analogous to cervical colposcopy. Generally, during HRA, a complete examination of the perianal skin and the anal canal, up to the distal rectum, is performed. This is done using a microscope, with biopsies performed of any suspicious lesions, with particular attention paid to the squamocolumnar junction (SCJ) and the anal transformation zone (see Figure 1). During HRA, anal cytology and digital anorectal examination are also performed.

The sensitivity and specificity of anal cytology is such that individuals may either be over-investigated or under-investigated, depending on which cytology result is used as the HRA referral threshold (see Table 2).[14] For instance, relying on a cytology result of HSIL to predict the presence of biopsy-proven, histologic HSIL has low sensitivity, and thus would potentially miss significant lesions. Alternatively, relying on

continued on page 6

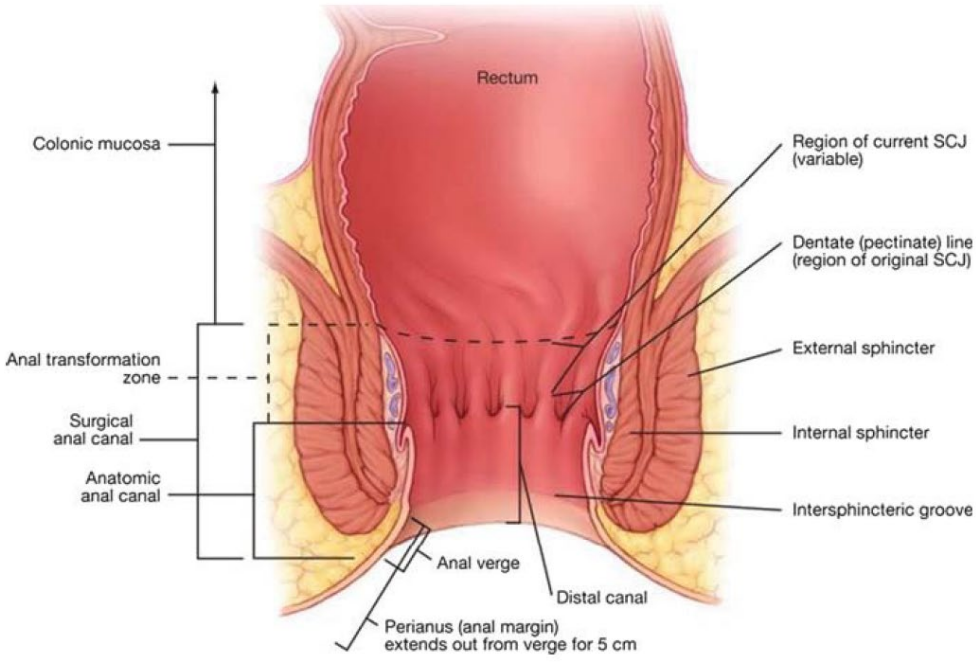


Figure 1: Anatomy of the anal canal and perianal area

Source: Darragh TM, B. J., Jay N, Palefsky J, Ed. (2011). (Darragh TM 2011).

A primer on Anal Cancer screening continued from page 1

any abnormality on cytology as your HRA referral threshold will lead to unnecessary HRA examinations. HPV testing can be a useful adjunct but is not available outside of research settings (see Table 2). In British Columbia, there is only one clinic performing anal cancer screening using HRA, with waitlists reaching up to two years for nonurgent referrals. In the rest of Canada, access to anal cancer screening is equally limited, with five clinics spread across three provinces, with roughly 10 trained HRA providers.

How to manage anal pre-cancers?

Anal HSIL is the cancer precursor lesion, and until recently, there was no evidence demonstrating a cancer prevention benefit from HSIL treatment. This changed with the publication of the landmark ANCHOR study in 2022 . In this study, individuals living with HIV and anal HSIL were randomized to either ablative therapy or surveillance. Following two years of follow-up, the treatment arm had a 57% lower cancer progression rate than the surveillance arm, leading the study's Data Safety Monitoring Board to prematurely halt the study due to efficacy.

Table 2: Performance characteristics of anal cytology and HPV for the detection of histologic HSIL

	Sn (%)	Sp (%)	PPV (%)	NPV (%)
Cytology				
Any abnormal Papa	84	39	31	88
HSIL	21	91	45	78
HPV-DNA+				
HPV-16/18	62	77	53	83
HPV16/18/31/33/45	81	58	44	89
Any oncogenic HPVb	96	33	37	95

Abbreviations: HSIL, high-grade squamous intraepithelial lesion; NPV, negative predictive value; PPV, positive predictive value; Sn, sensitivity; Sp, specificity.
[a]Indicates any abnormality on Pap smear (i.e. HSIL, LSIL or ASCUS); [b]HPV16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, and 68.

Anal cancer screening: looking to the future

In the context of long waitlists and limited resources for anal cancer screening clinics, the suboptimal performance of anal cytology, and the current lack of guidelines, it is challenging to know how to approach decisions around anal cancer screening. The forthcoming guidelines from the International Anal Neoplasia Society, which will provide recommendations on when, in whom and how frequently to screen for anal SCC, will be a good start. Additionally, there is ongoing work examining the utility of other biomarkers to be used either *in lieu* of, or in conjunction with, cytology. Together, these advances should help inform more evidence-based approaches to how best to triage patients for assessment in the anal cancer screening clinic.

Key Points

- Like cervical cancer, the majority of anal cancers are caused by HPV.
- Certain key populations, including but not limited to MSM living with HIV, individuals with a history of vulvar cancer/pre-cancer, and those who have had a solid organ transplant, are at elevated risk for anal cancer over their lifetime. Generally, within these groups, older age also increases one's risk.
- Screening for anal cancer can be done using anal cytology, which is graded according to the Bethesda system (e.g. negative, LSIL, ASCUS, ASC-H, HSIL). Anal cytology is neither sensitive nor specific enough to be relied upon as standalone test to predict histologic HSIL. For instance, with an estimated sensitivity of 21%, using a cytology result of HSIL as a threshold for HRA referral will miss a large number of significant lesions.
- Once diagnosed, histologic HSIL – the anal cancer precursor lesion – should be ablated in order to prevent malignant progression. Though this has only been shown in a clinical trial in individuals living with HIV, it is generally the standard of care for all individuals diagnosed with anal HSIL.
- In late 2023, anal cancer screening guidelines are anticipated from the International Anal Neoplasia Society (IANS). These are expected to make recommendations on the following: key populations to screen (e.g. individuals living with HIV); age to initiate screening; and, frequency of screening. The IANS website is an excellent resource for clinicians on anal cancer and HSIL www.iansoc.org
- For any inquiries around anal cancer screening, or the anal cancer screening clinic at St. Paul's Hospital, please contact the article author troy.grennan@bccdc.ca

References

1. Palella FJ, Jr., Delaney KM, Moorman AC, et al. Declining morbidity and mortality among patients with advanced human immunodeficiency virus infection. HIV Outpatient Study Investigators. [see comment]. N Engl J Med 1998;338(13):853-60.
2. Lohse N, Hansen AB, Pedersen G, et al. Survival of persons with and without HIV infection in Denmark, 1995-2005. Ann Intern Med 2007;146(2):87-95.
3. Silverberg MJ, Chao C, Leyden WA, Xu L, Tang B, Horberg MA, et al. HIV infection and the risk of cancers with and without a known infectious cause. AIDS 2009; 23:2337–2345.
4. Deeken JF, Tjen-A-Looi A, Rudek MA et al. The rising challenge of non-AIDS-defining cancers in HIV-infected patients. Clin Infect Dis 2012; 55(9): 1228-1235.
5. Clifford G, Georges D, Shiels MS, et al. A meta-analysis of anal cancer incidence by risk group: Toward a unified anal cancer risk scale. Int J Cancer 2021; 148(1):38-47.
6. Parkin M, Bray F. The burden of HPV-related cancer. Vaccine 2006; 24 (Suppl 3): S11-S25

continued on page 11

Join us at the virtual and in-person BC Cancer Summit!

The Summit will feature:

- Dr. Jillian Horton, award-winning medical educator, writer, musician and podcaster who leads the development of new programs related to physician wellness and winner of the 2020 AFMC-Gold Humanism Award.
- Joe Gallagher, PHSA's first vice president, Indigenous Health and Cultural Safety, and formerly the founding chief executive officer of the First Nations Health Authority, the first and only health authority of its kind in Canada.

Register at bccancersummit.ca

Early bird registration closes September 29

Bringing life-saving cancer care closer to home

By Heather Findlay, chief operating officer, BC Cancer and
Dr. Kim Nguyen Chi, chief medical officer, BC Cancer

BC Cancer, together with the Ministry of Health and our health authority partners, is bringing cancer treatment closer to home with the planning of four new cancer centres across the province. In the coming decade, we plan to open new centres in Surrey, Burnaby, Kamloops and Nanaimo to keep up with the increasing demand for cancer care.

The new centres are part of our 10-year cancer action plan, which outlines immediate steps to prevent, detect and treat cancers, delivering improved care now while preparing for the growing needs of the future.

In B.C., one in two people will be diagnosed with some form of cancer in their lifetime. With the rapidly growing populations in Surrey, Burnaby, Kamloops and Nanaimo, there is a great need for expanded cancer care services to provide life-saving care closer to home.

This year we reached major milestones with our projects underway and are excited to share our progress:

Kamloops and Nanaimo

In May, we joined Minister Adrian Dix, Premier David Eby, and our health authority partners, Island Health and Interior Health, to announce the approval of the concept plans for the new cancer centres in Nanaimo and Kamloops. The new Nanaimo Cancer Centre will be at Nanaimo Regional General Hospital and the new Kamloops Cancer Centre will be located at Royal Inland Hospital. Together with our health authority partners, the BC Cancer Redevelopment Team is currently working on the business plan to determine the project scope, clinical services, schedule and budget for submission to the Ministry of Health in the fall.

Burnaby

In August, we marked a major milestone with the approval on our business plan for the Burnaby Hospital Phase 2 and BC Cancer Centre project. With business plan approval, we will now move into the procurement stage, which involves the selection of partners that will design and build the facility. The new cancer centre at Burnaby Hospital will complement the services provided at the hospital and will include treatment, supportive care, research, education and innovative technologies, such as virtual health.

Dr. Kim Chi Heather Findlay

Surrey

We are currently in the final stages of selecting a firm to design and build the new Surrey hospital and BC Cancer Centre. We expect to announce the successful proponent this fall, and from there, we will launch into the design and construction phase for this project. Surrey's new hospital and cancer centre will be built in Cloverdale beside the Kwantlen Polytechnic University campus at 5500 180 Street. The new cancer centre will complement the services and care provided by BC Cancer – Surrey and help meet the demand for expanded cancer care services in this region.

We will continue to work in partnership with our health authority partners to engage with the people with the most in-depth knowledge of cancer care: our patients and their families, staff and physicians. We will also connect with our local communities and Indigenous partners to gather feedback on the design to ensure that our new cancer centres are built with culturally-safe and person-centred care in mind.

For more information about our redevelopment projects, visit bccancer.bc.ca/about/projects-priorities If you have any questions, email bccancer.redevelopment@phsa.ca.

For information on the 10-year cancer action plan, visit bccancer.bc.ca/cancerplan

Left to right: Nanaimo cancer centre approval announcement with Dr. Kim Chi, chief medical officer, BC Cancer; Sarah Roth, president and CEO, BC Cancer Foundation; Heather Findlay, chief operating officer, BC Cancer; Leah Hollins, board chair, Island Health; Emmy Manson, representative from Snuneymuxw First Nation; David Eby, Premier of British Columbia; Sheila Malcolmson, Nanaimo MLA and Minister of Social Development and Poverty Reduction; Adrian Dix, Minister of Health.

Campbell River – Cancer Care Clinic evolution and rural life attraction

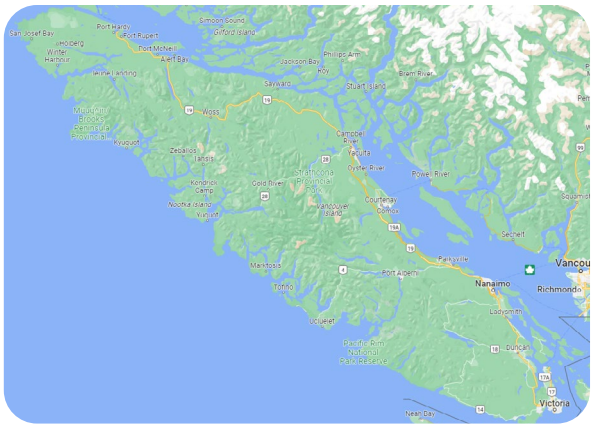
By Dr. Sian Shuel, Medical Education Lead FPON, with Dr. Jim Proctor

With the sound of free-range turkeys in the background and the serene ocean view in mind, I had the opportunity to connect with Dr. Jim Proctor, mentor and longest currently working General Practitioner in Oncology (GPO) in Campbell River on Vancouver Island. Upon completing his medical degree at UBC and before becoming a GPO, Dr. Proctor started in the community as a family medicine locum and then opened his family practice. In addition to his office work, his duties at the time included covering the emergency room for his patients and following admitted patients – both his own and those without a family physician.

Around 2002, a family physician colleague and chemotherapy nurse champion began assessing patients with cancer out of a designated chemotherapy bed in the local emergency department. Shortly after that, Dr. Proctor was approached to join the small team to help ensure patients in the area could access systemic therapy with less travel and financial burden. A year or so later, Dr. Proctor completed BC Cancer's then-newly developed GPO Education, now a prerequisite for all GPOs working in BC and Yukon and celebrating its 20th year in 2024.

From a single bed in the emergency department at Campbell River Hospital then to a small room in the inpatient medical ward, the Community Oncology Network (CON) clinic now boasts a ten-chair chemotherapy delivery room, a treatment room for procedures such as bone marrow biopsies, paracenteses and pleurocenteses, a solarium, space for the chemotherapy clerk and an office for GPOs to conduct their patient visits.

From a two-person team in the early 2000s, Campbell River now has five chemotherapy nurses, four part-time GPOs (with a fifth GPO currently training) and a dedicated clerk, all of whom work to ensure the unit runs five days a week to meet the increasing needs of patients in the area. Additional cancer care-related services in Campbell River include family physicians, a surgeon with a colorectal fellowship, a gastroenterologist, a wound care nurse, dieticians and pharmacists. The CON clinic also works to meet the needs of patients living north of Campbell River in communities such as Alert Bay, Port McNeill and Port Hardy, west to Gold River and Tahsis, east to Quadra Island and Cortez Island and south to Black Creek.



Upon speaking of geography, we reminisce about the community where we practiced, the beautiful view and the small-town feel. Dr. Proctor also appreciates the fresh air coming off the ocean, that he can bike and ski out his back door and that his family is in the area.

After working as a GPO for about 20 years, Dr. Proctor now works part-time and continues to love his GPO work. He notes that the most challenging part is sharing difficult news – having patients undergo three months of treatment with side effects, then telling them the treatment didn't work. However, despite the often-difficult diagnosis and prognosis, the clinic is still a positive place to be, with patients often focusing on the day they have before them. The highly functional team within the community and the support from the oncologists in Victoria are another positive. Dr. Proctor remarks that without the oncologists' help, the CON clinic wouldn't work, and despite the system challenges, upon overall reflection, he's primarily grateful for living in Canada and for the cancer care system.

Contact Dr. Sian Shuel at sian.shuel@bccancer.bc.ca

Calling all GPO'S and BC CANCER NPs! Join us for GPO Case Study Day @ the BC Cancer Summit

Saturday November 18, 2023
8:45 a.m. – 2:45 p.m.

