Melanoma Network of Canada
Sun Safe Sun Aware

Melanoma

What you need to know

5th Edition

Have Questions?
Please call 1-877-560-8035 or email info@melanomanetwork.ca

This booklet is provided free of charge by the Melanoma Network of Canada.

Acknowledgments

We would like to acknowledge and thank the following individuals who provided their expertise and review for the development of this booklet:

- **Annette Cyr**, Chair, Melanoma Network of Canada
- **Dr. Marcus Butler**, Medical Oncologist, Princess Margaret Cancer Centre, Toronto, Ontario
- **Dr. Danny Ghazarian**, Consultant Dermatopathologist, University Health Network (Princess Margaret /Toronto General/Toronto Western Hospitals), Professor, University of Toronto
- **Dr. Saima Hassan**, Surgical Oncology, University of Toronto/Sunnybrook Research Institute
- **Margo Kennedy**, MSW, RSW, Oncology Social Worker, Princess Margaret Cancer Centre, Toronto, Ontario
- **Dr. Elaine McWhirter**, Medical Oncologist, Juravinski Cancer Centre, Hamilton, Ontario
- **Dr. Teresa Petrella**, Medical Oncologist, Odette Cancer Centre, Assistant Professor, University of Toronto
- **Dr. John Walker**, Medical Oncologist, Cross Cancer Institute, Edmonton, Alberta
- **Dr. Frances Wright**, Professor Surgery, Sunnybrook Health Sciences Centre - University of Toronto

The information contained here is for reference and education only. Please consult your physician for specific information on personal health matters.

Melanoma Network of Canada
Sun Safe Sun Aware

The Melanoma Network of Canada (MNC) is a national, patient-led, charitable organization. The mission of MNC is to support individuals whose lives have been changed by melanoma. We are advancing the prevention of melanoma through advocacy and education.

Melanoma Network of Canada
Phone: 905-901-5121 | Toll Free: 1-877-560-8035
www.melanomanetwork.ca

Charitable Registration # BN 85491 3050 RR0001

Contents

About This Booklet

The purpose of this booklet is to help people diagnosed with the most common form of melanoma - cutaneous melanoma - to learn about this form of skin cancer and how it is treated. While the booklet is focused on cutaneous melanoma, we have included a section on rarer forms of melanoma, including **mucosal melanoma**, **uveal melanoma** (please see our booklet - *A Guide to Uveal Melanoma*) and **desmoplastic melanoma**. This booklet includes treatment options for all stages of melanoma that are available in Canada at the time of publication. Please speak to your health care team to determine any options available to you in your treatment centre. Not all treatment options apply to every person with melanoma, nor do we detail options for treatment for rarer forms of melanoma. For those details, please discuss with your medical team.

The more you know, the more you can be active in making choices about your own care. Being part of your care helps you feel more in control and can lessen the anxiety associated with a diagnosis. Working with your treatment team may also help you be more confident with your treatment.

It is a good idea to read the whole booklet first, then focus on the sections that apply to your phase of care.

This booklet also includes examples of questions you may want to ask your doctor at different stages of your treatment. Asking questions can help you learn about the disease and be active in treatment decisions. Any time you visit your doctor or the treatment clinic you may want to take notes about your condition and your treatment. Ask for copies of any test results so that you have them for easy reference or to review for questions later. Some centres may have access online for your test results. Please check with your hospital for further information. It is also a good idea to take a friend or family member to appointments – to take notes, listen, or ask questions. Having someone there as a second pair of eyes and ears is helpful and can be a good support for you.

This booklet does not discuss other types of more common skin cancers, such as basal cell carcinoma or squamous cell carcinoma. Please visit our website (**www.melanomanetwork.ca**) for further information and treatment of these skin cancers.

The Skin

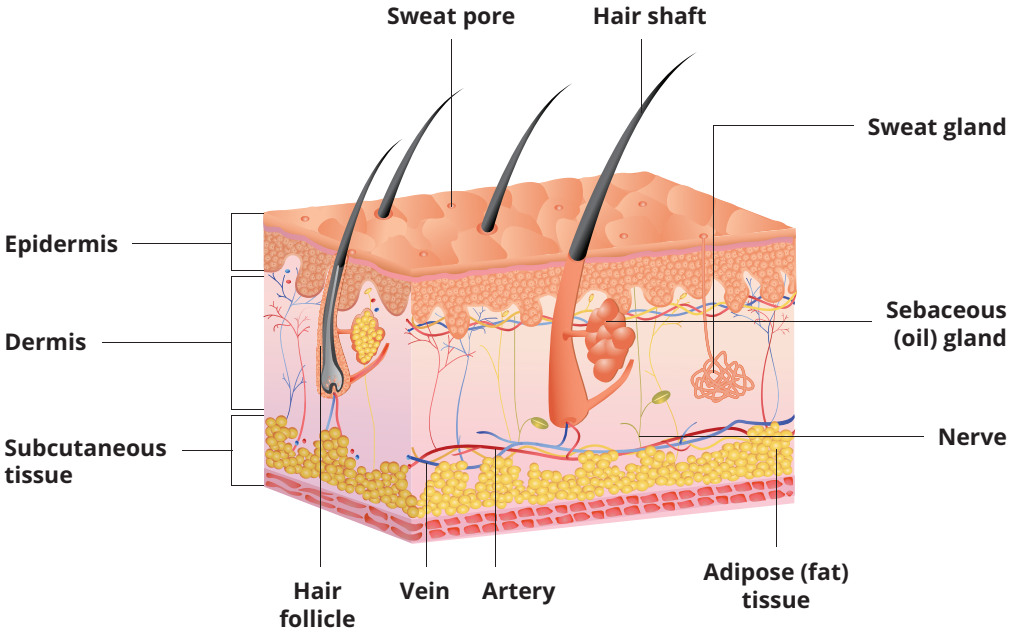
Importance of the Skin

Your skin plays an important role in your body. In fact, your skin is the largest organ of your body, covering its entire surface. Skin is a protective layer that performs many tasks:

- Skin provides the first line of defence against injury and infection. It is the largest immune organ and can multi-task to provide a balanced immune system. Healthy skin helps prevent infection, recognize allergens and can repair damage as it occurs.
- Skin prevents the body from losing water and drying out. This is important as your body is largely made up of water.
- Skin protects you from heat. Sweat glands release a watery fluid, cooling the skin.
- Skin helps to produce vitamin D.
- Skin protects you from damage that can be caused by **ultraviolet (UV) light**. The sun, sunbeds and sunlamps produce UV light.

Layers of the Skin

The skin is made up of three main layers, the epidermis, the dermis and the subcutaneous tissue. The **epidermis** is the thin top layer of skin you can see. Several **cell** types make up the epidermis. Cells are the microscopic building blocks that make up tissues, such as skin. **Melanocytes** are pigment cells found in the bottom of the epidermis. Melanocytes produce **melanin**, the pigment that gives skin its colour. When skin is exposed to UV light, melanocytes make more melanin to try to protect the body from damaging radiation.



The **dermis** is a thick layer below the epidermis. The dermis contains several types of cells and structures.

- **Blood vessels**: carry nutrients and oxygen to the skin and remove waste products.
- **Lymph vessels**: return blood plasma, the liquid part of the blood, from the tissues to the heart.
- **Sweat glands**: produce sweat, a watery substance that helps to cool the body.
- **Sebaceous glands**: produce sebum, an oily substance that helps protect skin from drying out.
- **Connective tissue**: surrounds these structures and holds them in place. Connective tissue allows the skin to stretch.
- **Hair follicles**: produce your hair.

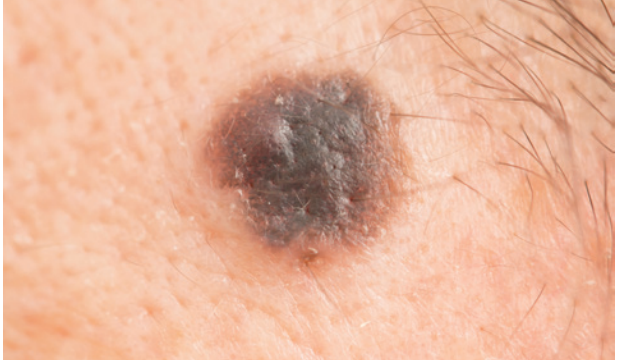
The **subcutaneous tissue**: is beneath the dermis. It attaches the skin to the muscle underneath. It contains connective tissue and fat. The subcutaneous tissue stores energy and body heat. It also absorbs shock to protect the body.

Cell Growth: Normal Cells and Cancer Cells

Cells are microscopic structures in the body that group together into tissues. Tissues include organs, bone, muscle, fat, and skin. Genes are the instructions in cells for making new cells and controlling how cells behave. The body needs new skin cells to replace those that have died and to heal injuries. Normally, your body makes new cells only when they are needed. Cells divide to form new cells until enough cells have been made. The cells then stop dividing. The body controls how many cells are made and where they are made.

Cancer cells have escaped the body's control. Abnormal changes (mutations) in genes can turn normal cells into cancer cells. Cancer cells continue growing and dividing, even when more cells are not needed or dying (cell proliferation). Eventually, cancer cells form a mass called a **tumour**. The first tumour formed is called the **primary tumour**. Cancer cells may also be abnormal in other ways. They can break off from the tumour and travel anywhere in the body through blood vessels or lymph vessels and continue to grow and divide. **Lymph nodes**, small immune glands that work as filters for harmful substances and attack and destroy germs, are located along lymph vessels.

Cancer cells often lodge in lymph nodes. A new tumour, in parts of the body far from the first or **primary** tumour, is called a **metastasis**. Metastases can replace or compress normal tissues and prevent them from working as they should. A metastasis close to the primary tumour is called a **local or satellite metastasis**. If a tumour grows at a distant site from the primary tumour, it is referred to as a **distant metastasis**. Melanoma that has spread to a local lymph vessel, but not to lymph nodes, is called an **in-transit metastasis**.



Melanoma

Melanoma is a cancer of the **melanocytes**, the pigment cells of the skin. Melanoma can occur anywhere on the skin and commonly develop in an existing or new mole. The mole may change over time. Telltale signs of a problem may include a black or brown stain spreading from the mole, oozing, itching or bleeding. In men, melanoma is often found on the head, neck, and back – common areas of sun (UV radiation) exposure. In women, melanoma is often found on the back, extremities such as arms, and lower legs. Melanoma is less common in people with dark skin but still poses a risk. However, in dark-skinned people, melanoma is more commonly found under the nails of the fingers or toes, on the palms of the hands, or soles of the feet.

Melanoma forms in the epidermis and can grow down into the dermis. The deeper a melanoma grows into the dermis, the higher the risk of spreading through lymph vessels or blood vessels. Once it reaches the dermis, melanoma can easily spread through the blood and lymph vessels to virtually anywhere in the body. Melanoma is more dangerous than other more common forms of skin cancer because it is more likely to spread if not identified early. However, most melanomas - about 84 out of 100 - are found early before a spread and are likely to be 'cured' by treatment (usually by excision). It is important to be monitored for life, after a diagnosis. Monitor your skin for changes, protect your skin and eyes from UV damage, and see your dermatologist at least annually.

The rates of melanoma are increasing rapidly as people spend more time in the sun. In fact, UV light from the sun or tanning beds is considered to be the leading cause of 85% of melanomas in Canada, according to the World Health Organization. So we know that most of this disease is preventable. In Canada, melanoma is now the 7th most common cancer and is one of the most prevalent cancers in our youth population ages 15 to 29 years.[1] By 2019, new diagnoses of melanoma in Canada will exceed 8,000 cases, resulting in more than 1,500 deaths annually.[1]

Moles: Benign Tumours That Start in the Melanocytes

A **mole** (nevus) is a benign skin tumour that develops from melanocytes. Almost everyone has some moles. Nearly all moles (nevi) are harmless, but having some types can raise your risk of melanoma. See Risk Factors for Cutaneous Melanoma (page 10), for more information about moles.

A **Spitz nevus** is a kind of mole that sometimes looks like melanoma. It's more common in children and teens, but it can also be seen in adults. These tumours are generally benign and don't spread. Sometimes doctors have trouble telling Spitz nevi from true melanomas, even when looking at them under a microscope. Therefore, they are often removed, just to be safe.

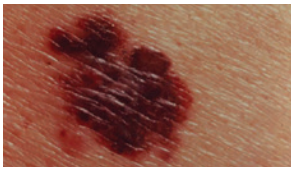
Spread of Melanoma

Melanoma cells use lymphatic channels to spread locally to skin and nearby regional lymph nodes in a process called metastasis. Melanoma cells can also use blood vessels to spread to distant organs such as the brain, liver, and lungs. Cancer cells that spread to the skin nearby, but are confined to that particular limb, are called **in-transit disease**. Once cancer cells spread to lymph nodes or distant organs, they may colonize and grow. Only once the cells have grown large enough will they become apparent during a physical exam or in radiologic imaging.

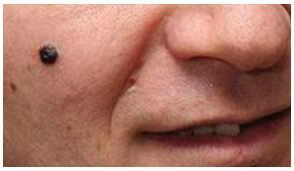
Lymphatic spread in melanoma may follow some patterns:

- Melanomas in the arms have a tendency to spread to lymph nodes in the armpit.
- Melanomas in the legs tend to spread to lymph nodes in the groin.
- Melanomas originating in the trunk or back have a more varied pattern and can spread to the armpit or groin.

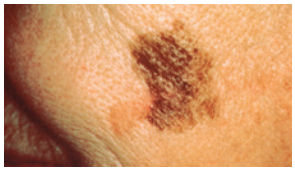
Melanomas can look very different from each other. Some melanomas may have all the ABCDE signs (see the explanation of the signs of melanoma on page 12). Others may have only one or two of the ABCDE features. Advanced melanomas may have changes in their texture or feel. The melanoma may become hard or bumpy. The surface of the melanoma may ulcerate (appear scraped or raw, and it may ooze or bleed). The melanoma may be itchy, sore, or even painful.



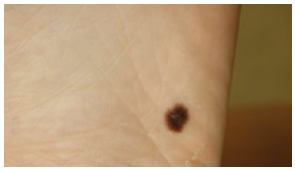
Superficial spreading melanoma: Image courtesy of National Cancer Institute



Nodular melanoma: Image courtesy of University of California



Lentigo maligna melanoma: Image courtesy of Skin Cancer Foundation



Acral lentiginous melanoma: Image courtesy of National Cancer Institute

Types of Cutaneous Melanoma

Doctors classify melanoma into four major types. Classification is based on their colour, shape, location, and how they grow.

Superficial Spreading Melanoma

This is the most common type of melanoma, making up almost 70% of melanomas diagnosed.[2] Other names for this cancer include malignant melanoma and cutaneous melanoma. As the name suggests, **superficial spreading melanoma** usually presents as a thin patch often looking like a dark brown or black stain spreading outwards from a new or existing mole (known as radial growth) before it invades vertically into the dermis, the lower layer of skin. The time it takes to spread can be fast or it can last for a relatively long time, ranging from months to decades. This type of melanoma is more commonly seen in areas of skin that have been exposed to UV light, especially areas of previous sunburn. Superficial spreading melanoma is often first identified by patients or family members (over 50% are found by patients or family first) using the ABCDEs of melanoma (see page 12).[3] In most situations the early changes are purely visual and it is the later stages that may result in symptoms like itching or bleeding.

Nodular Melanoma

Nodular melanoma (NM) is a firm, domed bump. It grows quickly down through the epidermis into the dermis. Once there, it can **metastasize**, or spread to other parts of the body. Nodular melanoma is the second most common subtype of melanoma, accounting for 15% to 30% of all melanomas and approximately 40% to 50% of melanomas thicker than 2 mm.[2] Nodular melanoma is typically dark brown or black, may crust or ulcerate. As in all subtypes of melanoma, nodular melanoma can be a pink, red or skin-toned colour (amelanotic) and rarely can also be colourless, especially in people with very fair complexions.

Nodular melanoma does not typically follow the ABCDEs of other melanomas, as it generally has uniform borders and colour, symmetry and small diameter. It is often difficult to diagnose and therefore it is important that physicians and patients be wary of new or changing lesions. A dermatologist will often use a dermatoscope to help in the diagnosis of melanoma. **Dermoscopy** is a widely used noninvasive diagnostic technique. It improves the diagnostic accuracy for pigmented lesions in comparison with examination with the unaided eye. Dermoscopy helps in the early diagnosis of NM because dermoscopic features are typically more suggestive of malignancy than clinical ones. [4,5]

Nodular melanoma has a more rapid growth rate, more biologically aggressive behaviour, and an increased number of mitoses (which is unchecked cell growth, often referred to as the mitotic rate), compared with other melanoma subtypes. It also is commonly raised and bleeds frequently. [6,7]

The **EFG** acronym to identify NM has been developed, summarizing the most frequent clinical features of NM:

- **Elevation**
- **Firm** on palpation, and
- Continuous **growth** for 1 month. [8]

Lentigo Maligna Melanoma

Lentigo maligna is also called melanoma *in situ* of the solar type when the melanoma cells are confined to the surface epithelium, the most superficial layer of the skin, with no invasion or penetration of the deeper layer, the dermis. This subtype accounts for 10-15% of all cases.[2] It occurs in chronically sun damaged skin, particularly in the elderly, so is generally found on the upper arms, face, ears or neck, and most often on the nose and cheek. As this is a very early stage of the disease, complete excision with appropriate clear margins is basically curative. Once the melanoma cells invade the dermis, then it is called lentigo maligna melanoma. Under this condition the prognosis depends on the depth of invasion, ulceration, mitoses and other parameters listed in the pathology report.

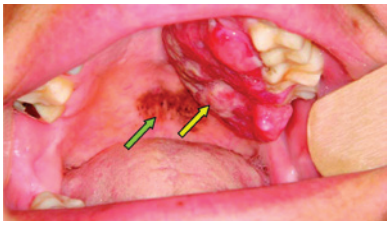
Acral Lentiginous Melanoma

Acral lentiginous melanoma can look like a dark spot or a bruise that does not get better. This subtype accounts for less than 5% of all cases.[2] It can occur on the palms of the hands and soles of the feet. Acral lentiginous melanoma under a nail may look like a dark stripe. Like other flat forms of early melanoma, it may be recognized by the ABCDE rules, but may also be amelanotic (non-pigmented, usually red in colour). People of African and Asian races most often develop this melanoma, but it may occur in any skin type.

Rare Types of Melanoma

Mucosal Melanoma

Mucosal melanoma is a rare, biologically aggressive form of melanoma, making up only 1 to 2% of melanoma cases.[9] As with other areas of the skin, melanocytes, the pigment-producing cells of the body, are also present in the mucosal surfaces of the body, lining the sinuses, nasal passages, oral cavity, vagina, anus and other areas. Just like melanocytes in other parts of the body, these can transform into cancerous cells, resulting in mucosal melanoma.



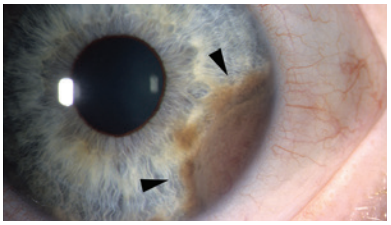
Mucosal melanoma
Image Source: The Oncologist Journal

Over 50% of mucosal melanoma develops in the nasal passages or sinus cavities in the mucous membrane or in the mouth or throat.[9] A further 20% develops on the female genital tract, approximately 24% are in the anal or rectal area, and 3% occur in the urinary tract. This form of melanoma is not related to being exposed to the sun, unlike most melanoma skin cancers. It is usually diagnosed at a late stage and tends to grow and spread quickly.