4 Mainpro+ credits

An interactive case based learning opportunity for GPOs and NPs working in Oncology covering:

- Recently Implemented Systemic Therapies at BC Cancer
- Current Management of Chronic Lymphocytic Leukemia
- Practical Management of Radiation-Induced Skin Toxicities
- Practical Cardio-Oncology for the Systemic and Radiation GPO

Registration available at:
https://bccancersummit.ca

For more information,
email fpon@bccancer.bc.ca

Learn with your peers. Enhance the cancer care you provide.

ABCGPO will be holding a meeting following Case Study Day. The recent workload survey results will be presented.

HPV and Oropharyngeal Carcinoma

By Dr. Pam Gardner
Program Medical Director in Oral Oncology, BC Cancer

Dr. Pam Gardner

Head and Neck squamous cell carcinomas (HNSCCs) have traditionally been linked to the carcinogenic effects of alcohol and tobacco. With public health efforts to reduce the prevalence of smoking in high income countries, there has been a decline in the incidence of HNSCCs. However, at the same time human papillomavirus (HPV) infections have emerged as an important risk factor that has increased the incidence of oropharyngeal cancers (OPSCCs) over the same period. While there are more than 200 HPV types identified, the World Health Organization classifies 14 mucosal HPV types (HPV-16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66 and 68) as high risk for cancer causation with HPV-16 alone accounting for at least 85% of HPV-positive (HPV+) OPSCCs.[1]

HPV+ OPSCCs represents a growing etiologically distinct subset of head and neck cancers with unique epidemiological, clinical, and molecular characteristics that differ from those of HPV-negative (HPV-) cancers.[2] It is an epidemic that remains relatively unfamiliar to most physicians, potentially delaying diagnosis and treatment. Knowledge of this epidemic, a high index of suspicion, and an understanding of how the tumors present in clinical practice can help physicians to make an early diagnosis, and reduce patient morbidity from cancer treatments associated with advanced disease stages.

HPV is one of the most commonly sexually transmitted infections in Canada and while the incidence of HPV-related OPSCCs are increasing, the natural history of HPV has not been well described. Most HPV infections occur without any symptoms and will clear within a year or two without treatment, whereas in some people, HPV infections can persist. A persistent HPV infection is a risk factor for OPSCC yet risk factors for oncogenic HPV persistence remain poorly understood.

In one of the longest and largest prospective studies of oncogenic oral HPV infection (n=1833 participants) that looked at extracted DNA from oral rinse and gargle specimens, the results showed that HPV-16 was the most common oncogenic infection detected (105 of 676) and the majority of oncogenic oral HPV infections cleared quickly (median 1.4 years, range 0.5-3.9 years). After 7 years of follow-up, 5.5% (n=37) of oncogenic oral HPV infections were still persistently detected. Most (70%) incident infections cleared by 2 years, and 97% cleared by 7 years, suggesting that long-term persistence of incident infections is rare. In contrast, only 47% of prevalent infections cleared by 2 years and 71% at 7 years. Specifically for HPV-16, clearance was 51% at 2 years and 76% at 7 years. A lower HPV-16 viral load was statistically significantly associated with clearance when compared to a higher viral load. One male participant who had oral HPV-16 consistently detected at 10 study visits over 4.5 years was subsequently diagnosed with an HPV+ OPSCC.[3]

Early natural history studies suggested that risk factors for persistent oral HPV infection include male sex, cigarette smoking and immunosuppression.[4,5] A higher risk of oral HPV infection is associated with an increased number of recent (within the past 3 months) oral and vaginal sex partners.[6] Sexual behavior is also considered to be an established risk factor for HPV+ OPSCC with a strong association observed between numbers of lifetime oral sex partners and incidence of the disease.[7,8]

OPSCC comprises tumors located in the posterior pharyngeal wall, soft palate, tonsillar complex and the base of tongue and the most common presentation is of a neck mass and/or a sore throat. It may also present as dysphagia, obvious mass, globus sensation, odynophagia or otalgia.[9] Common dental pathology including periodontal disease, dental decay or tooth abscesses do not typically present with lymphadenopathy or sore throat. Most patients present with small primary tumors (T1 or T2) and nodal metastases and a small subset will present with cervical lymphadenopathy alone. Neck masses should ideally be evaluated using confirmatory ultrasonography and fine needle biopsy sampling.[10]

Treatment of patients with OPSSC involves surgical excision, primary radiotherapy or concurrent chemo-radiotherapy. While there is an improved prognosis with HPV+ OPSCCs, all treatment modalities result in significant long term morbidity of the head and neck including loss of teeth, permanent and severe xerostomia, osteoradionecrosis of the mandible/maxilla, trismus, tissue fibrosis,

continued on page 11

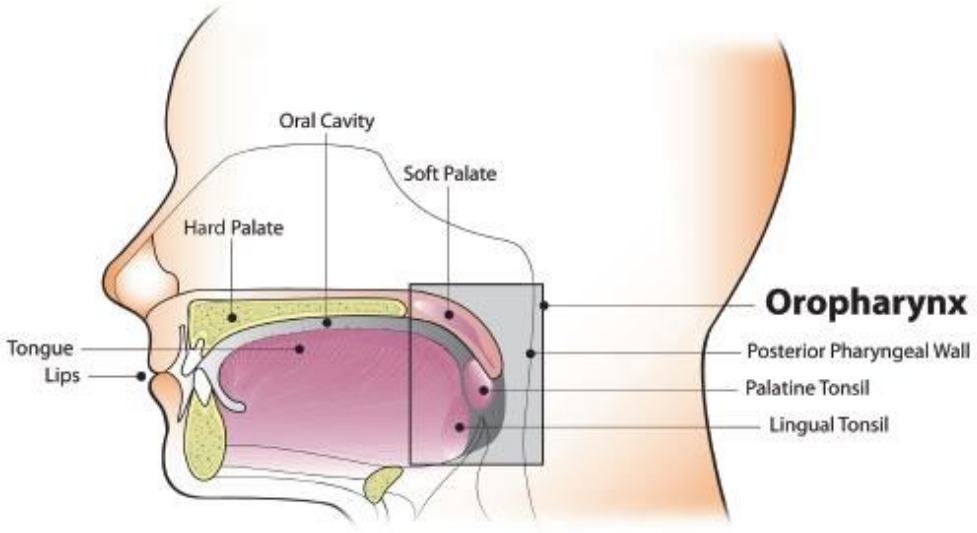


Diagram from the Centers for Disease Control and Prevention website.
www.cdc.gov/cancer/hpv/basic_info/hpv_oropharyngeal.htm

HPV and Oropharyngeal Carcinoma continued from page 10

speech and swallowing issues.

Despite the epidemic of HPV+ OPSCCs, there are currently no effective screening methods for HPV+ OPSCCs and premalignant OPSCC lesions remain to be identified.

While further research is needed for improved understanding of the molecular basis and clinical course of this disease in order to guide efforts towards early detection, reduce the significant health and economic burden of OPSCCs, and ultimately improve patient outcomes, an awareness of oral signs and symptoms will assist physicians in making an early diagnosis.

References

1. Liederbach E et al. The national landscape of human papillomavirus-associated oropharynx squamous cell carcinoma. *Int J Cancer* 2017;140:504-512
2. Craig SG, et al. Recommendations for determining HPV status in patients with oropharyngeal cancers under TNMB guidelines: a two-tier approach. *Br J Cancer*, 2019;120:827-833
3. D'Souza G, Clemens G, Strickler HD, Wiley DJ, et al. Long-term persistence of oral HPV over 7 years of follow-up. *JNCI Cancer Spectrum*. 2020;4(5):pkaa047
4. Pierce Campbell CM, Kreimer AR, Lin H-Y, et al. Incidence and clearance of oral human papillomavirus type 16: the HPV Infection in Men (HIM) study. *Cancer Prev Res (Phila)*. 2015;8(3):190-196
5. Beachler DC, Sugar EA, Margolick JB, et al. Risk factors for acquisition and clearance of oral human papillomavirus infection among HIV-infected and HIV-unaffected adults. *Am J Epidemiol*. 2015:181(1):40-53
6. D'Souza G et al. Sex differences in risk factors and natural history of oral human papillomavirus infection. *J Infec Dis* 2016;213:1893-1896
7. Gillison ML, CHaturvedi AK, Anderson WF & Fakhry C. Epidemiology of human papillomavirus-positive head and neck squamous cell carcinoma. *J Clin Oncol* 2015;33:3235-3242
8. Gooi Z, Chan JYK & Fakhry C. The epidemiology of the human papillomavirus related to oropharyngeal head and neck cancer. *Laryngoscope* 2016;126:894-900
9. McIlwain WR, Sood AJ, Nguyen SA & Day TA. Initial symptoms in patient with HPV-positive and HPV-negative oropharyngeal cancer. *JAMA Otolaryngol* 2014;140:441-447
10. Khalid MB et al Initial presentation of human papillomavirus-related head and neck cancer: a retrospective review. *Laryngoscope* 2019;129:877-882

A primer on Anal Cancer screening continued from page 6

7. De Ruiter A, Mindel A. Anal intraepithelial neoplasia. Eur J Cancer 1991; 27:1343–1345.
8. Bjorge T, Engeland A, Luostarinen T, Mork J, Gislefoss RE, Jellum E, et al. Human papillomavirus infection as a risk factor for anal and perianal skin cancer in a prospective study. Br J Cancer 2002; 87:61–64.
9. Watson AJM, Smith BB, Whitehead MR, Sykes PH, Frizelle FA. Malignant progression of anal intra- epithelial neoplasia. ANZ J Surgery 2006; 76:715–717.
10. Palefsky JM, Holly EA, Hogeboom CJ, Ralston ML, DaCosta MM, Botts R, et al. Virologic, immunologic, and clinical parameters in the incidence and progression of anal squamous intraepithelial lesions in HIV positive and HIV negative homosexual men. J Acquir Immune Defic Syndr 1998; 17:314– 319.
11. Peto J, Gilham C, Fletcher O, Matthews FE. The cervical cancer epidemic that screening has prevented in the UK. Lancet 2004; 364: 249-256.
12. Robinson D, Coupland V, Moller H. An analysis of temporal and generational trends in the incidence of anal and other HPV-related cancers in Southeast England. Br J Cancer 2009; 100: 527-531.
13. Silverberg MJ, Lau B, Achenbach CJ, et al. Cumulative incidence of cancer among HIV-infected individuals in North America. Ann Intern Med 2015; 163: 507-518.
14. Nayar R, Wilbur DC. The Pap test and Bethesda 2014. Acta Cytologica 2915; 59: 121-132.
15. Darragh TM, Colgan TJ, Cox JT, et al. The Lower Anogenital Squamous Terminology Standardization Project for HPV-associated lesions: background and consensus recommendations from the College of American Pathologists and the American Society for Colposcopy and Cervical Pathology. J Low Genit Tract Dis 2012; 16(3): 205-242.
16. Hillman RJ, Cuming T, Darragh T, et al. 2016 IANS International Guidelines for Practice Standards in the detection of anal cancer precursors. J Low Genit tract Dis 2016; 10: 283-291.
17. Palefsky JM, Lee JY, Jay N, et al. Treatment of anal high-grade squamous intraepithelial lesions to prevent anal cancer. New Engl J Med 2022; 386: 2273-2282.

Innovative Oncology models of care continued from page 4

References

1. Cancer Quality Council of Ontario. Programmatic Review on the Diagnostic Phase: Environmental Scan.; 2016.
2. Gorin SS, Haggstrom D, Han PKJ, Fairfield KM, Krebs P, Clauser SB. Cancer care coordination: A systematic review and meta-analysis of over 30 years of empirical studies. *Ann Behav Med*. 2017;51(4):532-546.
3. Mittmann N, Beglaryan H, Liu N, et al. Examination of health system resources and costs associated with transitioning cancer survivors to primary care: A propensity-score–matched cohort study. *J Oncol Pract.* 2018;14(11):e653-e664.
4. Zhao Y, Brettle A, Qiu L. The effectiveness of shared care in cancer survivors-A systematic review. I*nt J Integr Care*. 2018;18(4):2.

Cervical Cancer in British Columbia: a screening update

Dr. Jordan A. Lewis Dr. Lily Proctor

By Dr. Jordan A. Lewis, Obstetrics and Gynecology Resident, University of British Columbia,
Dr. Lily Proctor, Gynecologic Oncologist, BC Cancer

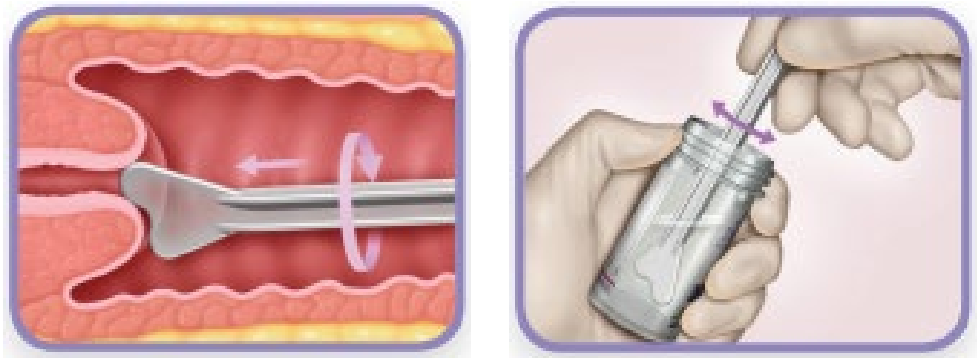
Cervical cancer is one of the only cancers with the potential to be entirely preventable—yet despite this, the Canadian Cancer Society predicts that British Columbia would see at least 200 new cervical cancer diagnoses and 50 cervical cancer-related deaths in 2022.[1] In 2017, BC saw a similar incidence of cervical cancer, and among these patients an alarming 66% of squamous cell carcinoma and 46% of adenocarcinoma cervical cancer cases either had never been screened or did not receive timely screening.[2]

British Columbia pioneered one of the first population-based cervix screening programs, leading to a 70% decrease in cervical cancer incidence between 1955 to 1985 by offering routine pap tests to eligible individuals.[2] It is now universally recommended that anyone with a cervix of baseline risk aged 25-69 years old undergo screening with a pap test every three years. In 2020, the Canadian Partnership Against Cancer (CPAC) organized a Canadian 'Action Plan for the Elimination of Cervical Cancer in Canada' to improve immunization and screening programs for cervical cancer by 2030. Specifically, CPAC aims to ensure 90% of eligible individuals remain current with their cervical cancer screening, and 90% of abnormal results have timely and appropriate follow up.[3] Having these effective and reliable screening protocols in place enables the opportunity to identify and diagnose cancerous or pre-cancerous lesions, ultimately increasing the chance of surgical cure.

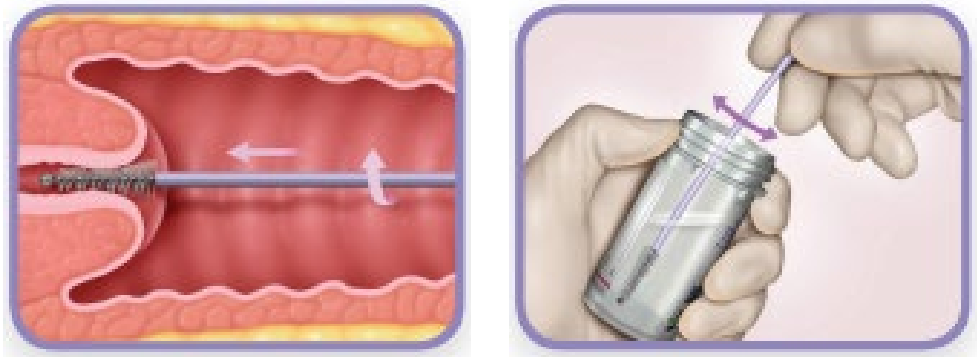
Unfortunately, one of the many distressing side effects of the COVID-19 pandemic raised by BC practitioners is the significant delay in receiving patients' pap smear results. The BC Cancer laboratory services website estimated that turnaround times for pap test reporting were 14-16 weeks from specimen collection – significantly longer than the previously average timeline of less than 4 weeks.[4] The Cervical Cancer Screening Laboratory (CCSL) processes up to 325,000 pap tests annually.[2] During peak isolation, it had been reported that as few as one third of eligible patients requiring cervical screening had timely appointments due to significant challenges in scheduling in-person examinations,[5] leading to an influx of "catch up" screening tests once restrictions were lifted. With specimen numbers well

continued on page 13

Figure 1: Endocervical brush/spatula protocol technique (adapted from Hologic Quick Reference Guide).[9]



First obtain sample from ectocervix using plastic spatula and rinse in container solution by swirling vigorously up to 10 times. Discard.