The median age at diagnosis is over 70 years, with women diagnosed more frequently than men.[9] Mucosal melanoma has a unique staging system, separate from cutaneous melanoma. Early detection, which is very often difficult because of the location of the disease, allows the best hope for cure. Unfortunately, most individuals diagnosed also have micrometastatic disease that cannot be easily detected and will experience multiple local recurrences before the clinical development of distant disease. Approximately a third of patients have nodal involvement when detected, and the overall 5-year survival rate is only 25%.[9] Despite aggressive surgical resection and use of adjuvant treatments like immunotherapy and chemotherapy, the prognosis remains poor.[9]

Uveal Melanoma

Uveal melanoma is an aggressive form of melanoma that affects the eye and is also known as primary intraocular melanoma or choroidal melanoma. It makes up less than 3% (or 150 cases per year) of all melanoma cases in Canada[1] and about 4,000 cases worldwide. Uveal melanoma has a poor prognosis with up to 50% of those diagnosed developing metastatic disease.[10,11] If the cancer spreads beyond the eye, only approximately 40% of patients will survive for one year.[12] While there is ongoing research into effective treatments, effective treatment options are somewhat limited.



Uveal melanoma
Image Source: Skin Cancer Foundation

Uveal melanoma refers to melanocytes of the uvea that become cancerous. This can occur in any part of the uvea: the iris, the ciliary body and/or the choroid. Uveal melanoma cases occur nearly 85% of the time in the choroid, another 10% in the ciliary body and approximately 5% in the iris.[13] Pathological staging is based mainly on the size of the mass, its location, and the presence or absence of metastases.

Although uveal melanoma (eye) and cutaneous melanoma (skin) both affect melanocytes, they are distinct cancers as they have different genetic mutations, they behave differently, and cutaneous melanoma is much more common (nearly 40 times more common).

The cause of uveal melanoma is unclear. Unlike skin melanoma, which is often closely linked to UV radiation damage from the sun or other sources, there is no hard evidence to support causal relationship. However, there are factors that are linked to increased risk for uveal melanoma. These include:

1. Light eye colour, such as blue or green eyes;

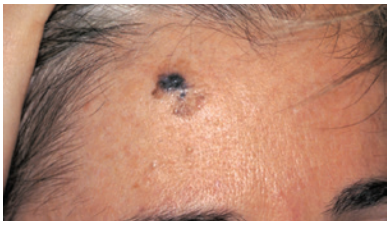
2. Fair skin colour;

3. Being older in age. The median age at diagnosis is 55 years old.

Although research studies have found an association with these factors, uveal melanoma can occur in any person regardless of age, gender or race. A more detailed information booklet on uveal melanoma, titled *A Guide to Uveal Melanoma* is available from the Melanoma Network of Canada at **www.melanomanetwork.ca**.

Desmoplastic Melanoma

Desmoplastic melanoma (DM) is a relatively rare type of melanoma, accounting for less than 4% of primary cutaneous melanomas.[14] It develops in the thick, inner layer of skin (dermis) or the layer of connective tissue that surrounds the mucosa (submucosa) and often appears as a lump that is the same colour as your skin.



Desmoplastic melanoma
Image Source: Fitzpatrick's Color Atlas & Synopsis of Clinical Dermatology Klaus Wolff, Richard Allen Johnson, Dick Suurmond Copyright 2005, 2001, 1997, 1993 by The McGraw-Hill Companies.

It tends to grow down into the skin and has a tendency for persistent local growth, with infrequent nodal metastases. Desmoplastic melanoma can present with or without pigmentation; men are affected twice as often as women, and most commonly affects older patients. The three most common locations for DM include chronic sun exposed areas on the head and neck (53%), extremities (26%), and trunk (20%).[14] Treatment of DM usually involves surgical excision and in some advanced cases, adjuvant radiation may be offered. More recently, DM has had very positive responses to treatment with immune-activating anti-PD-1/PD-L1 therapies, pembrolizumab (Keytruda) or nivolumab (Opdivo). These drugs block the interaction between the proteins PD-1 and PD-L1. During cancer development, PD-1 and PD-L1 inhibit the immune system and allow tumour cells to escape detection and continue to grow. By blocking their interaction, immune-activating drugs restimulate the immune system to detect and destroy cancer cells.[9,15]

Evaluating Melanoma

If your doctor suspects you may have melanoma, you may be referred to a **dermatologist**, a doctor who specializes in diseases of the skin.

Medical History

Your doctor should ask about any medical conditions you have had and your current symptoms, such as a change in a mole, any other marks on your skin, any history of melanoma or other skin cancers, and risk factors for cutaneous melanoma. Your doctor will also ask you about your immediate family and any skin cancers family members may have had.

Risk Factors for Cutaneous Melanoma

Scientists have identified many factors that increase the risk of developing melanoma, such as:

- **Sun exposure**: Exposure to ultraviolet radiation from the sun (UVA and UVB) is the most important risk factor for melanoma.
  - **Sunburn with blistering**: Even one severe, blistering sunburn increases the risk of melanoma.
  - **Lifetime sun exposure**: The total amount of sun exposure is a risk factor.
  - **Tanning**: Even people who tan without burning have an increased risk of melanoma because of increased total sun exposure.
- **Artificial sources of UV radiation**: Sunlamps and tanning beds produce UV light. Therefore, they increase the risk of melanoma. Using these artificial sources of UV light before the age of 30 greatly increases the risk of melanoma, but the danger exists for all ages.
- **Personal history of melanoma**: People who have had melanoma have an increased risk of developing another melanoma.
- **Family history of melanoma**: Having at least two close relatives with melanoma is a risk factor for melanoma. Close relatives include parents, siblings, and children. Melanoma can run in families.
- **Fair skin and light hair**: People with pale skin, who burn easily, have an increased risk of melanoma. These people may have blond or red hair, blue or gray eyes, or numerous freckles.
- **More than 50 moles**: Normal moles are smaller than a pea (¼") and have an even colour. They can be pink, tan, or brown. They are round or oval and smooth. Having many moles increases the risk of skin cancer.

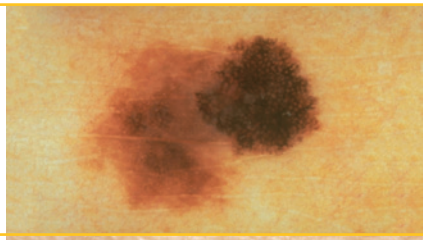
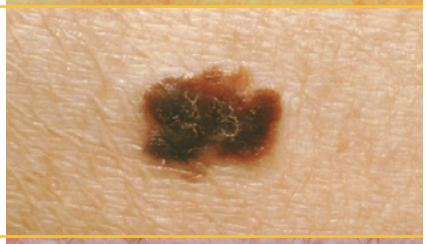
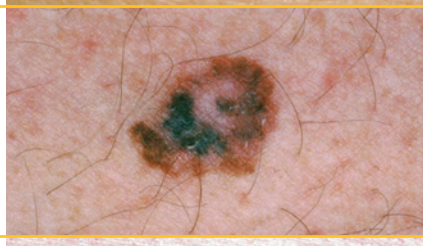
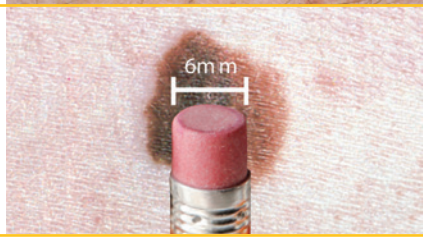
- **Atypical moles (dysplastic nevi)**: Nevus is the medical term for mole. These moles look a little like normal moles but also have some features of melanoma. They are often larger than other moles and have an abnormal shape or colour. They can appear on skin that is exposed to the sun as well as skin that is usually covered, such as on the buttocks or scalp. Dysplastic nevi often run in families. A small percentage of dysplastic nevi may develop into melanomas, but most dysplastic nevi never become cancerous. They may contain several colours, and they may have an irregular edge. Most often, a dysplastic nevus is flat with an irregular or scaly surface. A dysplastic nevus has a greater chance than a normal mole of turning into melanoma, although the risk is low.
- **Dysplastic nevus syndrome (also known as familial atypical multiple mole melanoma syndrome, or FAMMM)**: People with this inherited condition have many dysplastic nevi and usually a close relative who has had melanoma. People with this condition have a very high risk of melanoma, so they need to have very thorough, regular skin exams by a dermatologist. Sometimes full body photos are taken to help the doctor recognize if moles are changing and growing. It is recommended that these patients be taught to do monthly skin self-exams as well.
- **Age**: People with a family history of melanoma may develop the disease at a young age. However, about half of melanomas develop in people older than 50 years.
- **Medications**: Some medications, like antibiotics, hormones, or antidepressants, increase sensitivity to the sun. These medications can also increase the risk of melanoma.
- **Immune suppression**: The **immune system** fights infection and removes damaged cells. Some diseases and some medications weaken the immune system. This can increase the risk of melanoma.

Physical Examination

The doctor inspects your skin for any **lesions**, or abnormalities. If a melanoma is suspected, the doctor should refer you to a **dermatologist** as quickly as possible. A dermatologist is a doctor who is an expert in diseases of the skin. A dermatologist or a doctor should do a thorough skin check, including the scalp, between the toes and fingers, even around the genitals. Ideally, your dermatologist will look at any suspicious moles or lesions through a **polarized dermatoscope**. A dermatoscope is a handheld device that uses polarized light to magnify an area ten times and is beneficial in correctly identifying melanomas - particularly ones that may be difficult to identify by the naked eye alone. The doctor may also check other parts of your body for signs of skin cancer.

Signs of Melanoma

Normal moles tend to have an even colour and are mostly round or oval in shape. They also tend to be less than 6 mm in size (smaller than the width of a pencil's eraser). The first sign of melanoma may be a change in a mole – a small pigment spot on the skin. This change may affect the shape, colour, size, surface, or texture of the mole. Melanoma may also develop as a new mole. In some cases, the primary mole or lesion may not be identified and it may be a swollen lymph node that may be the initial area of concern. The **ABCDE** acronym in the chart below summarizes the more common signs of melanoma. While this is a useful tool to help identify melanoma, many melanomas do not fall into this pattern. Another consideration is to look for the 'ugly duckling' - a mole or lesion that does not look like others that you have. If it is changing, itching, bleeding or scabbing, have a biopsy done.

A – Asymmetry	The two halves of the mole have different shapes.	
B – Border	The edge of the mole is irregular. It may look blurred, ragged, or notched. Pigment may spread into the skin around the mole.	
C – Colour	The colour of the mole is uneven. The mole may have different shades of tan, brown, and black, sometimes with blue, gray, red, pink, or white.	
D – Diameter	While melanomas are usually greater than 6 mm (the size of a pencil eraser) when diagnosed, they can be smaller.	
E – Evolving	The mole has changed in the past few weeks or months. It may be itchy, scaling or bleeding.	Example: 

Source: American Academy of Dermatology **www.aad.org**

Skin Biopsy

If your doctor or dermatologist finds a suspicious mole, a **biopsy**, or removal of tissue for examination under a microscope, is taken of the mole. The doctor first numbs the skin with an injection of a local anaesthetic. The entire lesion and a border of normal skin around it should be removed to allow for the most accurate diagnosis by a **pathologist** or **dermatopathologist**. A pathologist is a physician who interprets and diagnoses the changes caused by disease in tissues and body fluids. A dermatopathologist is a specialist doctor that focuses on the study of skin diseases at a microscopic and molecular level.

There are several types of biopsy:

- **Excisional biopsy**: This is the preferred type of biopsy. The doctor uses a scalpel to remove the entire growth and some tissue around it. This is the most common type of biopsy when melanoma is suspected. A deep shave biopsy, also called 'saucerization' or 'scallop' biopsy is commonly used to remove an entire mole (lesion) and should not be confused with a superficial shave biopsy.
- **Incisional biopsy**: Sometimes a lesion is very large or in a place where it can't be easily removed. In these cases, an incisional biopsy is done. An incisional skin biopsy removes only part of the lesion.
- **Punch biopsy**: The doctor uses a sharp, hollow instrument to remove the lesion and some normal tissue around it. This type of biopsy may be used for specific areas of the body, such as the face.
- **Shave biopsy**: These are not recommended for pigmented lesions of the skin for suspected melanoma. A shave biopsy can actually hinder an accurate diagnosis of skin cancer and therefore lead to inadequate treatment, culminating in recurrence of skin cancer, a possible spread of the cancer and avoidable death.

In some cases, melanoma may be found somewhere in the body without ever finding a spot on the skin (the original primary). On rare occasions, melanoma skin lesions go away (called, **spontaneous regression**) on their own without any treatment, but may leave some of their cancerous cells to spread to other parts of the body. Certain rarer forms of melanoma can also start in internal organs (mucosal melanoma for example), and if melanoma has spread widely throughout the body, it may not be possible to tell exactly where it started.

You may want to ask your doctor these questions before having a biopsy:

- What type of biopsy do you suggest for me?
- How will you perform the biopsy?
- Where will the biopsy be done? In your office?
- How long does a biopsy take?
- Will the biopsy hurt?
- Will you remove the entire growth?
- What are the risks of a biopsy? What about infection or bleeding?
- Will the biopsy leave a scar? What will it look like?
- Will the tissue be examined by a dermatopathologist?
- When will I find out the results?
- If I have cancer, what are the next steps and who will talk to me about treatment?

Diagnosing Melanoma

Once the biopsy has been completed, the tissue sample will be sent off to a lab for review by a **pathologist**. A pathologist is a doctor who evaluates cells and tissues with the aid of a microscope and other tools to diagnose disease. A biopsy sample is sent to the pathology laboratory for preparation, starting with a process that preserves the tissue and cells. The pathologist then examines the tissue with the naked eye, embeds it in wax, slices the tissue very thinly, and mounts it on glass slides to be stained using different tissue dyes. The pathologist can then examine the biopsy under the microscope to diagnose melanoma. The process takes time, anywhere from a few days to a couple of weeks, depending on the difficulty of the biopsy. A dermatopathologist, a pathologist who specializes in diagnosis of diseases of the skin is sometimes consulted. This may take extra time.

The pathologist will send back a report to your dermatologist or doctor to confirm the initial findings. If melanoma is confirmed, depending on the depth of the lesion and other factors, additional surgery may be required. Fortunately, the majority of melanomas are detected early and the initial biopsy and surgical excision is all that is required in most cases. The pathologist's findings are included in a pathology report. Typical melanoma pathology reports include other information such as the following:

- **Melanoma type**: based on the microscopic examination
- **Breslow thickness or depth**: an important prognostic factor used by pathologists to describe how deep the melanoma cells have penetrated into the skin. Breslow thickness measures in millimetres the distance between the upper layer of the epidermis and the deepest point of tumour penetration. The thinner the melanoma, the better the chance of a cure. Therefore, Breslow thickness is considered one of the most important factors in predicting disease progression.
- Presence of **skin ulceration**: whether or not the tumour's top skin layer is intact (non-ulcerated) or broken or missing (ulcerated). Often the melanoma bleeds when it is ulcerated.
- **Tumour-infiltrating lymphocytes**: presence or absence of white blood cells that may be present in primary melanomas.
- How fast the melanoma cells are growing and dividing (**mitotic rate**)
- **Angiolymphatic invasion**: melanoma cells have invaded into the lymph vessels or blood vessels.
- Growth of melanoma around nerves (**perineural invasion or neurotropism**)
- **Microsatellitosis**: microscopic tumours that have spread nearby the primary melanoma tumour.
- Growth of melanoma inside blood vessels or lymphatics (**lymphovascular invasion**)
- **Tumour regression**: the presence of white blood cells called lymphocytes that suggest that the immune system is attacking the cancer cells.

• Completeness of excision or **peripheral margin status** - the presence or absence of cancer cells in the normal tissue around the sides of a tumour removed during initial biopsy or subsequent surgery.

It is a good idea to ask for a copy of the pathology report. If there is anything you do not understand, ask your oncologist. Pathology results determine staging of disease and help guide treatment options.

Surgical Tests Prior to Final Staging

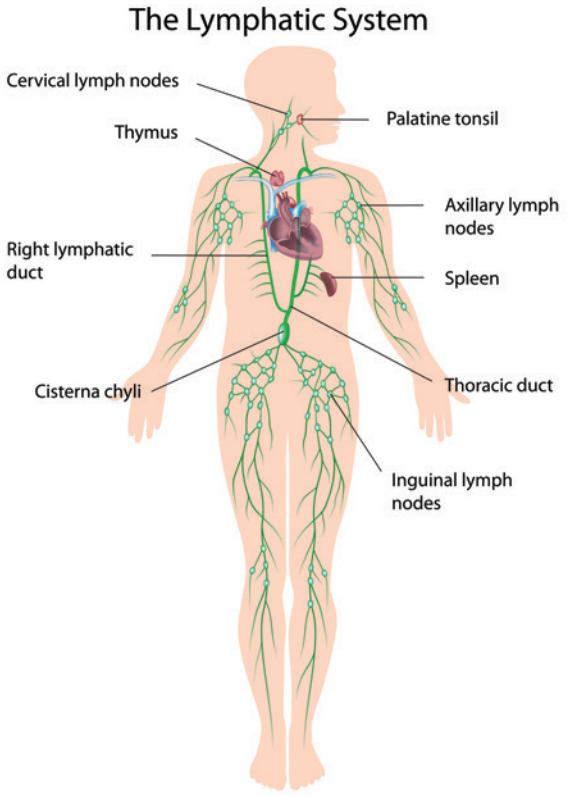
Patients who have very thin early stage *in situ* melanoma diagnosed will likely require a small surgical excision with a 5 mm margin around the lesion. For others with melanomas, even though it appears that the lesion has been removed, it is important to undergo a second **wide local excision (WLE)** to remove additional tissue (a 1 to 2 cm margin), to ensure that there is little chance of microscopic disease remaining in the surrounding tissue. The amount of tissue removed is guided by surgical standards that take into account factors such as the depth of the lesion and location on the body.

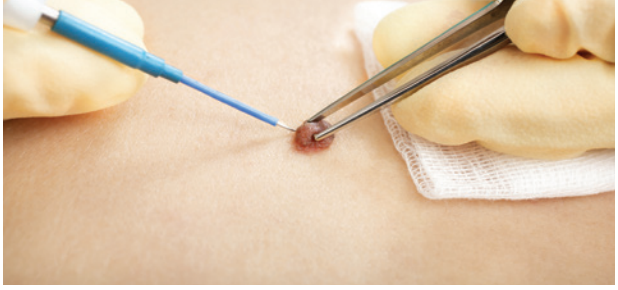
This second procedure may take place in hospital under local anesthesia or under a general anesthetic if a sentinel node biopsy is also being performed. If it appears that a wide local excision will result in a large skin defect, a plastic surgeon may be consulted in order to patch an area of skin using a skin flap or a graft, normally from the thigh, to close the defect in the operating room.