Obtain endocervix sample using brush, ensuring only bottom-fires are exposed when inserted into cervix. Rotate up to ½ turn in one direction. Rinse brush in container solution by swirling vigorously and pushing brush against vial wall. Discard.

Tighten cap securely, record patient information on the vial with cytology requisition form, and place in specimen bag for processing

Cervical Cancer in British Columbia continued from page 12

above baseline, we found ourselves facing a significant delay in pap test reporting and timely intervention.

To combat this backlog and accelerate results, a transition to liquid-based cytology (LBC) was undertaken in BC.[6] LBC has been used by many provinces for primary cervical cancer screening, including Alberta, Ontario, Saskatchewan, and Manitoba.[7] LBC uses a similar spatula and/or cytobrush as in conventional cytology sample collection. Instead of submitting the sample on a glass side, the liquid sample is transferred to a container with an alcohol-based fixative (Figure 1). This allows for collaboration with off-site diagnostic laboratories to report LBC results (such as Quest and Hologic), to ultimately allow for the CCSL to focus on expedient reporting of conventional cytology pap smears still awaiting analysis. Both methods are clinically equivalent for detecting cervical lesions, and there remain no differences with respect to the follow-up algorithm based on screening result. As of July 2022, training sessions and supplies were offered for select clinics and providers with no added cost. Practitioners and clinics with a high volume of testing were initially prioritized, with full transition to all 6000 providers who offer pap tests in BC now completed.

As part of our provincial and national goal to fight cervical cancer, it is of utmost importance to remain committed and current with all ways we can provide accessible and equitable screening and prevention practices. In addition to updating current practice to accommodate BC's LBC transition, our greatest influence comes from active identification, screening and retention of eligible patients. This includes being mindful of patients in our practice who may be less likely to participate in screening—including, but not limited to, new immigrants, Indigenous, low income, non-English speaking, transgender, gender-diverse, and non-binary patients. To encourage screening retention, we must continue to learn and improve upon offering culturally safe and trauma-informed care, and ensure we have the resources available to promote a welcoming and inclusive clinical space. Moving forward, the ultimate goal is to transition to primary HPV-based screening to target the many barriers faced by these populations, and we encourage you to learn more about BC's at-home cervix screening pilot project as it continues to expand to BC communities.[8] Furthermore, while screening works at the level of secondary prevention, targeting primary prevention of cervical cancer through frequent counselling and recommendation for HPV vaccination continues to have the most significant impact on combatting cervical cancer.

Some of your patients or colleagues may have questions regarding current and changing screening practices in BC and our provincial transition plan to LBC cervical screening. ***The process for provider collection liquid-based cytology (LBC) will be the same for provider testing for HPV in the future.*** For further information regarding the LBC transition and specimen collection, questions may be directed to the Cervical Cancer Screening Laboratory, or you can visit the following website: bccancer.bc.ca/health-professionals/clinical-resources/laboratory-services/cervical-cancer-screening

References

1. Brenner DR, Poirier A, Woods RR, Ellison LF, Billette JM, Zhang SX, Yao C, Finley C, Fitzgerald N, Saint-Jacques N, Shack L, Turner D, Holmes E, for the Canadian Cancer Statistics Advisory Committee. Projected estimates of cancer in Canada in 2022. CMAJ 2022; May 2;194:E601-7.
2. Cervix Screening Program Overview. BC Cancer, 2022. Accessed online August 18, 2022. www.bccancer.bc.ca/screening/Documents/Cervix-Program-Overview.pdf
3. Action plan for the elimination of cervical cancer in Canada, 2020-2030. Accessed online August 18, 2022. www.partnershipagainstcancer.ca/topics/elimination-cervical-cancer-action-plan
4. BC Cancer. Laboratory Services. Accessed online August 18, 2022. www.bccancer.bc.ca/health-professionals/clinical-resources/laboratory-services
5. Baaske A, Brotto LA, Galea LAM, Albert AY, Smith L, Kaida A, et al. Barriers To Accessing Contraception and Cervical and Breast Cancer Screening During COVID-19: A Prospective Cohort Study. J Obstet Gynaecol Can. 2022.
6. BC Cancer. Transition to Liquid Based Cytology Q&A for providers. Accessed online August 18, 2022. www.bccancer.bc.ca/lab-services-site/Documents/20220627%20LBCTransition%20QA%20new.pdf
7. Canadian Partnership Against Cancer. Cervical Cancer Screening in Canada: Environmental Scan. Toronto: Canadian Partnership Against Cancer; 2018. Accessed online August 18, 2022. www.partnershipagainstcancer.ca/wp-content/uploads/2019/01/Cervical-Cancer-Screening-Scan-EN-2018.pdf
8. At-Home Cervix Screening Pilot Project. Accessed online August 18, 2022. https://screeningbc.lpages.co
9. Protocol: endocervical brush/spatula quick reference guide (Hologic). Accessed online August 31, 2022. www.hologic.com/sites/default/files/DS-05867-001_002.pdf

Monoclonal proteins: When should we look for them and what should we do when we find them?

By Dr. Stephen Parkin, Clinical Assistant Professor, Vancouver General Hospital

Introduction

Dr. Stephen Parkin

The presence of a monoclonal protein (M-protein) on serum or urine studies implies the presence of either a clonal plasma cell or lymphocyte population responsible for its production. The clinical importance of this can vary widely from patient to patient. In many cases, the clonal population and M-protein are at sufficiently low levels that no clinical issues are encountered, termed monoclonal gammopathy of undetermined significance (MGUS). MGUS is important as it is common (present in ~5% of patients over 70 years old[1] using routine screening tests and nearly 20% if highly sensitive tests are used)[2] and comes with an approximate 1% per year risk of progression to a more serious disorder.[3] In other cases, the clonal hematologic population may be at much higher levels and may be associated with clinical findings as is seen in patients with multiple myeloma and subtypes of B-cell lymphoma. These can be life threatening conditions that benefit from appropriate therapy. There are also a number of M-protein associated conditions that can lead to important clinical sequelae irrespective of the level of hematologic clone or M-protein, which are collectively termed the monoclonal gammopathies of clinical significance (MGCS). AL amyloidosis is an important example of an MGCS in which a light chain monoclonal protein deposits in various organs as amyloid fibrils leading to organ dysfunction. This condition can present in multiple ways, most commonly with heart failure or nephrotic syndrome as a result of cardiac and renal amyloid deposits.[4]

It is important for all physicians to have a basic understanding of the clinical situations in which monoclonal protein testing is indicated, as well as how to assess the significance of a monoclonal protein once identified.

How and when to test for a M-protein

There are a number of circumstances in which screening for a monoclonal protein is appropriate (Table 1). These are generally findings that may represent a symptomatic monoclonal protein associated disorder, the most common of which include multiple myeloma, indolent B-cell lymphomas (including Waldenstrom's macroglobulinemia), and AL amyloidosis. In these situations, it is reasonable to order both serum and urine protein electrophoresis (SPEP/UPEP). SPEP will identify most clinically significant intact monoclonal immunoglobulins that are composed of a heavy chain (typically IgG, IgA, or IgM) and a light chain (kappa or lambda).[5] UPEP is important to detect monoclonal light chains (without an associated heavy chain) which are usually not detected on SPEP alone.[5] The serum free light chain (SFLC) assay can also be used to sensitively assess the level of free light chains, with a monoclonal light chain inferred by the unbalanced elevation of kappa or lambda light chains (elevated involved light chain value and an abnormal kappa/lambda ratio).[5] This assay can be more difficult to interpret in the setting of renal dysfunction or inflammation however, as levels of polyclonal light chains can become elevated in these settings and this is not reflective of a monoclonal protein.

Table 1: Indications for Monoclonal Protein Testing

- Unexplained laboratory abnormalities, including:
  - Anemia
  - Elevated creatinine
  - Hypercalcemia
  - Hypogammaglobulinemia
  - Hypergammaglobulinemia
  - Elevated total serum protein and/or low serum albumin
  - Rouleaux on peripheral blood smear (a sign of elevated serum proteins)
  - Autoimmune thrombocytopenia or hemolytic anemia
  - Proteinuria/albuminuria
- Unexplained back or other bone pain
- Lytic bone lesions or atraumatic fractures
- Lymphadenopathy/hepatosplenomegaly
- Unexplained heart failure, particularly with infiltrative findings (eg. left ventricular hypertrophy)
- Unexplained peripheral neuropathy

Determining the significance of a monoclonal protein

Once identified, a monoclonal protein must be interpreted in the clinical context of the patient. The first and most important question is whether there are findings concerning for multiple myeloma (such as anemia, hypercalcemia, renal dysfunction, or bone pain/lesions), lymphoma (lymphadenopathy/organomegaly, B symptoms, or cytopenias), or AL amyloidosis (heart failure, nephrotic syndrome, peripheral neuropathy, amongst others). If present, this warrants more urgent evaluation by hematology/oncology. Other rare MGCS entities can present with a wide spectrum of clinical findings, most commonly causing cutaneous, renal, neurologic, or various inflammatory manifestations. These rare conditions should be considered if there are otherwise unexplained symptoms in a patient with a monoclonal protein. A summary of MGCS entities is beyond the scope of this article, but good clinical reviews are available.[6,7]

In the absence of any of these clinical findings, features of the monoclonal protein testing can guide further work up. In the absence of concerning symptoms or laboratory findings, low concentration monoclonal proteins (<15 g/L on SPEP without a significant monoclonal light chain on UPEP/SFLC assay) are very

continued on page 15

Monoclonal proteins continued from page 14

likely to represent MGUS whereas higher concentrations (especially >30 g/L) warrant more expedited workup to rule out more serious conditions. Importantly, MGCS entities such as AL amyloidosis can occur even at low M-protein concentration so a low level monoclonal protein does not automatically imply MGUS and review for any concerning clinical symptoms remains important. The isotype of M-protein can also alter the differential diagnosis being considered. IgG and IgA M-proteins can be produced by clonal plasma cells (more commonly) or lymphocytes and can therefore be associated with almost any monoclonal protein associated disorder. IgM M-proteins are almost always produced by clonal lymphocytes making multiple myeloma very unlikely in these patients and raising suspicion for the possibility of B-cell lymphoma. Figure 1 shows an approach to the work-up of a M-protein once identified.

Conclusion

M-protein associated conditions range from asymptomatic low risk conditions (MGUS) to life threatening diseases (like multiple myeloma) and therefore recognizing the clinical situations in which monoclonal protein testing is appropriate as well as an understanding of how to assess the significance of a monoclonal protein once found is an important skill for any physician.

References

1. Kyle RA, Therneau TM, Rajkumar SV, Larson DR, Plevak MF, Offord JR, et al. Prevalence of monoclonal gammopathy of undetermined significance. N Engl J Med. 2006;354: 1362–1369.
2. El-Khoury H, Lee DJ, Alberge J-B, Redd R, Cea-Curry CJ, Perry J, et al. Prevalence of monoclonal gammopathies and clinical outcomes in a high-risk US population screened by mass spectrometry: a multicentre cohort study. Lancet Haematol. 2022;9: e340–e349.
3. Kyle RA, Larson DR, Therneau TM, Dispenzieri A, Kumar S, Cerhan JR, et al. Long-Term Follow-up of Monoclonal Gammopathy of Undetermined Significance. N Engl J Med. 2018;378: 241–249.
4. Al Hamed R, Bazarbachi AH, Bazarbachi A, Malard F, Harousseau J-L, Mohty M. Comprehensive Review of AL amyloidosis: some practical recommendations. Blood Cancer J. 2021;11: 97.
5. Willrich MAV, Katzmann JA. Laboratory testing requirements for diagnosis and follow-up of multiple myeloma and related plasma cell dyscrasias. Clin Chem Lab Med. 2016;54: 907–919.
6. Dispenzieri A. Monoclonal gammopathies of clinical significance. Hematology Am Soc Hematol Educ Program. 2020;2020: 380–388.
7. Ríos-Tamayo R, Paiva B, Lahuerta JJ, López JM, Duarte RF. Monoclonal Gammopathies of Clinical Significance: A Critical Appraisal. Cancers . 2022;14. doi:10.3390/cancers14215247

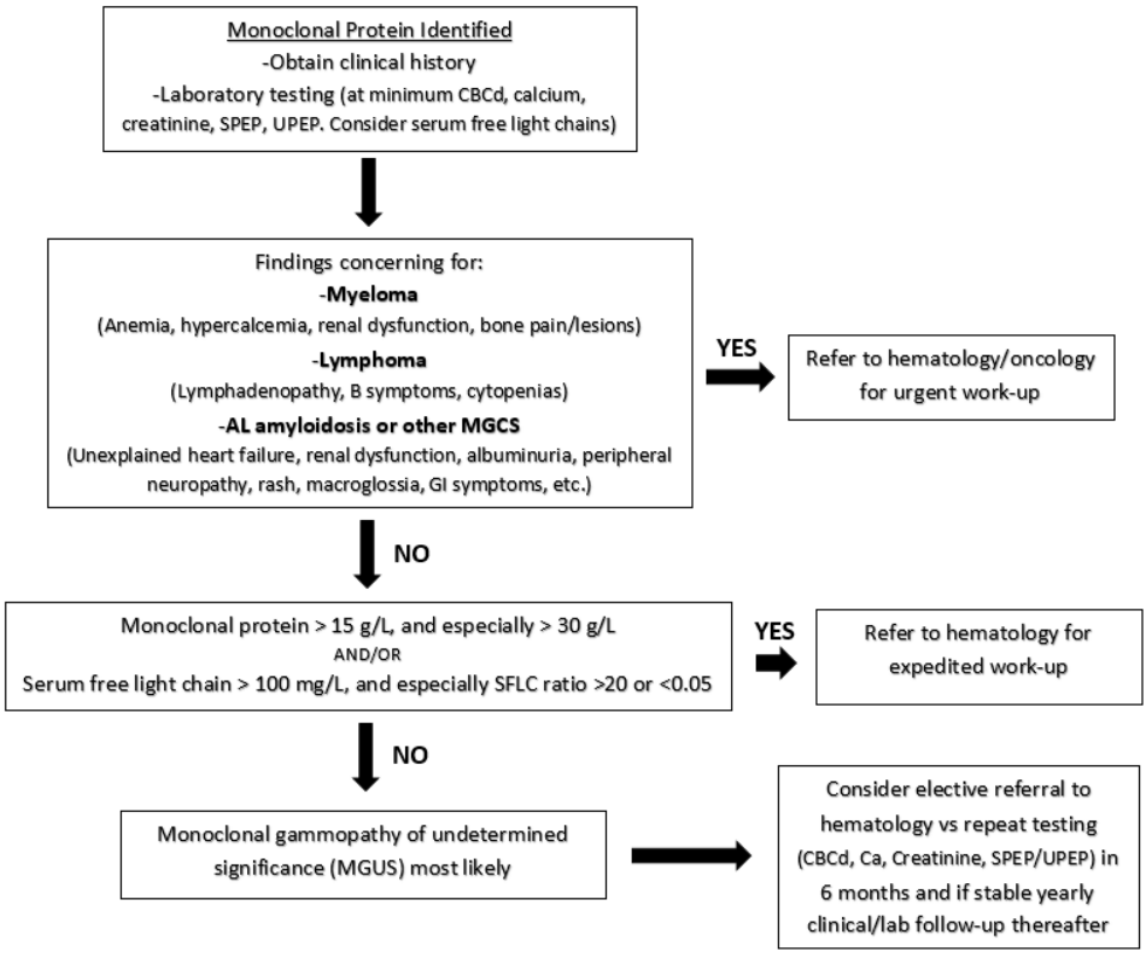


Figure 1 – Approach to the work-up of a monoclonal protein

Childhood and AYA (adolescent and young adult) cancer survivors: The risk of late effects

By Dr. Karen Goodard,
Clinical Radiation Oncologist, BC Cancer

Introduction

Dr. Karen Goodard

Over the past few decades, enormous strides have been made to improve the outcomes for pediatric and AYA (adolescent and young adult) cancer patients living in developed/high income countries. Currently, over 80% of children with cancer who have access to contemporary therapy are expected to survive into adulthood.[1] Increased rates of survival have been driven by coordination of multidisciplinary care, therapy intensification and improved supportive care during treatment.