Sentinel Lymph Node Biopsy

Biopsies of areas other than the skin may be needed in some cases.

The **sentinel lymph node** is the first lymph node or nodes to which cancer is likely to spread from a primary tumour. A sentinel lymph node biopsy (SLNB) is performed to determine if the melanoma has spread to the lymph nodes. A radioactive tracer dye, and possibly a blue dye, is injected and followed to the sentinel lymph node. This is generally located in one of the major lymph node basins in either the cervical (neck), axillary (armpit), or inguinal (groin) basin. Surgery is then conducted under general anesthetic to remove the sentinel nodes, (generally there are two to three sentinel nodes). The lymph nodes are then sent to the pathologist for review. A sentinel lymph node biopsy is done when there is no evidence (through physical exam or by CT scan or other diagnostic imaging) of lymph node metastases or distant metastases, but in cases where there is a higher chance that the melanoma may have spread. Possible side effects of the biopsy include numbness, pain, bruising and lymph fluid





build up at the surgical site. Most side effects are temporary and the risk of developing **lymphedema** (swelling of a limb affected by removal of lymph nodes), for this type of biopsy is rare.

If there are no melanoma cells in the sentinel nodes, no more lymph node surgery is needed because it is very unlikely the melanoma would have spread beyond this point. If melanoma cells are found in the sentinel node, the remaining lymph nodes in this area may be removed (please see the section below regarding radical lymphadenectomy) and looked at as well. Alternatively, your surgeon may offer you ultrasound monitoring of the lymph node basin for the following five years.

Patients with melanoma 0.75 mm to <1 mm will discuss the benefit of a sentinel lymph node biopsy, given the results of the initial biopsy. For intermediate or thick melanomas 1 mm to > 4 mm, a sentinel lymph node biopsy is generally recommended for survival benefit, locoregional control and prognostic information.

Fine Needle Aspiration (FNA) Biopsy

Patients with palpable lymph nodes or suspicious lymph nodes may undergo a fine needle aspiration of the lymph node to detect the presence of cancer cells. This type of biopsy is not as invasive as some other types of biopsies, but it may not always collect enough of a sample to tell if a suspicious area contains melanoma.

For an FNA biopsy, the doctor uses a thin, hollow needle and syringe to remove a small sample of tissue of a lymph node or a tumour. The needle is smaller than the needle used for a blood test. A local anesthetic is sometimes used to numb the area first. This test rarely causes much discomfort and does not leave a scar.

If the lymph node is just under the skin, the doctor can often feel it well enough to guide the needle into it. For a suspicious lymph node deeper in the body or a tumour in an organ such as the lung or liver, an imaging test such as ultrasound or a CT scan is used to help guide the needle into place.

Excisional Lymph Node Biopsy

An excisional lymph node biopsy is often done if a lymph node's size suggests the melanoma has spread to the lymph node but an FNA biopsy of the node wasn't done or didn't find any melanoma cells.

A small incision is made in the skin. A local anesthetic is generally used if the lymph node is just under the skin, but a patient may need to be sedated or even receive general anesthesia if the lymph node is deeper in the body.

Radical Lymphadenectomy

If the sentinel lymph node biopsy results test positive for melanoma in more than one node, a radical lymphadenectomy may be recommended. A radical lymphadenectomy (also known as a lymph node

dissection), is a surgical procedure in which most or all of the lymph nodes in the tumour basin are removed. It is usually performed under general anesthesia and patients usually stay in the hospital overnight.

An incision is made in the skin above the area of the affected lymph nodes. The lymph nodes, nearby lymphatic tissue, and some underlying soft tissue are then removed and evaluated. Patients will require a drain that will stay in place for several weeks to help eliminate the buildup of fluid from the surgery. Complications of the procedure may include lymphedema, numbness, tingling, or pain in area of surgery. Lymphedema could be a permanent side effect in up to 50% of patients, depending on where the lymph nodes are removed. Lymph nodes in the groin or under the arm normally help drain fluid from the limbs. If they are removed, fluid may build up. This can cause limb swelling, which may or may not go away. If severe enough, it can cause skin problems and an increased risk of infections in the limb. Bandaging, professional lymphatic drainage massage and compression garments can help some people with this condition. For more information, see our booklet entitled *Managing Lymphedema for the Melanoma Patient*.

You may wish to ask your doctor these questions about surgery:

- What surgery do you recommend for me? Why?
- What is involved in the surgery?
- Do I need to stay in the hospital?
- Will I have pain after the surgery? How will you manage my pain?
- Am I likely to need antibiotics to prevent infection?
- What problems do I need to watch for after surgery?
- Will there be a scar?
- Are there any long-term side effects?
- Will I need home care assistance, and if so, how is that coordinated?
- Who will I call if I run into issues following the surgery?

Surgery Side Effects

Pain medications are provided after all types of surgeries. Since the pain medications commonly cause constipation, medications for constipation are commonly provided as well. The common side effects of surgery are bleeding and infection. Infection can either be treated with antibiotics or opening of the wound to allow drainage of pus and bacteria.

Lymph node surgeries sometimes have wound healing problems and can commonly cause an accumulation of lymph fluid in the limb, called lymphedema. Lymphedema can occur soon after the surgery or much later. The long-term effects of lymphedema can be transient or permanent. Talk to your treatment team if you are having bothersome side effects after surgery, or in certain cases, to effectively manage or reduce issues of lymphedema. Please also refer to our booklet *Managing Lymphedema for the Melanoma Patient* which is available in hard copy or downloadable from our website at **www.melanomanetwork.ca**.

Diagnostic Tests

Once the presence of melanoma is confirmed, your doctor may wish to perform other tests, especially if you have symptoms or if there is concern that the melanoma may have spread.

Blood Tests

Blood tests are not used to diagnose or find melanoma. Abnormal levels of certain enzymes in the blood can be an indicator of disease. **Lactate dehydrogenase (LDH)** is a blood test and LDH level can be high, which may be an indicator for issues but alone is not an accurate indicator for the presence of disease.

Imaging

Different forms of imaging allow doctors to see internal tissues and organs. This helps determine if the melanoma has spread anywhere in the body. Imaging is not used for people with stage 0 melanoma or low-risk stage I disease. For intermediate-risk stage I disease and stage II disease, imaging is used mostly to evaluate specific symptoms, such as pain. Imaging is not a routine test in early melanoma. For stage III and stage IV disease, imaging is used to evaluate specific symptoms. It is also used to assess the degree of spread of the melanoma. The type of imaging depends on symptoms and the likely location of melanoma spread.

- **Chest x-ray**: A chest x-ray may be performed for some stage I and II melanomas. It is often performed for stage III and IV melanomas.
- **Ultrasound**: A ultrasound maybe performed to assess the remaining lymph nodes in the lymph node basin (head and neck, axilla or groin) when the sentinel node had melanoma metastases.
- **Computed tomography (CT) scan**: A CT scan takes multiple x-rays of part of the body from different angles. This produces a three-dimensional image. Injection of a contrast agent helps highlight the area of concern. A CT scan is the best type of imaging to detect melanoma in the lung.
- **Magnetic resonance imaging (MRI)**: An MRI uses radio waves and magnets to take pictures of organs and other parts of the body. An MRI is the best type of imaging to find melanoma in the brain.
- **Positron emission tomography (PET) scan**: An injection of radioactive glucose, or sugar, is given before this test. The scan identifies areas with the most glucose, especially cancer cells, which collect glucose.

You may want to ask your doctor these questions about tests for melanoma:

- What tests do you suggest for me?
- Where will the tests take place? Do I need to go to the hospital?
- How long do the tests take?
- Will it hurt? Will I be given a local anesthetic?
- What happens if I'm pregnant?
- Do I need to prepare for tests?
- Do I need to bring a list of my medications?
- Can I bring someone with me?
- How long does it take to recover? Do I need any medication after the tests?
- When will I know the results? Who will explain them to me?
- If a biopsy is done, will I get a copy of the pathology report?
- If I have cancer, who will talk with me about the next steps? When?
- Will I be able to access the results of my tests online?

Staging Melanoma

When all surgical and imaging tests have been completed and pathology reports have been received, the doctors will try to figure out if the cancer has spread, and if so, how far. This process is called **staging**. It helps determine how serious the cancer is and how best to treat it. Doctors also use a cancer's stage when talking about prognosis and survival statistics. A preliminary **clinical stage** is assigned after the physical examination and initial biopsy. The final pathology report determines the **pathologic stage** and helps to determine the treatment options.

Melanoma stages are based on several factors. The staging system used for melanoma is the American Joint Committee on Cancer (AJCC) TNM system, which is based on three key pieces of information - **T** (thickness of the tumour); **N** (lymph node involvement); **M** (metastasis):

T: **The thickness of the tumour**. How deep has the cancer grown into the skin? The thickness of the melanoma is called the **Breslow** measurement. In general, melanomas less than 1 millimetre (mm) thick (about 1/25 of an inch) have a very small chance of spreading. As the melanoma becomes thicker, it has a greater chance of spreading.

Is the cancer ulcerated? Ulceration is a breakdown of the skin over the melanoma. The ulceration status tells us whether or not the tumour's top skin is present or broken or missing (ulcerated). Melanomas that are ulcerated tend to have a worse outlook.

The T category is further divided into levels 1 to 4, based on how deep the tumour has grown into the skin, measured in millimetres (mm).

N: **The spread (metastasis) to lymph nodes**. Has the cancer spread to nearby lymph nodes?

M: **The spread (metastasis) to distant sites**. Has the cancer spread to distant lymph nodes or distant organs such as the lungs or brain?

Each letter is then assigned a numerical value that provides more details about the cancer associated with it. The results of this analysis are grouped into five stages (0, I, II, III, and IV).

- **Early melanoma** is defined as stage I and stage II disease.
- **Advanced melanoma** is defined as stage III and stage IV disease.

The staging system outlined below uses the pathologic stage. We have provided a simplified version of the latest TNM system as of January 2018. It is important to know that melanoma cancer staging can be complex. If you have any questions about the stage of your cancer or what it means for your treatment ask your doctor to explain it in a way you understand. And for further breakdown on the details of the staging system, please visit our website **www.melanomanetwork.ca**

Table. TNM Pathological Staging Overview

Stage	Tumour	Node	Metastasis
0	Tis	N0	M0
IA	T1a or T1b	N0	M0
IB	T2a	N0	M0
IIA	T2b or T3a	N0	M0
IIB	T3b or T4a	N0	M0
IIC	T4b	N0	M0
IIIA	T1a/b or T2a	N1a or N2a	M0
IIIB	T0 T1a/b or T2a T2b or T3a	N1b or N1c N1b/c or N2b N1a/b/c or N2a/b	M0
IIIC	T0 T1a/b or T2a/b or T3a T3b or T4a T4b	N2b/c or N3b/c N2c or N3a/b/c Any N ≥N1 N1a/b/c or N2a/b/c	M0
IIID	T4b	N3a/b/c	M0
IV	Any T, Tis	Any N	M1

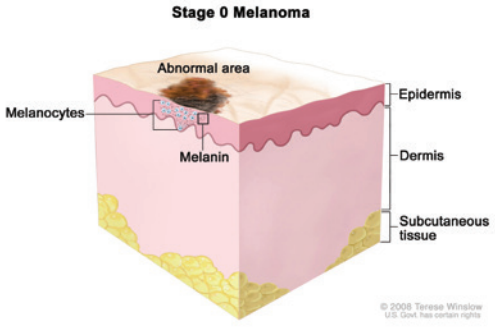
N, number of tumour-involved lymph nodes; M, number of metastases at distant site; T, primary tumor thickness.

Source: Melanoma Research Alliance

Stage 0 (Melanoma *In Situ*)

In stage 0, abnormal melanocytes are found in the epidermis, the very top of the skin and have not spread to the dermis (the second layer of skin below the epidermis). It has not spread to lymph nodes or distant sites. Stage 0 is also called melanoma *in situ*.

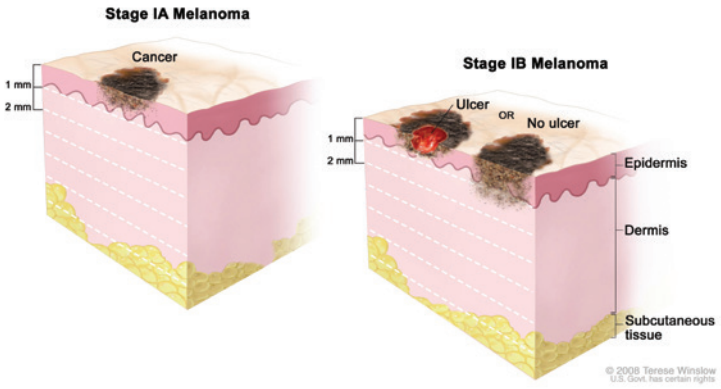
Surgery to remove the melanoma and a border of normal skin completes treatment. The prognosis is excellent at this stage. Ongoing monitoring by a dermatologist is recommended at least annually for life, with regular monthly skin self-checks by the patient.



Stage I

In stage I, cancer has formed. The cancer has not spread to nearby lymph nodes or distant sites. Stage I is divided into stages IA and IB.

- **Stage IA**: In stage IA, the tumour is up to 1 mm thick, with or without ulceration.
- **Stage IB**: In stage IB, the tumour is more than 1 mm but not more than 2 mm thick, with no ulceration.

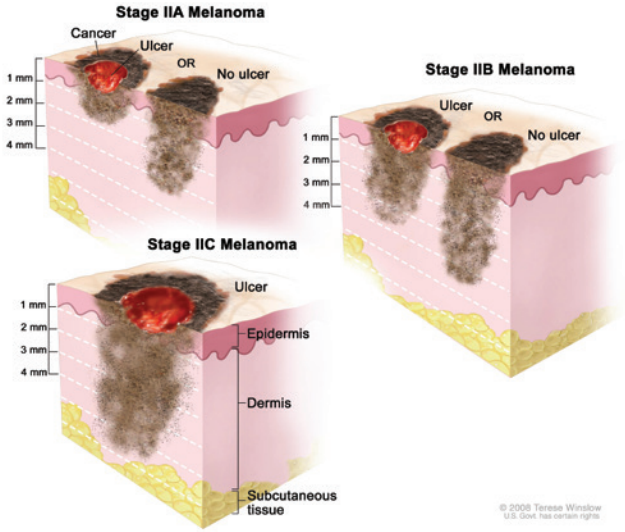


Treatment of stage I includes a second surgery to remove a wider border of normal skin around the biopsy site (a wide local excision). In some cases, a sentinel lymph node biopsy may be recommended, particularly where the tumour is over 1 mm in thickness. Ongoing monitoring by a dermatologist is recommended at least annually for life, with regular monthly skin self-checks by the patient.

Stage II

In stage II, the cancer has not spread to nearby lymph nodes or to distant sites. Stage II is divided into levels IIA, IIB, and IIC.

- **Stage IIA**: In stage IIA, the tumour is either:
  - more than 1 mm but not more than 2 mm thick, with ulceration; or
  - more than 2 mm but not more than 4 mm thick, with no ulceration.
- **Stage IIB**: In stage IIB, the tumour is either:
  - more than 2 mm but not more than 4 mm thick, with ulceration; or
  - more than 4 mm thick, with no ulceration.
- **Stage IIC**: In stage IIC, the tumour is more than 4 mm thick, with ulceration.



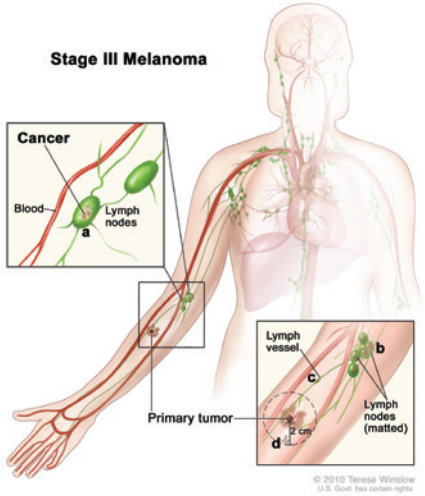
Treatment of stage II includes a second surgery to remove a wider border of normal skin around the biopsy site (wide local excision). The risk of recurrence, or return of the melanoma, or spread to another part of the body, is moderate in stage IIA. Some people with larger tumours (stage IIB or IIC), have a higher risk of recurrence and may benefit from additional treatments. Sentinel lymph node biopsy is recommended for these patients.

Stage III

In stage III, melanoma has spread to nearby lymph vessels or lymph nodes. The tumour may be any thickness, with or without ulceration. Stage III is divided into four levels - A, B, C and D.

Stage IIIA: The primary melanoma is no more than 2 mm thick. It may or may not be ulcerated. It has spread to no more than three lymph nodes detected by pathology (not palpable nodes). It has not spread to distant sites.

Stage IIIB: Either the primary melanoma site cannot be found and it has spread to only one lymph node or it has spread to very small areas of nearby skin (satellite metastasis) or lymphatic vessels, without spreading to distant sites; **OR**



The primary melanoma is no more than 4 mm and may or may not be ulcerated. It has spread to up to three lymph nodes or to very small areas of nearby skin (satellite tumours) or lymphatic channels. It has not spread to distant sites.

Stage IIIC: The primary melanoma site cannot be found **AND** it has spread to up to four or more lymph nodes **OR** it has spread to two or more lymph nodes and to very small areas of nearby skin (satellite metastasis) or lymphatic vessels, without spreading to distant sites; **OR**

The primary melanoma is no more than 4 mm and may or may not be ulcerated. It has spread to one or more lymph nodes or to very small areas of nearby skin (satellite tumours) or lymphatic channels or lymph nodes clumped together. It has not spread to distant sites; **OR**

The melanoma is between 2.1 mm and 4 mm and may or may not be ulcerated **AND** has spread to one or more lymph nodes or has spread to very small areas of nearby skin (satellite tumours) or lymphatic channels or lymph nodes clumped together. It has not spread to distant sites; **OR**

The melanoma is thicker than 4 mm, is ulcerated has spread to no more than three lymph nodes or to very small areas of nearby skin (satellite tumours) or lymphatic channels. It has not spread to distant sites.

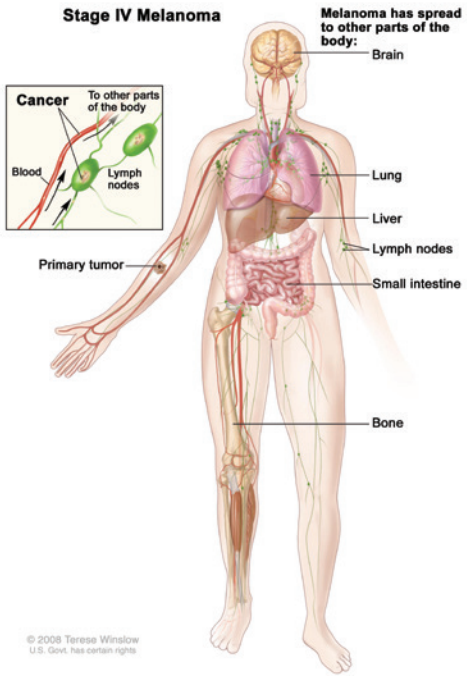
Stage IIID: The primary melanoma is thicker than 4 mm, is ulcerated **AND** has spread to four or more lymph nodes **OR** has spread to very small areas of nearby skin (satellite tumours) or lymphatic channels. It has not spread to distant sites.