As a result of therapy, many adult survivors of childhood and AYA cancer are cured of their cancer but face future long-term health problems and risks. These chronic health conditions are called Late Effects (LEs). Patients treated and cured of cancer with intensive chemotherapy and radiation therapy (RT) face future health problems that can be very significant and affect multiple organ systems.[2].

When do late effects occur?

Late effects can occur months to many years after therapy is completed. The convention is that a LE occurs more than 5 years after diagnosis. Unfortunately, the risk of LEs related to RT does not decrease with time – the opposite is true.[3] The risk of LEs continues to increase with time after initial therapy. This does not fit well with many of the ideas we have about patient care or the way in which our current medical system is set up. We are taught to "fix" health problems and then move on. I care for a survivor of AYA cancer who required a heart transplant many years after mediastinal radiotherapy for Hodgkin lymphoma when she was 22 years old. When the symptoms of her heart disease first started, she had been told by many specialist physicians that the severe valve disease, arrhythmias and coronary artery disease couldn't possibly be the result of previous RT, because the treatment was given too long ago.

How serious can late effects be?

Adult childhood cancer survivors (ACCS) are at excess risk of late mortality even 40 years from diagnosis and require life-long follow-up guided by knowledge of their previous cancer and therapy. In one very important study, ACCS treated with RT and intensive chemotherapy, recalled for evaluation of their health many years after therapy, had an 80% risk of at least one serious, life-threatening LE by the time they were 40 years old and many ACCS in this study had multiple, chronic health conditions.[4] Research has also shown that AYA patients (treated between the age of 16 and 39 years) are also at very significant risk for long-term health problems after cancer therapy.[5]

What causes late effects associated with childhood and AYA cancer therapy?

As multimodality, intensive treatment is often used for childhood and AYA cancers, many different factors determine the risk of late effects (LEs).

Patient factors

Pediatric cancer patients are more likely to have an underlying hereditary cancer syndrome than older patients. This may predispose them to an increased risk of LEs such as the development of a second cancer.

Interesting research shows that some of the factors which increase the risk for chemotherapy related side effects are genetic.[6]

The younger the child is at the time of RT, the more likely it is that they will suffer from significant organ damage due to reduced growth and development within the treatment field.[7]

Tumor factors

The tumor itself can lead to LEs. For example, Wilms tumor is a childhood kidney cancer that often destroys one kidney before it is detected and that organ has to be surgically removed. In the long-term, this leads to an increased risk of hypertension.

Treatment factors

Surgery can affect organ function – for example many Hodgkin lymphoma patients in the past had splenectomies as part of a staging laparotomy to establish if their spleen was involved by disease. Splenectomy is no longer indicated in Hodgkin lymphoma patients, but there are patients who received therapy 30 years or more and have asplenism. It is essential that they are given appropriate vaccinations to reduce the risk of overwhelming sepsis.[8]

Chemotherapy: The long-term side effects of chemotherapy depend on the type and amount of drug received. Examples include:

Adriamycin (a type of anthracycline chemotherapy) is associated with a risk of damage to the heart muscle (cardiomyopathy).[6]

Cyclophosphamide (an alkylating agent) is associated with a risk of long-term infertility and increased risk for the development of second cancers.[9]

Cisplatin is associated with high frequency hearing loss and renal damage, which my result in low magnesium levels and early renal failure. In young adults, cisplatin is also associated with a risk of long-term peripheral neuropathy.[10]

Radiation therapy: Long-term side effects of radiation therapy (RT) may occur many years after treatment. The severity of RT related LEs depends on many factors and can be difficult to predict precisely. These factors include the age of the patient at the time of therapy (the younger the patient is, the more likely it is that growth will be affected), the amount of RT given, the organs within the RT treatment field (some organs are very sensitive such as the kidneys), whether chemotherapy is given concurrently with the RT and some individual, genetic factors which are not well understood. While many long-term side effects are unusual, the risk of LEs associated with RT does not decrease with time.

Any patient who has received RT is at significant or "high" risk for LEs – some

continued on page 17

Childhood and AYA cancer survivors continued from page 16

patients who receive intensive chemotherapy are also considered to be in a high-risk category. Many patients who receive less intense chemotherapy alone (such as the treatment given for low-risk leukemia) are in a low-risk category for LEs and unlikely to have major long-term health problems.

What is the nature of these late effects?

Cancer treatment can affect many different organ systems and the nature of any LE will very much depend on all the different factors describe above.

Radiation therapy is the treatment modality most likely to be associated with significant LEs. Long-term side effects of RT include scarring, organ damage and reduced development within the treatment field leading to organ dysfunction/early failure. Scarring and damage to blood vessels leads to early onset vascular disease. Radiation therapy is associated with a significantly increased risk for the development of secondary cancers within the treatment field many years later. The risk of RT induced side effects increases with time after therapy.

Some ACCS groups are far more likely to be affected than others. Central nervous system tumor survivors often receive RT to the brain which affects development. They may have significant neurocognitive problems which affect their ability to work and integrate into society.

It is not surprising that many ACCS have significant psychological problems. Childhood cancer can result in post-traumatic stress and chronic anxiety. ACCS are far more prone to depression.[1]

Please see the clinical example to see how a single individual might be affected by previous multimodality cancer therapy.

What can be done to address late effects?

Practically speaking, it is good for health care providers (HCPs) to think of LEs in terms of current chronic health problems and potential long-term health risks. This helps to focus on the management of ongoing health problems, but also not to forget about appropriate long-term screening and lifestyle recommendations (to prevent or reduce the risk of these problems).

ASCO and the COG recommend the development of a "survivorship care plan" for patients at the time of discharge from oncology programs. This plan documents patients' previous cancer, treatment details and initial complications of that therapy together with an outline of future recommended focussed screening and life-style recommendations. Over time, these recommendations are very likely to change as we learn more about LEs and the health of cancer survivors.

At the BC Children's Hospital, it is has been routine for many years to provide patients and their families with information about the previous cancer and therapy prior to discharge from the program together with screening and lifestyle recommendations.

In BC, patients at significant risk for LEs are referred to the Late Effects, Assessment and Follow-up (LEAF) Clinic for ongoing care.

The LEAF clinic is a BC Provincial survivorship/ after-care program. Our goal is to provide:

- Medical care
  - Detect and monitor for LEs:
    - > Patients are transferred from the BCCH oncology program to the LEAF clinic for follow-up as they age out of pediatric care.
    - > We accept ACCS treated in other Canadian Provinces who have moved to BC.
    - > We contact ACCS treated in BC many years ago and ask if they would like to be evaluated for long-term health risks to check that they are receiving appropriate screening.
  - Organize screening investigations
  - Coordinate specialist and primary care
  - Provide lifestyle information and advice
- Psychosocial support
  - Patient and family counseling address psychological problems such as depression, anxiety and post-traumatic stress.
  - Provide practical assistance to access resources such as disability benefits
  - Develop
    - > Links with rehab programs
    - > Support groups
    - > Wellness program focusing on diet, exercise and mental well-being
- Education
  - We organize teaching and clinical attachments for HCPs (Medical and nursing undergraduates, residents, primary and specialist care providers).
  - We provide ACCS and their families with information about LEs and how to best try to mitigate and address these problems.
- Research
  - We are learning more about LEs through our clinical programs.

Our aim is to build a collaborative program focusing on how to reduce the risk and severity of late effects and improve survivor's quality of life. We use screening recommendations and clinical practice guidelines developed by groups such as the Children's Oncology Group[12] and the European PanCare Network.[13]

Appropriate screening is very important, but lifestyle choices significantly impact the risk of LEs. Healthy choices such as regular exercise, a healthy diet, avoiding smoking and excessive alcohol intake together with sun protection have been shown to reduce the risk of LEs in ACCS.

Adult childhood cancer survivors represent a growing patient population with a significant risk for developing medical complications over time. We provide a resource in British Columbia to address their medical needs.

If you care for a long-term cancer survivor in your practice and you would like advice regarding potential late effects, please do not hesitate to contact us.

Here is our contact information:
Late Effects, Assessment
and Follow-up (LEAF) Clinic
www.bccancer.bc.ca/our-services/services/late-effects-assessment-follow-up
Phone: 604-877-6070
Toll Free: 1-844-677-6070
Email: ACCS@bccancer.bc.ca

Resources

Here are some useful resources where you can learn more about the topics of childhood and AYA cancer survivorship and late effects:

Children's Oncology Group (COG) Survivorship Guidelines: https://childrensoncologygroup.org/survivorshipguidelines

National Cancer Institute (NCI): Late Effects of treatment for Childhood Cancer https://www.cancer.gov/types/childhood-cancers/late-effects-hp-pdq

continued on page 19

Childhood and AYA (adolescent and young adult) cancer survivor: clinical case

A 38-year-old man was contacted for "recall" at a survivorship/after care clinic. He was previously treated for acute lymphoblastic leukemia (ALL) with combination chemotherapy and radiation therapy (RT) when he was only 2 years old. His chemotherapy included Adriamycin and cyclophosphamide. He had received cranial RT (2000 cGy in 12 fractions to his whole brain) and spinal RT (1200 cGy in 5 fractions) – relatively low doses of RT.

He had not been evaluated by an oncologist for many years.

The long-term health risks which should be considered for this patient, include

THYROID NODULES AND LOW GRADE THYROID MALIGNANCY: Very low dose scattered radiotherapy increases the risk of thyroid cancer and benign nodules. The thyroid cancer that arises in these circumstances is a papillary carcinoma and is a very low-grade indolent tumor, which is rarely, if ever, life threatening. The treatment of thyroid cancer is surgical.

His thyroid gland should be examined clinically every year for nodules and it would be prudent to perform an ultrasound of the gland every 5 years or so for routine screening (if he does not have thyroid nodules). If he has nodules, then screening should be more frequent. Depending on the size and nature of the nodules, FNA may be indicated.

HYPOTHYROIDISM: Under-activity of the thyroid (hypothyroidism) is very common after head and neck radiation therapy. This would not be easy to detect clinically and he should have his serum TSH checked once a year. Hypothyroidism is easily treated by thyroid replacement therapy.

METABOLIC SYNDROME: He will be at increased risk of metabolic syndrome. This is associated with high blood pressure, an increased risk of obesity, higher than normal serum lipids and an increased risk of diabetes. Metabolic syndrome leads to accelerated cardiovascular and cerebrovascular disease. Regular exercise is recommended and his blood pressure should be checked annually. He should also have his fasting lipid profile and glucose checked every year.

The Heart and Stroke Foundation of Canada have an online resource outlining healthy lifestyles: www.heartandstroke.ca/get-healthy

CEREBROVASCULAR EVENT: He will be at increased risk of a cerebrovascular event causing a stroke or TIA. Both cerebral hemorrhage and thrombosis are more common many years after cranial radiation therapy due to direct damage to the cerebral blood vessels. This risk is small and probably in the range of 2% to 3% many years after therapy but is greatly increased by the presence of hypertension and metabolic syndrome.

CARDIOMYOPATHY: He received Adriamycin (an anthracycline) as part of his previous therapy and there is a small risk of cardiomyopathy associated with this therapy. He should have intermittent screening echocardiograms.

LOW GRADE MENINGIOMAS: Patients who have had whole brain radiotherapy are at risk for benign radiation induced meningiomas within the radiotherapy field. Meningiomas result from an overgrowth of the meningeal layer (a layer of tissue that surrounds the brain). We recommend that he should have a screening MRI scan of his head every 3 years starting at 10 years after completion of his radiation therapy.

SECOND MALIGNANCY: As a result of his previous radiation therapy, there is a small risk of a malignant secondary neoplasm. This would be very unusual. Unfortunately, it is not possible to effectively screen for these tumors. He should be informed to contact his family doctor or the survivorship clinic promptly should any new symptoms arise, such as significant headaches or new swelling.

He is at increased risk for the development of skin cancers (especially basal cell cancers within the previous RT field). He should avoid sunburn, wear a hat in the summer and use sunscreen. His skin should be examined at least once a year. These cancers are generally low-grade basal cell carcinomas, which grow very slowly and do not spread to other regions.

He received alkylating agent chemotherapy which can be associated with bladder cancer. Should he ever develop hematuria, he should have a screening cystoscopy.

He had alkylating agent chemotherapy which slightly increases the risk of second cancers later in life. It would be important that he never smoke.

He is at increased risk for colorectal polyps and cancers as a result of his previous spinal RT and alkylating agent chemotherapy. It would be prudent for him to have an early screening colonoscopy.

continued on page 19

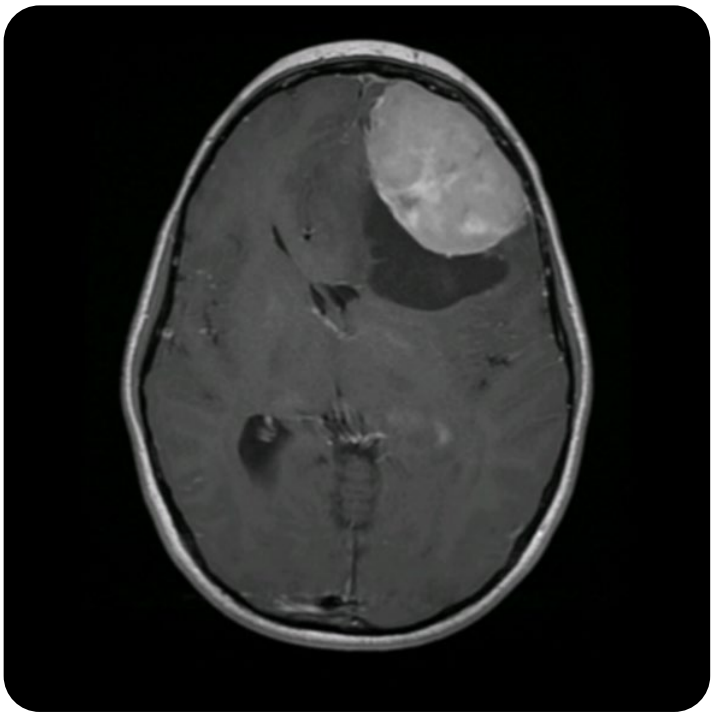


Figure 1: Axial T1 post gad1 showing a large, left frontal meningioma in a 38 year-old-man treated for acute lymphoblastic leukemia at 2-years-old.