Treatment of stage III may include a wider border of normal skin around the biopsy site. Sentinel lymph node biopsy is recommended for these patients to provide locoregional control and to identify patients who may benefit from adjuvant therapy, radiation and/or entry into adjuvant clinical trials. Adjuvant therapy following biopsy and surgery may be recommended and is discussed in our treatment section below.

Stage IV

In stage IV, the cancer can be any thickness and might or might not be ulcerated. It may or may not have spread to nearby lymph nodes, but has spread to other distant sites in the body, such as the lung, liver, brain, bone, soft tissue, or gastrointestinal (GI) tract. Cancer may have spread to places in the skin far away from where it first started.

Treatment of Stage IV involves a discussion with your oncologist for available treatments and the possibility of participating in clinical trials.



Persistent or Recurrent Disease

Melanoma can return after treatment.

- **Persistent melanoma** is a tumour that was not completely removed by treatment. It is found in the surgical scar. Persistent melanoma has not penetrated beneath the epidermis.
- **Recurrent melanoma** may be of several types. Local recurrence is reappearance of the melanoma in the vicinity of a previously removed melanoma or en route to the regional lymph node basin (in-transit metastasis).
- **Regional recurrence** is melanoma in the lymph nodes near the first melanoma.
- **Distant recurrence** is spread beyond the regional lymph nodes.

Investigation of persistent and recurrent melanoma begins with a biopsy. After that, additional tests depend on the stage of the disease, as described previously. The stage of the recurrence also determines the type of treatment given and the follow-up schedule. Clinical trial participation may be offered for recurrence.

Treating Melanoma

The main factors determining treatment options are depth of the tumour, presence of ulceration and lymph node involvement. Deeper melanomas are more likely to have spread. They are also more likely to **recur**, or come back after treatment. Melanomas less than 1 mm in thickness are unlikely to spread.

Treatment for melanoma can include the following:

- **Surgery**
- **Immunotherapy**, or treatment that stimulates the immune system to fight disease
- **Targeted therapy**, or treatment for people whose melanoma possesses specific genetic changes
- **Chemotherapy**, or treatment with drugs that kill cancer cells
- **Radiation**, or treatment that uses a high-energy beam to kill cancer cells

Cancer treatment involves a team of healthcare professionals. Your treatment team may include the following:

- A dermatologist
- A surgeon or surgical oncologist
- A **radiation oncologist**, a doctor who uses radiation to treat cancer
- A **medical oncologist**, a doctor who uses drug therapy to kill cancer cells that have spread from the primary melanoma

You may wish to ask your doctor these questions about melanoma treatment:

- What stage is my melanoma?
- What treatments are recommended for my stage of melanoma?
- Does my age, health, and other medical conditions affect my treatment options?
- What are the risks and benefits of each treatment for melanoma?
- Where will I be treated? Do I need to stay in hospital or can I go home after each treatment?
- What should I do to prepare for treatment?
- When can I start treatment?
- What is my chance of being free of melanoma after treatment?
- What side effects should I watch for during treatment?
- When can I resume my normal activities?
- What is the chance my cancer will return or spread?
- What do I do after treatment is finished?

Treatment Options

Adjuvant Treatment

Early melanoma that has not spread beyond the skin or nearby lymph nodes is usually treated with surgery (refer to pages 15 to 17 on surgery). **Adjuvant therapy** is additional cancer treatment given after the primary treatment (surgery), to lower the risk that the cancer will come back. Stage III patients that have had surgery and are considered to have no further evidence of disease (fully resected), still may be at higher risk for recurrence of melanoma.

Adjuvant therapy or clinical trials are typically offered to stage III patients after they have had a complete surgical resection of their melanoma. Please consult with your medical team to determine current treatments or clinical trials available for stage III patients or check the MNC website.

As of January 2020, adjuvant use of the targeted therapy combination Dabrafenib and Trametinib have been approved by Health Canada for use in the adjuvant setting. As well, the immunotherapies Pembrolizumab and Nivolumab have also been approved by Health Canada for use in the adjuvant setting. Please check our website, your oncology team or your private insurance (if appropriate) to determine coverage in your province.

Localized Therapy

Patients with melanoma that have non-resectable in-transit disease may be offered treatment that is injected directly into the skin tumours. For patients with low-volume disease, the drug therapy aldesleukin (or IL-2, interleukin 2, or Proleukin), can help stimulate the immune system to attack tumours when locally injected. This consists of injections performed in the cancer centre every two weeks for usually up to eight sessions.

Occasionally, other therapies such as isolated limb infusion or isolated limb perfusion are used for patients with a greater volume of disease and involve local recirculation of chemotherapy in the affected limb. This treatment is performed in the operating room, requiring general anesthesia and the patient usually stays in the hospital for a few days after the procedure.

Systemic Therapy

Melanoma Stage IIIC Unresectable to Stage IV

Melanoma that has spread to other parts of the body and is not treatable by surgery may be treated with systemic therapy. Systemic therapy, which may be given by pills or by intravenous, treats the entire body to kill any melanoma cells. Systemic therapy is a type of therapy that treats the entire body and may be given by pills or by intravenous. Sometimes, particularly if the melanoma has spread to the brain, radiation therapy may be recommended.

There are two major types of systemic therapy: **biological therapy,** (**which includes immunotherapies, targeted therapies and cytokines**), and **chemotherapy**. Systemic therapy may be used when melanoma has spread beyond the skin. A single type of treatment or a combination of treatments may be given. Combination regimens are complex and usually given in specialized centres. A second systemic therapy (**second-line therapy**) may be given if the first one was ineffective or if it has stopped working.

Biological Therapies

Immunotherapy

Immunotherapies are a new class of drugs that have been developed to stimulate a person's own immune system to recognize and destroy cancer cells. Several immune checkpoint inhibitors are now available that seem to release the brakes of the immune system, allowing it to mount a stronger and more effective attack against cancer cells. These drugs target proteins on immune cells that act like brakes, or checkpoints. By releasing these immune brakes, the drugs allow a stronger and more powerful immune attack against cancer.

Since 2012, several types of immunotherapies have been approved in Canada for the treatment of advanced unresectable or metastatic melanoma (stages IIIC – Stage IV), including pembrolizumab (Keytruda), nivolumab (Opdivo) and ipilimumab (Yervoy).

Side effects of these drugs can include fatigue, cough, itching, skin rash, decreased appetite, constipation, joint pain, and diarrhea. Other more serious side effects occur less often. As these drugs work by basically removing the brakes from the body's immune system, sometimes the immune system starts attacking other parts of the body. This can cause serious or even life-threatening problems in the lungs, intestines, liver, hormone-making glands, kidneys, or other organs.

It's very important to report any new side effects to your health care team promptly. If serious side effects do occur, treatment may need to be stopped and you may be prescribed high doses of corticosteroids to suppress your immune system.

Current immunotherapy drugs:

Ipilimumab (Yervoy): This immunotherapy helps the body's immune system recognize and destroy melanoma cells. It blocks CTLA-4, a protein on T cells that normally helps keep them in check. Ipilimumab is given intravenously. One dose is given every three weeks for four treatments. Ipilimumab can lengthen life in people with advanced disease with melanoma that can't be removed by surgery or that has spread to other parts of the body (stage IIIC – IV). Often, ipilimumab is prescribed in combination with nivolumab, which has resulted in longer progression-free survival and a higher objective response rate than ipilimumab alone.

Pembrolizumab (Keytruda): This drug is an immune checkpoint inhibitor that targets PD-1, a protein on immune system cells (called T cells), that normally helps keep these cells from attacking other cells in the body. Keytruda can be used to treat melanomas that can't be removed by surgery or that have spread to other parts of the body. By blocking PD-1, this drug boosts the immune response against melanoma cells. This can often shrink tumours and help people live longer. Keytruda is normally given as an intravenous (IV) infusion every 3 weeks.

Nivolumab (Opdivo): This is an immune checkpoint inhibitor that targets PD-1, a protein on immune system cells (called T cells) that normally help keep these cells from attacking other cells in the body. By blocking PD-1, this drug boosts the immune response against melanoma cells. This can often shrink tumours and help people live longer. These drugs are given as an intravenous (IV) infusion every 2 weeks. Often, nivolumab is prescribed in combination with ipilimumab, which has resulted in longer progression-free survival and a higher objective response rate than ipilimumab alone.

Targeted Therapies

A targeted therapy is a type of cancer drug that targets melanoma cancer cells. It precisely identifies and attacks cancer cells, while doing less damage to healthy or normal cells. Targeted therapy blocks cancer growth, beyond just interfering with cancer cells. It can kill a cancer cell without harming healthy cells. It differs from standard chemotherapy which acts on all rapidly dividing cancer cells and normal cells.

How do targeted therapies work?

The goal of targeted therapy is to shut down mutated protein molecules to slow the growth of melanoma cells – without harming healthy tissue. Targeted therapy is systemic, which means that the drugs travel through the bloodstream to all parts of your body.

About half of melanoma patients have a particular genetic mutation in the BRAF (pronounced bee-raf) protein that is causing the cancer to grow. A BRAF mutation triggers cells to develop abnormally and divide out of control. Targeted therapy drug combinations (below) block the activity of the mutated BRAF protein and the MEK protein that is also a part of this growth pathway. The result may slow or stop the growth and spread of melanoma. The combination of BRAF plus MEK inhibitors shrinks or eliminates tumours for longer periods of time than using either type of drug alone.

If you have advanced unresectable or metastatic melanoma, a biopsy of your tumour will likely be tested to see if the cancer cells have a BRAF mutation. Drugs that target the BRAF protein (or the MEK proteins) aren't likely to work in patients whose melanomas have a normal BRAF gene.