Childhood and AYA clinical case continued from page 18

INCREASED RISK OF EARLY OSTEOPOROSIS: As a result of his prior intensive chemotherapy, he is at slightly increased risk of development of generalized bone density loss as he gets older. Regular exercise, a healthy diet containing sufficient calcium (1000 mg per day) and vitamin D (at least 1000 IU a day) is very important.

AVASCULAR NECROSIS: This can occur after intensive therapy for childhood leukemia including high dose steroids and can result in pain and loss of function in joints. This can occasionally occur as a late complication of therapy and if joint pain develops in the future, this diagnosis should be considered.

INFERTILITY: Alkylating agent chemotherapy can be associated with a risk of infertility.

IMMUNE DYSFUNCTION: Humoral immunity is affected by previous intensive chemotherapy. Antibody levels to previous vaccinations are likely to be reduced. He may need revaccination (MMR booster) depending on the vaccinations he received after completion of his chemotherapy.

DEPRESSION AND ANXIETY: Depression and anxiety are common among childhood cancer survivors.

LEARNING DISABILITY: His previous radiation therapy at a young age and intrathecal methotrexate can be associated with poor short term memory and difficulty concentrating.

CATARACTS: Radiation therapy is associated with a risk for the development of cataracts (cloudiness or opacification of the lens of the eye). This would not be a serious risk to his vision and would be treated easily with surgery.

The Children's Oncology Group has general guidelines for follow-up after treatment for childhood and AYA (adolescent and young adult) cancer at: http://www.survivorshipguidelines.org

Many aspects of these guidelines are very likely to change over time, but give a useful overview of the different long-term health risks associated with his previous therapy. It is extremely likely that these guidelines will change in the years to come as we learn more about long-term health problems in ACCS.

Assessment: He was found to have a meningioma, a basal cell cancer of his forehead, hypertension and metabolic syndrome. Colonoscopy was positive for 3 colorectal adenomatous polyps.

This is a MR image of his meningioma which was not associated with any acute neurological symptoms and required surgical resection.

He has recovered from surgery for his meningioma (which had likely been present for many years prior to contact with the survivorship clinic). His basal cell cancer was treated by a dermatologist. His adenomatous colon polyps were removed via colonoscopy and his risk for bowel cancer is now reduced. He is addressing his metabolic syndrome with diet and exercise. His hypertension is now treated to reduce the risk of cerebrovascular disease. These health problems were detected by focussed screening informed by knowledge of his previous cancer therapy.

Childhood and AYA cancer survivors continued from page 17

University of British Columbia CME module about Late Effects: https://elearning.ubccpd.ca/course/view.php?id=44

References

1. Butler E, Ludwig K, Pacenta HL, Klesse LJ, Watt TC, Laetsch TW. Recent progress in the treatment of cancer in children. CA *Cancer J Clin*. 2021;71(4):315-332. doi: 10.3322/caac.21665.
2. Landier W, Skinner R, Wallace WH, et al. Surveillance for late effects in childhood cancer survivors. *J Clin Oncol*. 2018;36(21):2216-2222. doi: 10.1200/JCO.2017.77.0180.
3. Han JW, Kim HS, Kim BS, et al. Increasing and worsening late effects in childhood cancer survivors during follow-up. *J Korean Med Sci*. 2013;28(5):755-762. doi: 10.3346/jkms.2013.28.5.755.
4. Hudson MM, Ness KK, Gurney JG, et al. Clinical ascertainment of health outcomes among adults treated for childhood cancer. *JAMA*. 2013;309(22):2371-2381. Accessed 20130612. doi: //dx.doi.org/10.1001/jama.2013.6296.
5. Chao C, Bhatia S, Xu L, et al. Chronic comorbidities among survivors of adolescent and young adult cancer. *J Clin Oncol*. 2020;38(27):3161-3174. doi: 10.1200/JCO.20.00722.
6. Ding Y, Du K, Niu Y, Wang Y, Xu X. Genetic susceptibility and mechanisms underlying the pathogenesis of anthracycline-associated cardiotoxicity. *Oxid Med Cell Longev*. 2022;2022:5818612. doi: 10.1155/2022/5818612.
7. Paulino AC, Wen BC, Brown CK, et al. Late effects in children treated with radiation therapy for wilms' tumor. *Int J Radiat Oncol Biol Phys.* 2000;46(5):1239-1246.
8. Bisharat N, Omari H, Lavi I, Raz R. Risk of infection and death among post-splenectomy patients. *J Infect.* 2001;43(3):182-186.
9. Travis LB, Curtis RE, Glimelius B, et al. Bladder and kidney cancer following cyclophosphamide therapy for non-hodgkin's lymphoma. *J Natl Cancer Inst.* 1995;87(7):524-530.
10. McTiernan A, Jinks RC, Sydes MR, et al. Presence of chemotherapy-induced toxicity predicts improved survival in patients with localised extremity osteosarcoma treated with doxorubicin and cisplatin: A report from the european osteosarcoma intergroup. *Eur J Cancer.* 2012;48(5):703-712.
11. Zebrack BJ, Zeltzer LK, Whitton J, et al. Psychological outcomes in long-term survivors of childhood leukemia, hodgkin's disease, and non-hodgkin's lymphoma: A report from the childhood cancer survivor study. *Pediatrics*. 2002;110(1 Pt 1):42-52.
12. Mulder RL, van Kalsbeek RJ, Hudson MM, Skinner R, Kremer LCM. The critical role of clinical practice guidelines and indicators in high-quality survivorship after childhood cancer. *Pediatr Clin North Am.* 2020;67(6):1069-1081. doi: 10.1016/j.pcl.2020.07.003.
13. Hjorth L, Haupt R, Skinner R, et al. Survivorship after childhood cancer: PanCare: A european network to promote optimal long-term care. *Eur J Cancer.* 2015;51(10):1203-1211. doi: 10.1016/j.ejca.2015.04.002.

Prostate Cancer and support groups

By Norm Dooley, Patient Partner, BC Cancer Supportive Care Program

Most men diagnosed with prostate cancer are alike in their fear and uncertainty. Each is unique, however, in how he comes to terms with the condition.

My story of cancer induced anxiety and final reconciliation is one that was assisted by a local prostate cancer support group. It began with a chance encounter with a lab requisition form a decade ago. On the way to the lab for an unrelated test, I remembered that I had not asked my doctor for a PSA test, noticed the PSA box and checked if off, and then went for the test. Two days later, I got a call from my physician directing me to the Prostate Centre at VGH. The urologist did not seem overly concerned about my test results and suggested that we "wait and see". I relaxed. Eighteen months, several PSA tests and one biopsy later, I was diagnosed with aggressive cancer. My once sanguine urologist suggested that I would die if the cancer was not treated right away. I began to worry.

Anxiety is compounded by delays and lack of information. It took a while for the next round of tests— a bone scan and a CT scan—to take place. A consultation with a radiation oncologist was also suggested. But none of these came quickly. As I waited, I worried more. I found myself sitting alone some nights contemplating death over a glass of brandy. I was also perplexed by the decision as to the form of treatment to have.

Questions swirled around the treatment decision. Could my cancer be treated effectively at all? What form of treatment was most effective? On what basis should I choose a form of treatment? What piece of information is most critical? If successful, how long would I have until recurrence? Just how much importance should I give to the side effects of either radical surgery or extensive radiation, and how should they be weighed in my decision? I needed more information.

My appointment with a radiation oncologist finally came and I was fortunate to be assigned someone who had both time and patience. He answered all of my seven pages of questions that I had brought along. He was calm and attempted to assuage my anxiety. He was also someone who had a real appreciation of what a PC support group might do for me. He suggested that before making a treatment decision that I read more about the condition and that I also attend a session of the Vancouver support group.

A few days later, I walked into my first group session. It was filled with "old timers"—men who had had been treated years earlier—together with a few "newbies" like me. The session was engaging. There was a speaker from a cancer research field. People were open and keen to talk about their own experience. The atmosphere was relaxed, and I noticed that those who came regularly found the sessions helpful long after their treatments had been completed. I also sensed that I was among others who understood how I felt and who wanted to be of assistance to someone like me. Members of the group had important information that related directly to my state.

There was a tremendous reservoir of collective experience and knowledge about prostate cancer residing within the group. I also noted that many of the attendees had been treated many years earlier—some as many as twenty years— and were still healthy and active. The group had a calming effect. As a newly diagnosed, I had a strong need to meet and talk with people who had been through a process that I was about to begin. It was reassuring to know that I was truly not alone and that I would get through the treatment phase.

I returned to the group the following month and I continue to attend years later. As time has passed, the support group has played a positive role in my life by increasing my understanding of prostate cancer, and by introducing me to people who have been good models of how to deal with the condition. Over that time, I have distilled several characteristics of what makes a good support group work for someone like me.

While some prefer to deal with their cancer on their own, others need to talk with someone who has been through the experience earlier. The support group provides such a channel. Sessions provide a time for small group sharing—unstructured opportunities for people to raise questions and talk about their conditions openly. This is a kind of support that is hard for family members and friends who have not had cancer to replicate.

I learned that there is a wide variety of information and skills needed by men with prostate cancer. Support groups funnel information on cancer research, and treatment innovations. nutrition, the role of exercise, urinary incontinence, sexual dysfunction and health and life-style management. My support group has hosted some ninety different presentations on subjects related directly to or associated with cancer and its impacts over the last decade.

I also discovered that Prostate Cancer is a condition that can stay with you for the remainder of your life. Some of the side effects of my primary treatment began to emerge only years later and had to be

continued on page 21

Family Practice Oncology Network (FPON) Continuing Medical Education Webcasts

The Network strives to provide directly relevant, accessible oncology continuing medical education opportunities for primary care providers in BC, the Yukon and beyond. Webcasts are presented in partnership with UBC's Division of Continuing Professional Development and are held 8-9:00 a.m. (Pacific time) the third Thursday of every month (except July, August and December). Our complimentary Webcasts provide opportunity to participate in topical, interactive oncology continuing medical education opportunities from anywhere with Internet access and are delivered via ZOOM. Future topic information and links to Registration can be found on our website www.bccancer.bc.ca/health-professionals/networks/family-practice-oncology-network/continuing-medical-education#Webcasts

Upcoming Webcasts

October 19: Prostate Cancer Screening and Early Prostate Cancer Management (Dr. Marie-Pier St.-Laurent):

By the end of this session, participants will be able to:

1. State current prostate cancer screening recommendations;
2. Describe the diagnostic process; and
3. Summarize management options for early prostate cancer.

November 16: Female Sexual Health & Cancer Survivorship (Dr. Melanie Altas)

Prostate Cancer and support groups continued from page 20

treated. Effective groups tailor their meetings to members at all points of the cancer experience. I also found out that PC is not always cured—only postponed. Recurrence is a real possibility, and with the return of cancer there also comes a new series of questions to answer and the need for information related to treatment decisions. An effective group recognizes that there are stages in the journey and responds.

I observed that as a result of their own cancer, many men want the opportunity to be of assistance to others. Despite the improved survival rates that occur following primary treatment, several group members, whom I met early on, have succumbed to their condition. Incredibly, my local group provided opportunities for those men, who knew that they were soon to die, the chance to volunteer and share their story with others right up to the end. The support group provided a link that enabled them to contribute to those who would live on. It was for them a form of personal legacy.

Prostate Cancer support groups help many men cope. And, they are incredibly cost effective, but only because of the dedication of a small group of volunteers in each of the 17 support groups across BC. They have no formal connection with the health care system nor with social support systems. Instead, groups are left to their own initiative and ingenuity to survive. Locations have to be found, participation must be maintained, meetings organized, speakers secured, and new communication technologies like Zoom, mastered and used. And those demands are constant month after month, year in and out.

Support groups face other challenges too. And this is where the medical community can be of real assistance. Here are a few ways by which health care professionals can make a real contribution to these groups' survival and success.

1. Support groups need people to support. Oncologists, urologists, family physicians, nurses and counsellors can help by making newly diagnosed patients aware of the local support group and suggesting that they attend a session. Most men do not stay involved with a support group for a time. They get what they need and go on. As a result, it is important that groups receive "newbies" on a regular basis to survive and fulfill their purpose.
2. Provide support group contact information that is posted in your facilities where patients can find it. Ask for brochures or business cards from your local group that you can distribute to your patients. BC Cancer in Vancouver regularly asks for the Vancouver group's contact information and provides it to new patients.
3. Be willing to attend and contribute from time to time. Groups need your expertise, and as a member I can attest that a presentation or question and answer period with a medical specialist or researcher at our meetings is extremely valuable. You can ask to be put on the speakers' resource list of your local group. Information and expertise is part of the life-blood of a good support group. We value your knowledge, and your presence adds medical authenticity to the group's work.
4. Invite support group representatives to on-going projects that you are involved in and especially those projects that involve improving patient care, patient awareness, and patient services.
5. Direct prostate cancer research projects to support groups. Both medical researchers and academics are frequently looking for people who have or have had prostate cancer, to participate in their research. Support groups are happy to assist in finding volunteers.

I know from my work as a patient partner at BC Cancer that the system is keenly interested in ensuring that it stays responsive to the people that it serves. Assisting Prostate Cancer support groups is another way to demonstrate that responsiveness. Importantly, in their own unique ways support groups can greatly assist the newly diagnosed with the challenges of dealing with their cancer.

PC SC Prostate Cancer Supportive Care

VANCOUVER PROSTATE CENTRE
A UBC & VGH Centre of Excellence

PROSTATE CANCER SUPPORTIVE CARE PROGRAM

Patients must register into the program.
Virtual group education sessions are available to all registered patients.
**** Clinical appointments are available only to BC patients. ****

INTRODUCTION TO PROSTATE CANCER & PRIMARY TREATMENT OPTIONS

A 1.5-hour virtual group education session for newly diagnosed prostate cancer patients, jointly presented by a urologist and a radiation oncologist. Diagnosis, treatment options and side effects are discussed, as well as how the PCSC Program can support you before, during and after treatment.

MANAGING THE IMPACT OF PROSTATE CANCER TREATMENTS ON SEXUAL FUNCTION AND INTIMACY

A 1.5 hour virtual group education session that focuses on the sexual consequences of prostate cancer treatments and how to optimize the sexual adaptation process, which includes both sexual and penile optimization. One-on-one appointments are also available with our sexual health clinician which includes a telephone consult with our sexual medicine urologist.

EXERCISE FOR PROSTATE CANCER PATIENTS

A 1.5-hour virtual group education session for patients wishing to increase their physical activity levels and to improve overall health with a long-term behavior change. One-on-one appointments are also available with our exercise physiologist.

RECOGNITION & MANAGEMENT OF TREATMENT RELATED SIDE EFFECTS OF ANDROGEN DEPRIVATION THERAPY (ADT)

A 1.5-hour virtual group education session for prostate cancer patients who are starting or are currently on hormone therapy (ADT). A nurse practitioner explains how ADT works and presents the possible side effects and ways to manage these side effects. One-on-one appointments are also available with our nurse practitioner.

PELVIC FLOOR PHYSIOTHERAPY FOR BLADDER & BOWEL CONCERNS

A 1.5-hour virtual group education session for patients pre and post-prostate cancer treatment to understand ways to reduce the effects of surgery and radiation therapy on bladder and bowel function. Our physiotherapist offers three complimentary one-on-one appointments for patients experiencing bladder and bowel concerns 12 weeks post-treatment.

COUNSELLING SERVICES

Six private, confidential appointments for prostate cancer patients with our registered clinical counsellor. Counsellors can help explore how to cope with difficult emotions and provide information about group programs and community resources.

METASTATIC DISEASE MANAGEMENT

A 1.5-hour virtual group education session for patients with metastatic prostate cancer. The topics of this session include an overview and treatment options for both types of metastatic disease: hormone sensitive and castrate resistant.

NUTRITION ADVICE FOR PROSTATE CANCER PATIENTS

A 1.5-hour virtual group education session for patients to learn how to use their diet to help reduce the risk of recurrence or progression of prostate cancer, manage treatment-related side effects and plan for a healthy future. One-on-one appointments are also available with our registered dietitian.

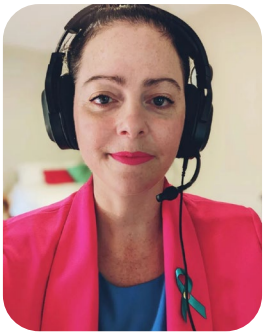
FOR MORE INFORMATION OR TO REGISTER, PLEASE CONTACT:

PCSC PROGRAM COORDINATOR
PH: (604) 875-4485 | E: PCSC@VCH.CA
VISIT OUR WEBSITE: WWW.PCSCPROGRAM.CA

How family doctors can help prevent Ovarian Cancer

Alicia Tone, PhD; Scientific Advisor, Ovarian Cancer Canada
atone@ovariancanada.org

Why prevention is key to changing outcomes for ovarian cancer



Alicia Tone

Ovarian cancer (OC) is the fifth most common cause of cancer deaths in Canadian women. Approximately 3,000 Canadians will be diagnosed in 2023; more than half will die within 5 years of diagnosis. While many individuals with OC are living longer and better with advances in treatment and supportive care, 75% of patients continue to be diagnosed at a late stage (stage III or IV) and long-term survival rates have not changed in 50 years.[1,2,3]

So why is OC so hard to detect at an earlier, potentially curable, stage? To understand this, it is important to appreciate that OC is not one disease; rather, the term "ovarian cancer" refers to a group of diseases that originate at or near the ovaries. Each type of OC is associated with a distinct tissue and/or cell of origin, risk factors, precursor lesions, molecular alterations, response to treatment and prognosis.[4] This complexity has resulted in a lack of reliable screening methods that can detect the different types of OC at an early enough stage to impact mortality.[5] While most individuals with OC report experiencing symptoms prior to their diagnosis (e.g., persistent bloating, difficulty eating, abdominal pain/discomfort, changes in urinary habits).[6] symptoms are typically non-specific and attributed to other causes. Furthermore, the most common and lethal type of OC, high-grade serous carcinoma, typically starts in the fallopian tubes and can spread when the primary tumour is still very small and before symptoms appear. While the scientific community is searching for new solutions for early detection and precision oncology, **prevention is our most effective tool for decreasing the incidence of, and mortality from, OC now.**

Ovarian cancer prevention: one size does not fit all

In order to determine the best prevention strategy, you must first understand an individual's estimated lifetime risk for OC.

Anyone born with ovaries is at some risk for OC; in the absence of other risk factors, the lifetime chance of developing OC is around 1.5% (1 in 70). For individuals in this "average risk" population, opportunistic salpingectomy (OS) – surgical removal of the fallopian tubes (but not ovaries) in individuals planning to undergo gynecologic surgery (e.g., tubal sterilization, hysterectomy) for reasons unrelated to OC – is the best option for decreasing OC risk.[7,8] The role of OS in OC prevention has previously been covered in the Spring 2022 Journal found at fpon.ca in the Journal of Family Practice Oncology section previous issues links.

A simplified pathway for preventing OC in the "high-risk" population is shown in Figure 1; the importance of genetic testing in this pathway cannot be understated. Clinical recommendations for management of previvors (individuals confirmed to be at high genetic risk for OC) are shown in Table 1.[9,10] In contrast to individuals at average risk for OC, those at high risk are recommended to undergo surgical removal of ovaries and fallopian tubes (risk-reducing salpingo-oophorectomy, RRSO). While surgical menopause resulting from RRSO can be life-altering, this procedure can also be lifesaving: OC risk is reduced by up to 98% if surgery is performed in accordance with age recommendations, and breast cancer risk in *BRCA1/2* mutation carriers is cut in half if RRSO is performed prior to natural menopause.[10,11,12,13]

continued on page 24

Figure 1. Prevention in individuals at high risk for OC: a simplified view.

1) Identify individuals who may be at increased risk for OC

- ✓ Inherited mutation in an OC risk gene in a close relative
- ✓ Family history of ovarian or other cancers - such as breast, endometrial, colorectal, pancreatic or prostate - on either side of the family
- ✓ Personal history of breast cancer
- ✓ Belonging to a specific ethnic community (e.g., Ashkenazi Jewish or French-Canadian) associated with higher prevalence of mutations in OC risk genes

2) Confirm increased OC risk through genetic testing

- ✓ Timely referral to genetic counselling
- ✓ Genetic testing of hereditary cancer genes, if appropriate

3) Reduce OC risk in confirmed previvors

- ✓ Timely referral to gynecologic surgeon
- ✓ Pre-surgical consult, risk-reducing surgery and appropriate after-care

Table 1. Lifetime risk and recommendations for risk reduction in individuals with inherited mutations in OC risk genes.

Gene/s	Estimated risk for OC*	Recommended age for risk-reducing salpingo-oophorectomy**
BRCA1	39-44% by age 70	35-40 years
BRCA2	11-18% by age 70	40-45 years
MSH2, MLH1, MSH6, PMS2, EPCAM ("Lynch Syndrome")	~10-20% by age 70	Timing individualized
RAD51C, RAD51D	~11-13% by age 80	Consider at 45-50 years
BRIP1	~6% by age 80	Consider at 45-50 years
PALB2	~5% by age 80	Based on family history or >45 years

*Mutation carriers are also at increased risk for other cancers, depending on the affected gene.
**Family history will also be considered when determining optimal timing for an individual patient.

How family doctors can help prevent ovarian cancer continued from page 23

Ovarian Cancer Canada's work with previvors, genetics clinics and gynecologic surgeons from across Canada has revealed many gaps and inequities that must be addressed in order to maximize the opportunity for OC prevention in Canada.[14,15] Of note, a lack of discussion on family cancer history with primary care physicians is likely contributing to missed opportunities from the outset: of 60+ previvors we spoke with 61% denied discussing their family's cancer history with their family doctor prior to genetic testing, and only 11% reported that it was their family doctor who recommend that they pursue genetic testing.

How can family doctors help?

Understanding an individual's estimated lifetime risk of OC is the necessary first step to knowing how best to support them in their journey to prevention. Table 2 outlines concrete steps that you can take to help your patient navigate the pathway to OC prevention, depending on their personal/family circumstances. The resources listed below may also be helpful for both primary care physicians and their patients.

- Ovarian Cancer Canada website ovariancanada.org
  - Prevention information and resources https://ovariancanada.org/?s=prevention This section of the Ovarian Cancer Canada website includes information on the role of genetics in OC, genetic counselling and testing, and surgical and non-surgical risk reduction strategies. It also contains links to relevant webinars and patient tools.
  - Talking to your family doctor about ovarian cancer. https://ovariancanada.org/resources/talking-to-your-family-doctor-about-ovarian-cancer includes a printable worksheet that is designed to help facilitate effective conversations on OC risk.
- BC Cancer Hereditary Program www.bccancer.bc.ca/health-professionals/clinical-resources/hereditary-cancer includes a referral form that outlines detailed criteria for genetic counselling/testing for hereditary cancer genes in BC.
- Canadian Association of Genetic Counsellors (CAGC) website. This website www.cagc-accg.ca includes a list of all genetics clinics in Canada, for patients outside of British Columbia.
- Gynecologic Cancer Survivorship Clinic https://brcainbc.ca/gynecologic-oncology-survivorship-clinic This clinic is led by Dr. Lesa Dawson MD FRCSC in Vancouver and specializes in the care of individuals at high risk for OC. For questions on specialized clinics outside of British Columbia, contact atone@ovariancanada.org
- SOGC Clinical Practice Guideline: Gynaecologic Management of Hereditary Breast and Ovarian Cancer www.jogc.com/article/S1701-2163(18)30522-X/pdf
- Commercially available genetic testing. The following companies offer clinical-grade genetic testing for individuals who do not

continued on page 27

Table 2. Steps that family doctors can take to prevent OC.

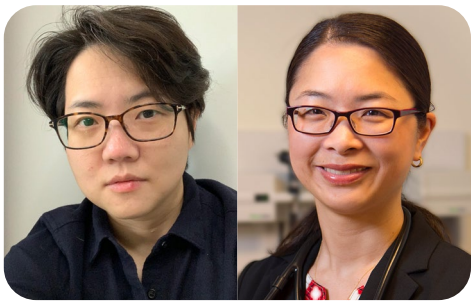
To help identify and manage individuals/families at high risk for OC	
If your patient:	**Then you should:**
✓ Has a family history (on either the maternal or paternal side) of ovarian, breast, pancreatic, prostate, colorectal and/or endometrial cancer; AND/OR ✓ Has a personal history of breast cancer; AND/OR ✓ Is a member of a high-risk ethnic community	✓ Send a referral for genetic counselling*
✓ Has been found to have an inherited mutation in an OC risk gene; AND ✓ Has not been personally diagnosed with OC	✓ Discuss risks and benefits of RRSO (risk-reducing salpingo-oophorectomy) ✓ Send a referral to a high-risk clinic or gynecologic surgeon who has experience performing RRSO
✓ Has been found to have an inherited mutation in an OC risk gene; AND ✓ Has been diagnosed with OC	✓ Encourage them to discuss their genetic result with their family members, and the importance of cascade genetic testing to understand their own risks
✓ Has been diagnosed with OC; AND ✓ Has not had genetic testing	✓ Reinforce** the potential benefits of genetic testing for both the patient themselves (treatment, prevention of other cancers) and their family members (prevention)
To help prevent OC in individuals at average risk	
If your patient:	**Then you should:**
✓ Does not have a relevant personal or family history of cancer, or ethnicity AND ✓ Is considering tubal ligation for permanent contraception	✓ Discuss opportunistic salpingectomy as a safe and effective contraceptive choice that also prevents OC
✓ Does not have a relevant personal or family history of cancer, or ethnicity AND ✓ Is undergoing a hysterectomy for reasons unrelated to OC	✓ Discuss benefit of opportunistic salpingectomy for OC prevention

*These genetics experts will then determine whether your patient should consider genetic testing of hereditary cancer genes. A listing of all genetic clinics can be found at the CAGC (Canadian Association of Genetic Counsellors) website.

**Your patient should be offered genetic testing as part of their ovarian cancer care

Primer on systemic therapies for advanced lung cancers in 2023

By Dr. Florence T.H. Wu (PGY-5, BC Cancer), Prof. Cheryl Ho (Medical Oncologist, BC Cancer Vancouver)



Dr. Florence Wu Cheryl Ho

Lung cancers remain the leading cause of cancer deaths (21%) in 2023.[1] Historically, before the introduction of lung cancer screening programs, ~50% of lung cancers are diagnosed at stage IV with metastatic dissemination. Prior to the era of precision oncology, 5-year survival rates had been in the order of <10% for stage IV lung cancers.

However, the landscape of systemic therapy options for unresectable or metastatic lung cancers has evolved dramatically in the recent 5 years, with the expansion of targeted options and inclusion of immunotherapy in the treatment algorithms.[2] Here we summarize five take-home messages for our primary care physician colleagues.

1. Molecular characterization is key.

Currently at BC Cancer, all non-small cell lung cancers (NSCLC) are subjected to immunohistochemistry testing for tumor cell expression of PD-L1 to assess appropriateness of first-line immunotherapy. In non-squamous NSCLC, additional immunohistochemical tests include ALK and ROS1 translocations with confirmatory fluorescent in-situ hybridization as needed. Non-squamous NSCLC is also further subjected to next-generation sequencing for DNA/RNA alterations using the Illumina Focus panel, to look for potential oncogenic drivers that can be managed with targeted therapy (Table 1). Non-smokers are more likely to have EGFR-mutated NSCLC, while smoking history is more strongly associated with KRAS mutations.[3] (Figure 1). Squamous NSCLC and small cell lung cancer (SCLC) do not undergo DNA/RNA sequencing because targeted therapies have not been identified yet for these subsets of patients.

continued on page 26

Table 1. Targeted therapy options for oncogene-driven advanced NSCLC.

Oncogene	Alteration	Targeted therapy
EGFR	Exon 19 deletion L858R mutation (exon 21) T790M resistance mutation	 osimertinib
EGFR	other rare mutations	afatinib, gefitinib, erlotinib
ALK	Fusion	crizotinib, ceritinib, alectinib, brigatinib
ROS1	Fusion	crizotinib, entrectinib
NTRK	Fusion	entretinib, larotrectinib
RET	Fusion	selpercatinib

Table 2. Immunotherapy options for advanced NSCLC or SCLC.

	PD-L1 Expression	Immune checkpoint inhibitor
Metastatic NSCLC with no driver alterations in EGFR/ALK/ROS1	≥50%	pembrolizumab
	Any	chemotherapy + pembrolizumab chemotherapy + nivolumab + ipilimumab
Extensive-stage SCLC	Any	chemotherapy + durvalumab chemotherapy + atezolizumab

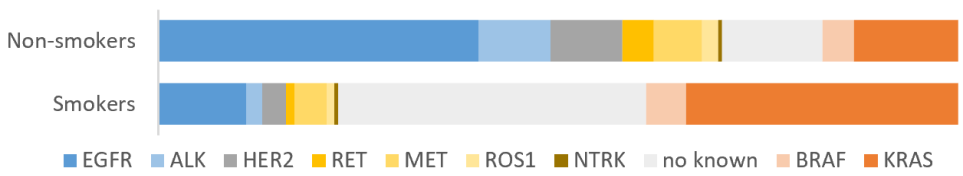


Figure 1. Prevalence of oncogenic drivers in non-squamous NSCLC differ based on smoking history.

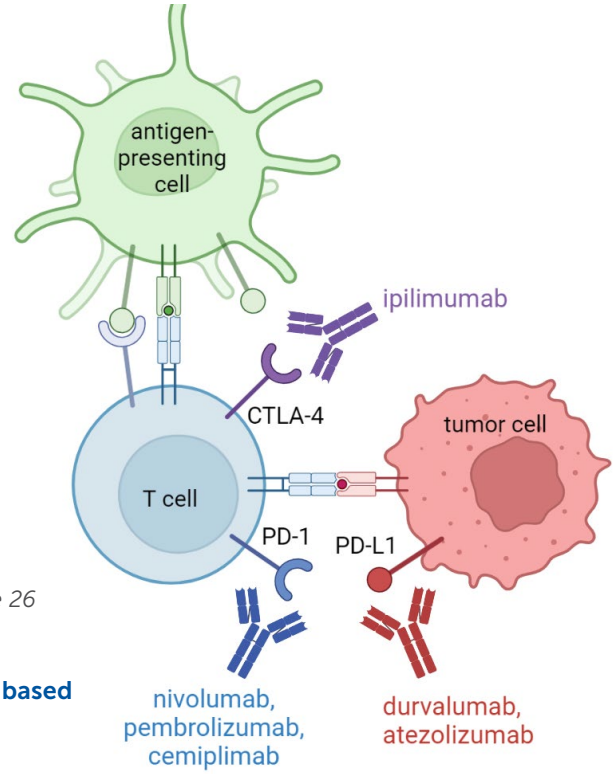


Figure 2. Mechanism of action of immune checkpoint inhibitors.
Figure created with BioRender.com (with permission for educational use in FPON).

Systemic therapies for advanced lung cancers continued from page 25

2. Targeted therapy options for non-squamous NSCLC are expanding.

Oncogenic drivers refer to DNA/RNA alterations (mutations, insertions, deletions) that lead to constitutive activation of intracellular pathways that drive cancer cell proliferation.[4] Table 1 is a list of targeted therapies for oncogene-driven advanced lung cancers that are currently funded in BC or are expected to be funded by the end of 2023. The advantages of targeted therapies include typically oral administration for patient convenience, better side effect profiles compared to chemotherapy, and improved outcomes in terms of disease control and survival. Targeted therapies are typically offered as first-line treatment and patients subsequently are treated with chemotherapy at the time of progression with each different line of therapy providing an improvement in survival.

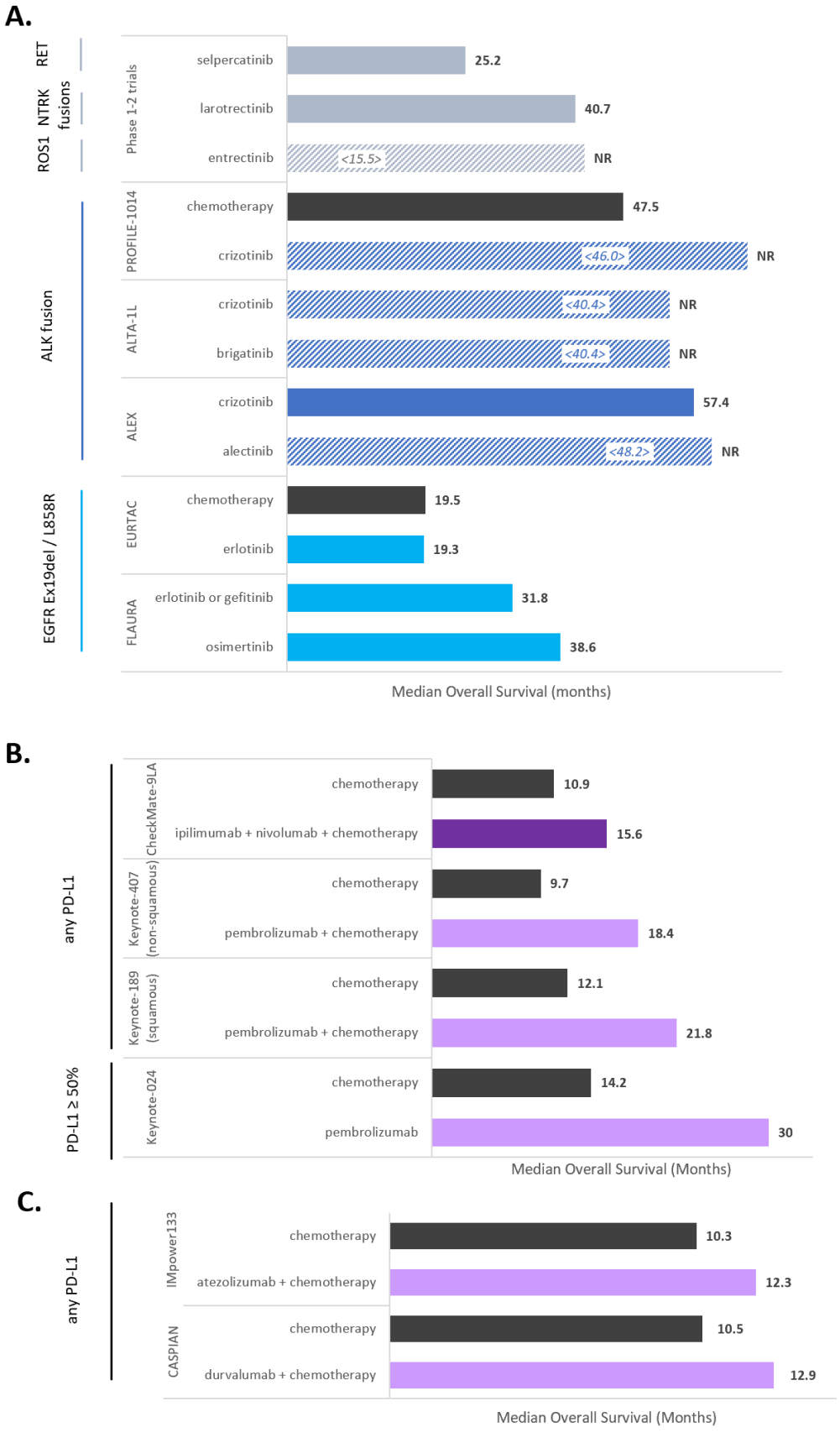
3. Immunotherapies are widely available.

Immune checkpoint proteins (PD-1, PD-L1, CTLA-4) are often hijacked by cancers to put a 'brake' on cytotoxic T cell activity against tumor cells. Immune checkpoint inhibitors (ICIs) are designed to release these brakes to re-activate anti-tumor immunity (Figure 2). Immunotherapy is generally less effective in patients with driver mutations hence the importance of molecular characterization before treatment initiation. Immunohistochemistry for PDL1 is also informative for treatment selection as the expression of PDL1 on tumor cells can predict response to immunotherapy.

Clinical trials have shown efficacy of first line pembrolizumab as a monotherapy in PD-L1 > 50% NSCLC. Single agent pembrolizumab is favored for PDL1-high patients because it is well tolerated and avoids the toxicity of chemotherapy. Irrespective of PDL1 expression, first-line pembrolizumab plus chemotherapy for 4-6 cycles or nivolumab plus ipilimumab plus chemotherapy for 2 cycles, followed by maintenance immunotherapy (+/- chemotherapy), are the currently funded options (Table 2). If patients are not suitable for first-line immunotherapy alone or in combination with chemotherapy, then atezolizumab, pembrolizumab or

continued on page 27

Figure 3. Survival benefits of first-line therapies for advanced NSCLC with (A) or without (B) oncogenic driver mutations and extensive-stage SCLC (C). Bolded numbers = median overall survival (OS). NR = not reached, with median follow-up shown italicized in brackets.



Systemic therapies for advanced lung cancers continued from page 26

nivolumab are available in the second-line setting after chemotherapy.

For advanced or extensive-stage small cell lung cancers (SCLC), atezolizumab and durvalumab are funded options used in combination with chemotherapy irrespective of PD-L1 expression. Immunotherapy in SCLC has demonstrated modest improvements in survival which may related to the different biology of this cancer compared to NSCLC.

4. Tailored systemic therapies confer clinically meaningful survival benefits.

Figure 3 summarizes median overall survival (OS) data from Phase 3 clinical trials conducted in the specific molecular alteration population. Data for entrectinib, larotrectinib, and selpercatinib are based on Phase 1-2 trials because these mutations are rare.

5. Side effects are manageable.

While side effects are a significant challenge for patients' quality of life, early recognition and prompt management can help avoid serious toxicities. Rates of toxicity-related discontinuations are generally low, in the order of <10%. Further guidance can be found online in the BC Cancer: Cancer Drug Manual www.bccancer.bc.ca/health-professionals/clinical-resources/cancer-drug-manual for individual drug mongraphs (click "Go to the Drug Index") and algorithms for classifying and managing immune-mediated adverse events (click "Go to Immunotherapy").

References

1. Siegel, R.L., Miller, K.D., Wagle, N.S., and Jemal, A. (2023). Cancer statistics, 2023. CA Cancer J Clin 73, 17–48. 10.3322/caac.21763.
2. Wu, F.T.H., Diab, M., Myers, R., Ho, C., Lam, S., and McGuire, A. (2023). Update on lung cancer. Canadian Journal of Respiratory, Critical Care, and Sleep Medicine, 1–5. 10.1080/24745332.2023.2226410.
3. Singal, G., Miller, P.G., Agarwala, V., Li, G., Kaushik, G., Backenroth, D., Gossai, A., Frampton, G.M., Torres, A.Z., Lehnert, E.M., et al. (2019). Association of Patient Characteristics and Tumor Genomics With Clinical Outcomes Among Patients With Non-Small Cell Lung Cancer Using a Clinicogenomic Database Supplemental content. JAMA 321, 1391–1399. 10.1001/jama.2019.3241.
4. Thai, A.A., Solomon, B.J., Sequist, L. V, Gainor, J.F., and Heist, R.S. (2021). Lung cancer. Lancet 398, 535–554. 10.1016/S0140-6736(21)00312-3.

How family doctors can help prevent ovarian cancer continued from page 24

meet provincial testing criteria. Tests are ordered through a healthcare provider, with genetic counselling services available.

- Invitae: Breast and Gyn Cancers Panel (link)
- LifeLabs Genetics: Hereditary Breast and Ovarian Cancer Test (link)
- GeneDx: Breast/Gyn Cancer Panel (link)

References

1. Brenner DR, Poirier A, Woods RR, Ellison LF, Billette JM, Demers AA, et al. Projected estimates of cancer in Canada in 2022. CMAJ. 2022;194(17):E601-E7.
2. Society AC. Survival Rates for Ovarian Cancer 2022 [Available from: www.cancer.org/cancer/ovarian-cancer/detection-diagnosis-staging/survival-rates.html
3. Lheureux S, Braunstein M, Oza AM. Epithelial ovarian cancer: Evolution of management in the era of precision medicine. CA Cancer J Clin. 2019;69(4):280-304.
4. Karnezis AN, Cho KR, Gilks CB, Pearce CL, Huntsman DG. The disparate origins of ovarian cancers: pathogenesis and prevention strategies. Nat Rev Cancer. 2017;17(1):65-74.
5. Menon U, Gentry-Maharaj A, Burnell M, Singh N, Ryan A, Karpinskyj C, et al. Ovarian cancer population screening and mortality after long-term follow-up in the UK Collaborative Trial of Ovarian Cancer Screening (UKCTOCS): a randomised controlled trial. Lancet. 2021;397(10290):2182-93.
6. Tone A, Boghosian T, Ross A, Baugh E, Altman AD, Dawson L, et al. Understanding the Experience of Canadian Women Living with Ovarian Cancer through the Every Woman Study (TM). Curr Oncol. 2022;29(5):3318-40.
7. ACOG Committee Opinion No. 774: Opportunistic Salpingectomy as a Strategy for Epithelial Ovarian Cancer Prevention. Obstet Gynecol. 2019;133(4):e279-e84.
8. Hanley GE, Pearce CL, Talhouk A, Kwon JS, Finlayson SJ, McAlpine JN, et al. Outcomes From Opportunistic Salpingectomy for Ovarian Cancer Prevention. JAMA Netw Open. 2022;5(2):e2147343.
9. Daly MB, Pal T, Berry MP, Buys SS, Dickson P, Domchek SM, et al. Genetic/Familial High-Risk Assessment: Breast, Ovarian, and Pancreatic, Version 2.2021, NCCN Clinical Practice Guidelines in Oncology. J Natl Compr Canc Netw. 2021;19(1):77-102.
10. Jacobson M, Bernardini M, Sobel ML, Kim RH, McCuaig J, Allen L. No. 366-Gynaecologic Management of Hereditary Breast and Ovarian Cancer. J Obstet Gynaecol Can. 2018;40(11):1497-510.
11. Finch AP, Lubinski J, Moller P, Singer CF, Karlan B, Senter L, et al. Impact of oophorectomy on cancer incidence and mortality in women with a BRCA1 or BRCA2 mutation. J Clin Oncol. 2014;32(15):1547-53.
12. Finch A, Evans G, Narod SA. BRCA carriers, prophylactic salpingo-oophorectomy and menopause: clinical management considerations and recommendations. Womens Health (Lond). 2012;8(5):543-55.
13. Kotsopoulos J, Hall E, Finch A, Hu H, Murphy J, Rosen B, et al. Changes in Bone Mineral Density After Prophylactic Bilateral Salpingo-Oophorectomy in Carriers of a BRCA Mutation. JAMA Netw Open. 2019;2(8):e198420.
14. Tone A. Ovarian cancer prevention in high-risk population: the patient & previvor perspective 2023 [Available from: www.bccancer.bc.ca/family-oncology-network-site/Documents/Tone.pdf
15. Tone A. Ovarian cancer prevention: understanding the Canadian landscape & the previvor experience 2021 [cited Gynecologic Cancer Initiative Research Rounds. Available from: www.youtube.com/watch?v=XSNgU5IAFkg

The management of incidentally found lung nodules

By Dr. Kenneth Wong, Clinical Associate Professor, UBC, Faculty of Medicine, Department of Radiology

Dr. Kenneth Wong

Incidental lung nodules are an all-too-common finding on CT imaging of the thorax. The most followed guidelines for the management of this incidental finding are published by the Fleischner Society. The Fleischner Society is a multidisciplinary international group of thoracic radiologist, pulmonologists, surgeons, pathologists, and other specialists. Their most recent revised guidelines from 2017 are for the management of both solid (Fig 1a & 1b) and subsolid (Fig 2a & 2b) nodules. A table has been included which summarizes these guidelines (Fig 3). These guidelines are not intended for patients with known primary cancer or immunocompromised patients. They are not intended for patients under the age of 35.

The recommendations are meant to exclude reimaging with CT those nodules with a less than 1% risk of cancer. Risk factors which would make incidental nodules higher risk would include older age, heavy smoking, larger nodule size, spiculated margins and upper lobe location. Those factors which make the risk of cancer greater than 1% will result in a recommendation of reimaging with CT. Lung nodule malignancy prediction calculators are available which give the likelihood of cancer based on the above risk factors. The Tammemagi risk prediction model otherwise known as the Brock model can be found online.

www.uptodate.com/contents/calculator-solitary-pulmonary-nodule-malignancy-risk-in-adults-brock-university-cancer-prediction-equation

It has been estimated that the presence of high-risk factors for nodules less than 6 mm in size increase the risk of cancer from less than 1% to 1-5%. For nodules 6-8mm in size with no other high risk factors the risk of cancer is up to 2%. For nodules greater than 8mm in size with no other high risk factors the risk of cancer is 3%.

Subsolid otherwise known as ground glass nodules are treated differently. If cancerous they are usually indolent cancers of the lungs such as adenocarcinoma in situ or minimally invasive adenocarcinoma. These lung cancers grow much slower justifying their longer follow up period of 5 years instead of 2 for solid nodules. Part solid and part subsolid nodules can also be found incidentally and have the longer follow-up periods.

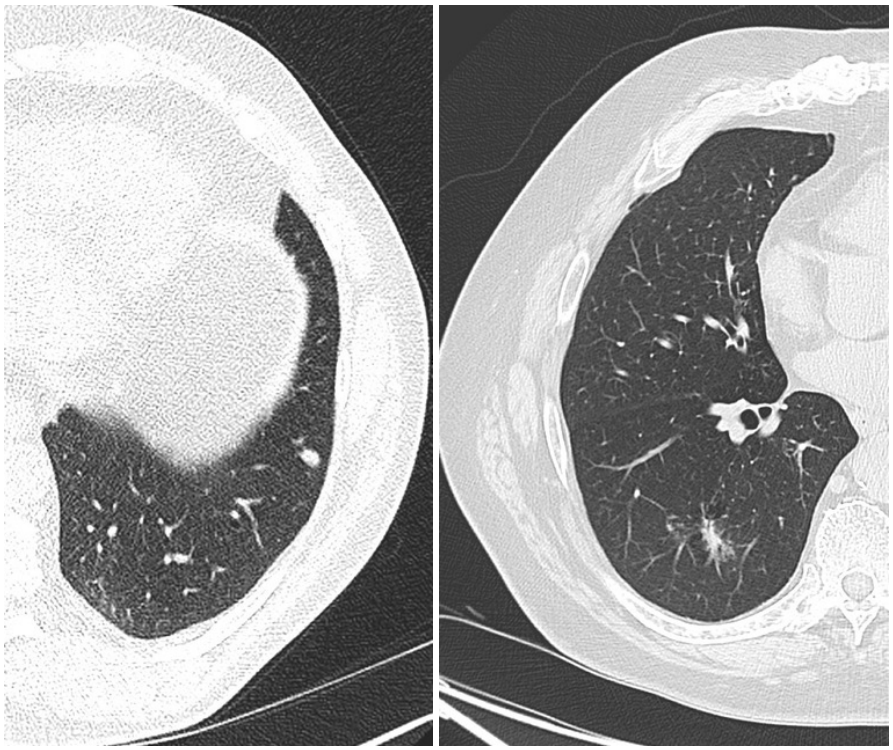


Figure 1a & 1b: Solid nodule

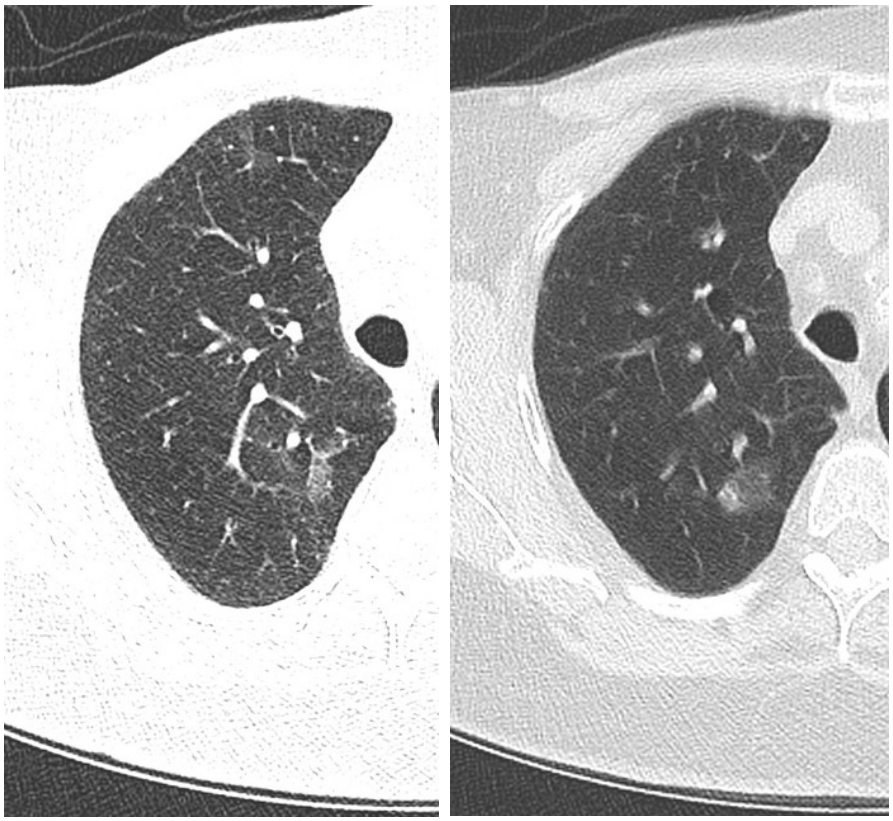


Figure 2a & 2b: Subsolid nodule

continued on page 29

Incidentally found lung nodules continued from page 28

For patients with multiple nodules, it is the most suspicious which is usually the largest nodule that indicates whether follow up is recommended. A range of months are recommended to allow clinicians the flexibility to order earlier CT imaging for those patients who are uncomfortable with longer interval follow-up. However whenever possible longer interval follow-up CT imaging would be the most ideal when looking for growth in a nodule. Any solid nodule that does not grow for 2 years or subsolid nodule that does not grow for 5 years are considered benign.

The almost universal use of voice recognition has made it possible for most radiologists to include this reference in the CT examination report usually with a version of the guidelines in table form.

Reference

MacMahon H, Naidich DP, Gamsu G, et al. Guidelines for the management of incidental pulmonary nodules detected on CT images: from the Fleischner Society 2017. Radiology: Volume 284: Number 1 – July 2017

Fleischner Society 2017 Guidelines for Management of Incidentally Detected Pulmonary Nodules in Adults

A: Solid Nodules*

	Size			
Nodule Type	<6 mm (<100 mm³)	6–8 mm (100–250 mm³)	>8 mm (>250 mm³)	Comments
Single				
Low risk†	No routine follow-up	CT at 6–12 months, then consider CT at 18–24 months	Consider CT at 3 months, PET/CT, or tissue sampling	Nodules <6 mm do not require routine follow-up in low-risk patients (recommendation 1A).
High risk†	Optional CT at 12 months	CT at 6–12 months, then CT at 18–24 months	Consider CT at 3 months, PET/CT, or tissue sampling	Certain patients at high risk with suspicious nodule morphology, upper lobe location, or both may warrant 12-month follow-up (recommendation 1A).
Multiple				
Low risk†	No routine follow-up	CT at 3–6 months, then consider CT at 18–24 months	CT at 3–6 months, then consider CT at 18–24 months	Use most suspicious nodule as guide to management. Follow-up intervals may vary according to size and risk (recommendation 2A).
High risk†	Optional CT at 12 months	CT at 3–6 months, then at 18–24 months	CT at 3–6 months, then at 18–24 months	Use most suspicious nodule as guide to management. Follow-up intervals may vary according to size and risk (recommendation 2A).

B: Subsolid Nodules*

	Size		
Nodule Type	<6 mm (<100 mm³)	≥6 mm (>100 mm³)	Comments
Single			
Ground glass	No routine follow-up	CT at 6–12 months to confirm persistence, then CT every 2 years until 5 years	In certain suspicious nodules < 6 mm, consider follow-up at 2 and 4 years. If solid component(s) or growth develops, consider resection. (Recommendations 3A and 4A).
Part solid	No routine follow-up	CT at 3–6 months to confirm persistence. If unchanged and solid component remains <6 mm, annual CT should be performed for 5 years.	In practice, part-solid nodules cannot be defined as such until ≥6 mm, and nodules <6 mm do not usually require follow-up. Persistent part-solid nodules with solid components ≥6 mm should be considered highly suspicious (recommendations 4A-4C)
Multiple	CT at 3–6 months. If stable, consider CT at 2 and 4 years.	CT at 3–6 months. Subsequent management based on the most suspicious nodule(s).	Multiple <6 mm pure ground-glass nodules are usually benign, but consider follow-up in selected patients at high risk at 2 and 4 years (recommendation 5A).

Note.—These recommendations do not apply to lung cancer screening, patients with immunosuppression, or patients with known primary cancer.

* Dimensions are average of long and short axes, rounded to the nearest millimeter.

† Consider all relevant risk factors (see Risk Factors).

Figure 3: Guidelines

Corridor Consult – Childhood Cancer

By Dr. Caron Strahlendorf, Division Head, Hematology/Oncology/Bone Marrow Transplantation, BC Children's Hospital

Dr. Caron Strahlendorf

A cancer diagnosis at any age is complex but especially when the patient is a child. The types of cancer that develop in children are often very different to that in adults and arise over the trajectory of childhood; from infants, children, pre-teens and teenagers. Cancer in children is rarely linked to lifestyle or environmental issues but may develop as a result of DNA changes in cells early in life. In Canada, more than 1000 new cases of cancer are diagnosed in children 0-15 years of age[1] with more than 80% of children today surviving, and we still are able to offer hope to the 20% of children who relapse.

What are the most common childhood cancers?

The most common types of cancer diagnosed in children 0-15 years of age are as follows:

- Leukemia (30%) – Acute Lymphoblastic Leukemia (ALL) more commonly than Acute Myeloid Leukemia (AML)
- Brain and other CNS tumours (28%)
- Lymphoma (12%) - both Non-Hodgkin's Lymphoma and Hodgkin's Lymphoma

However, there are many other forms of solid organ cancers seen in children making up the remaining 30%:

- Osteogenic sarcoma, Ewing Sarcoma, other sarcomas
- Neuroblastoma (most common extra-cranial tumour)
- Rhabdomyosarcoma
- Wilms Tumour (most common abdominal tumour)
- Retinoblastoma
- Rhabdoid Tumours
- Adult-type cancers like melanoma, and rare carcinomas

September is Childhood Cancer Awareness Month

What red flag symptoms warrant further evaluation?

Cancer in children is not usually front of mind when seeing a child in one's practice as it is such a rare occurrence. Many of the symptoms may mimic common viral illness and, depending on the age of the child, signs might be subtle and challenging in non-verbal children. Children who have more than 3 visits to the ED or doctor's office with the same symptoms increase the risk of the symptoms being due to cancer up to 10-fold. Parents know their children best and, if they are worried, hear them. Always try to examine the whole child particularly if returning with symptoms. Red flags to pay attention to include the following:

Complaints of constant tiredness, not playing, sleeping more than usual.

Headaches worse in the morning, persistent vomiting (especially early morning), and particular in a child with closed fontanelles indicating raised intracranial pressure.

Sudden vision changes, true diplopia, new onset squint or loss of red reflex needs prompt referral to specialist care.

One can see how, in the younger child, these symptoms may not be forthcoming. Recurrent or persistent fevers of unknown origin are concerning for leukemia or neuroblastoma, and infiltrative bone marrow will present with signs of pallor, bruising, infection or active bleeding. Pain waking a child at night needs careful examination. This would include excluding adenopathy, hepatosplenomegaly and exclude a mass in site of pain. New onset of obstructive symptoms, such as urinary retention, or sensory and motor changes needs urgent care.

When should we become concerned about growing pains?

Growing pains in children are not uncommon. About 10% of healthy kids will complain of leg pains – generally bilateral, usually in calves or thighs, often at the end of the day and, once resting, are able to fall asleep and are not woken by pain. Concerning for something sinister would be unilateral pain, pain waking the child at night, pain stopping them from activities or running around with friends, limping or wanting to be carried. If parents are worried enough to bring their child in because of "growing pains", examine the child well, look for signs of marrow dysfunction; a CBC is an easy way to ensure no cytopenias and exclude leukemia or marrow infiltration. If a bump is felt on exam an X-ray is a reasonable thing to do,

When a workup reveals an elevated WBC, when should we be concerned about leukemia and what other investigations are recommended?

Leukemia may increase the white cell count or, as in metastatic disease infiltrating the bone marrow, the white cell count may be very low. Always look at the entire blood count and see what "company the white cells are keeping"; are there other cytopenias, is the MCV elevated, are the platelets also trending down? Always look at the differential, if the cause of the elevated white cell count is all neutrophils with no other cytopenias, it is most likely infection and not leukemia. However, "other cells" or presence of blasts is a reason to urgently call the oncologist on call. Look for adenopathy, hepatosplenomegaly and, especially with a high white cell count, we will guide you to exclude tumour lysis (hyperkalaemia, hyperphosphatemia, hypocalcemia and hyperuricemia. An LDH is also useful, and CXR to exclude an anterior mediastinal mass. We will guide hyperhydration (with non potassium containing fluids) and transfer to pediatric oncology depending on stability of the child and the level of hemoglobin and platelet count.

Can you give examples of when one should consider referral to pediatric oncology?

In pediatric oncology we want to see the child with a *suspected* malignancy NOT once the diagnosis is made. Workup of the child can be coordinated in the pediatric setting with all procedures planned with a single sedation, molecular and cytogenetic testing

continued on page 31

Corridor Consult – Childhood Cancer continued from page 30

done that is essential for guiding therapy and prognosis, opens opportunities for clinical trials, and support of the family emotionally. We have no waitlist and are happy to discuss potential cases with referring practitioners so, if you SUSPECT a malignancy in a patient less than 17 years old, call the oncologist-on-call at 604 875 2161 (24 hours a day 7 days a week). Do not perform surgical interventions, biopsy or treat with steroids. Although we know it is difficult, please try to let the parents know why you are referring the child to us.

Once you have referred the child to us, diagnostic work up commences. Information and test results will be discussed with the parents and age-appropriate information will be conveyed to the child. Every new patient and family is seen by one of our social workers to assist them in dealing with the shock and the emotional and psychosocial aspects of coping with their new situation. Treatment is initiated at BC Children's Hospital. As a referring practitioner you will be kept in the loop and families like to know you will be there for them on their return home.

Caring for children and their families with cancer is a privilege. Our ability to cure more children is impacted by early referral, understanding biology, new and innovative therapies, clinical trials, and the resilience and joy that children bring to our work.

Useful resources

1. https://health-infobase.canada.ca/data-tools/cypc/
2. https://childrensoncologygroup.org
3. http://www.bcchildrens.ca/health-professionals/clinical-resources/oncology
4. http://www.bcchildrens.ca/health-professionals/refer-a-patient/oncology-referral
5. https://childrensoncologygroup.org/

Pediatric Oncology Hematology Education Day Friday, November 24, 2023

https://ubccpd.ca/learn/learning-activities/course?eventtemplate=528-pediatric-oncology-hematology-education-day

Changing of the seasons – Autumn and a time to reflect

By Dr. Catherine Clelland
Medical Director, Primary Care, BC Cancer

With the changing of seasons coming, the autumn is a time to reflect on where we have been over the past few months. Yet again, we have seen a record number of forest fires with the devastation of several communities in British Columbia and around the country. Over the past several decades there have been records set on a regular basis, interspersed with flood records. I was practicing full-service family medicine in Kelowna and remember well the summer of 2003, when the Okanagan Mountain Park Wildfire and the McLure Wildfire set provincial records of over 25,000 hectares with numerous structures destroyed and thousands of people evacuated. In 2009, a new record of 66,719 hectares was set with the Lava Canyon wildfire in the Chilcotin. 2010 saw 4 complex fires over 35,000 hectares and in 2014, there were 5 wildfires over 25,000 hectares with the largest at 133,098 hectares south of the Chelaslie river.

Dr. Cathy Clelland

Fast forward to 2021 when over 1600 wildfires burned over 868,000 hectares across the province followed by historic floods that took out much of the road infrastructure connecting the lower mainland with the rest of the province and country. Last year started with floods but by the end of October, BC Wildfire services recorded almost 1800 wildfires affecting just over 133,000 hectares. 2023 saw essentially the entire city of Yellowknife, NWT evacuated, with the healthcare systems and communities in general in BC, Alberta and Manitoba stepping up to the plate to support those in need. At the end of August there were still well over 100 fires listed as "out-of-control" with 12 listed as "Wildfires of Note" that are highly visible or pose a potential threat to public safety. BC will again set a new record when all is said and done. The longer-term impact of the resulting poor air quality both on those with chronic respiratory conditions and on cancers that are related to the inhalation of toxic particles in smoke is something we will need to keep an eye on for decades to come.

Our thanks go out to all the first responders and firefighters who have come to help directly with the fires and with the work of supporting those who have had to leave their homes. Communities coming together with neighbors helping neighbors with many of the basic needs like food and shelter. Through all this, humanity has shown how resilient it can be, but it is important to remember that studies have shown how the impact of these natural disasters can affect mental health and wellness in both the short and long term.

It falls to all of us not only as healthcare providers, but as parents, children, partners and friends to be aware of the "emotional thermometer" of not only those around us but also ourselves. We need to be mindful to encourage reaching out for help through community Family Physicians and other primary care providers, local Divisions of Family Practice and Primary Care Networks as well as organizations such as the Canadian Mental Health Association, BC Division https://cmha.bc.ca/documents/coping-with-natural-disaster-stress/ At this time, it is important for all of us to remember that we need to think about self-care and take steps to ensure we are in a place of mind to be able to care for our patients, our families, our friends and that person looking back at us in the mirror.

FOR MORE INFORMATION

To learn more about the Family Practice Oncology Network or become involved, please email FPON@bccancer.bc.ca or visit 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.

ISSN 2369-4173 (Online)
Key title:
Journal of family practice oncology

Publications Mail Agreement Number 41172510

Return all undeliverable Canadian Addresses to
BC Cancer, 600 West 10th Ave, Vancouver, BC V5Z 4E6