The following combinations of targeted therapies are being used in Canada:

Vemurafenib (Zelboraf) plus cobimetinib (Cotellic): This is a first-line treatment for patients with BRAF V600 mutation-positive unresectable stage IIIC or IV melanoma or metastatic melanoma. Vemurafenib targets the mutated BRAF protein, while cobimetinib acts against the MEK protein. The drugs are administered as pills taken daily. Side effects can include rash, nausea, diarrhea, swelling, fatigue and extreme sensitivity to sunlight (UV radiation). Rare but serious side effects can include heart damage, excess bleeding, loss of vision, lung problems and skin infections. Some side effects (such as the development of other skin cancers) are actually less common with the combination therapy.

Dabrafenib (Tafinlar) plus trametinib (Mekinist): This is a first-line treatment for patients with BRAF V600 mutation-positive unresectable stage IIIC or IV melanoma for metastatic melanoma. Dabrafenib acts as an inhibitor of the BRAF protein and slows down or stops the growth of cancer cells while trametinib acts against the MEK protein. The drugs are administered as pills taken daily. Side effects can include rash, nausea, fevers, headaches, anemia, changes in eyesight, diarrhea, swelling, and fatigue. Rare but serious side effects can include heart damage, excess bleeding, loss of vision, lung problems, and skin infections.

What should I ask my doctor about immunotherapies or targeted therapies?

Not all of these therapies work for all melanoma patients, because everyone is different and has a different genetic makeup. Here are some questions you may want to ask your doctors:

- Am I eligible for a targeted therapy or an immunotherapy? What are the alternatives if not?
- What is your experience using the targeted therapies or immunotherapies?
- Is there a combination therapy that is a good option for my melanoma treatment?
- How successful has the therapy you are recommending been for patients like me?
- What are the side effects of treatment?
- Will the drug be taken orally or by intravenous? Will I have to be at the hospital for treatment and if so, how often?
- Are there any clinical trials for the one of these therapies that I should consider?
- What other treatments are Health Canada-approved for treating advanced melanoma?
- What are the risks and benefits of the available treatment options?
- What are the goals for my treatment?
- How long will I stay on this treatment?
- Is the drug therapy covered by provincial government or on private insurance? If not, is it available for purchase and is there any assistance to offset the cost of therapy?
- Is there a clinical trial option that may be of better benefit for me compared to what is currently available for treatment?
- Will any of these therapies affect my fertility?

Chemotherapy

Chemotherapy is not very effective in treating melanoma and has been largely replaced by immunotherapies and targeted therapies. Chemotherapy uses powerful drugs to kill cancer cells, and may be given as a single drug or a **regimen**, or combination. These drugs may be given as pills or by injection or infusion into a vein. Chemotherapy is usually given in cycles lasting between two and four weeks. Chemotherapy drugs include carboplatin, paclitaxel, and dacarbazine.

Chemotherapy side effects

Side effects of chemotherapy depend on the specific agent. Chemotherapy kills rapidly dividing cells, like cancer cells. It also damages normal cells that divide quickly. Cancer cells cannot recover from chemotherapy, but normal cells can repair the damage. Chemotherapy may cause a number of side effects including mouth sores, hair loss, fatigue, nausea and vomiting, diarrhea or constipation, amongst others. Side effects generally stop once chemotherapy has finished.

Radiation

Radiation therapy uses a high-energy beam to kill cancer cells. Radiation, when recommended, is usually used after surgery to kill any potential remaining cancer cells. To minimize damage to normal tissue, many beams of radiation may be aimed from different angles to meet at the tumour. This delivers more radiation to the tumour than to healthy cells around it. Postoperative radiation may be considered in the following situations:

- The melanoma has spread from the lymph nodes or the lymph nodes are greatly enlarged.
- Disease remains after surgery or local control of disease is not possible through surgery.
- A great deal of melanoma is present in lymph nodes, and surgery is unlikely to remove all the cancerous cells.
- There is a need to manage and control pain for palliative care.

In other cases, radiation may be used pre-operatively to reduce the size of the tumour for a better surgical outcome.

Radiation and Brain Metastases

Melanoma has a high propensity to metastasize to the brain. In patients with a limited number of brain metastases, the options for treatment include surgical removal and/or radiation therapy. Radiation therapy can be delivered as either focused radiation to the metastases alone, called stereotactic radiosurgery (SRS), or radiation to the entire brain (whole brain radiotherapy - WBRT). SRS can decrease the risk of developing neurocognitive side effects (e.g. memory loss) compared to WBRT. However, WBRT also treats microscopic disease that may not be visible on imaging, which can decrease the risk of developing subsequent brain metastases. Which treatment is recommended often depends on a multitude of factors, including the life expectancy of the patient, the number of metastases in the brain, the size of those metastases, as well as the amount of disease outside the brain.

Radiation Side Effects

Radiation therapy is painless. However, other side effects may occur. Side effects depend on how much radiation you receive and the part of the body treated. Skin treated with radiation may be red, burning like a sunburn, dry, tender, and itchy. Hair loss may occur in the treated area. There also may be scar tissue and loss of feeling in the area of the radiation. Changes in the skin usually disappear within six to 12 months. Fatigue often occurs during radiation therapy. Energy levels generally return to normal after radiation. Rarely, radiation may lead to the development of a different tumour. Your treatment team can help you manage radiation side effects.

You may wish to ask your doctor these questions about radiation:

- How long does treatment last?
- How often will I have radiation?
- Will I feel any pain?
- What are the side effects of radiation?
- What problems do I need to watch for after radiation?
- Are there any long-term side effects?
- Will I have a scar?

Clinical Trials

Clinical trials are studies of new therapies to determine whether a medication is safe and effective. Generally, clinical trials compare new treatment with current therapies. Clinical trials may assess new medications and new combinations of treatments. This may include combinations of medications, and combinations of radiation, biological therapy, chemotherapy, and targeted therapy.

Clinical trial participation is often offered to people with high-risk stage II, stage III, or stage IV melanoma. People with persistent or recurrent melanoma may also be offered clinical trial participation. There may be clinical trials in melanoma available in your area. Talk to your

doctor if you are interested in being part of a clinical trial. For more information on the phases of clinical trials and what to consider, please visit our website **www.melanomanetwork.ca**. The Cancer View Canada website at **www.cancerview.ca** has a list of clinical trials in Canada. Other major clinical trial information is available from the U.S. National Institute of Health at **www.clinicaltrials.gov**.

You may wish to ask your doctor these questions about clinical trials:

- Are any clinical trials available that I could take part in?
- What is the study purpose?
- What tests and treatments are part of the study?
- What does the treatment do?
- Has the study treatment been tested before? For what types of cancer?
- Will I know which treatment I receive?
- What is likely to happen to me with, or without, this new treatment?
- What are my other options? What are their benefits and risks?
- What does taking part in the study mean to my daily life?
- Can I expect side effects during the study? Can they be prevented or treated?
- Does the study involve a hospital stay? If so, how often and for how long?
- Will taking part in the study increase my chance of recovery?
- Does the study include follow-up care?
- What is the phase of this clinical trial? (Phase 0-III)

Palliative Non-Curative Therapies

Should available treatments prove ineffective to control or eliminate the cancer, palliative non-curative therapies and support are available through your treatment centre. Palliative non-curative therapies are given without curative intent when no cure can be expected. It is treatment given to relieve the symptoms and reduce the suffering caused by cancer and other life-limiting diseases.

For patients with melanoma, this may include any of the previously discussed treatment therapies and interventions, including pain management. Palliative medicine provides medical treatments that focus on symptoms rather than curing illness.

The palliative care team will focus on providing relief from the symptoms, pain, physical stress, and mental stress of a terminal diagnosis. Palliative care providers can help the person and their family address concerns, expectations, needs, hopes and fears.

When receiving palliative care, many people experience an improved quality of life and reduced anxiety once symptoms have been well managed.

Second Opinion

A second opinion from another doctor about your diagnosis and suggested treatment can be a good idea in certain circumstances. The second doctor may agree with the proposed treatment plan or he or she may suggest a different approach. In either case, you will have learned more and may be more confident that you know the treatment options. It may take a few weeks to see a second doctor. The possible delay generally does not affect the treatment outcome. You may want to ask your doctor whether your treatment needs to start immediately.

Treatment Plan

A **treatment plan** is a useful tool to help you understand your therapy and feel in control. Developing a treatment plan can ease some of the anxieties of the initial unknowns after diagnosis. It can be a relief to know how your team will address your melanoma and give you an idea of what to expect. A treatment plan includes information about the melanoma, the planned treatment and possible side effects. It may also include information about any physical and emotional concerns or issues and your treatment goals. Your treatment plan may also include general health measures, such as quitting smoking or limiting alcohol. A treatment plan helps anyone with melanoma. It is, however, even more important for anyone with advanced disease. A treatment plan helps you and your treatment team be clear about your goals and wishes. Ask your treatment team for a written treatment plan.

You may wish to ask your doctor these questions about melanoma treatment:

- What stage is my melanoma?
- What treatments are recommended for my stage of melanoma?
- Do my age, health, and other medical conditions affect my treatment options?
- What are the risks and benefits of each treatment for melanoma?
- Where will I be treated? Do I need to stay in hospital or can I go home after each treatment?
- What should I do to prepare for treatment?
- When can I start treatment?
- What is my chance of being free of melanoma after treatment?
- What side effects should I watch for during treatment?
- When can I resume my normal activities?
- What is the chance my cancer will return or spread?
- What do I do after treatment is finished?
- Are there any clinical trials that may offer a better option compared with currently available treatments?

Following Up

Your follow-up plan depends on the stage of the melanoma and the guidelines of your province or cancer centre. Follow-up appointments allow your doctor to monitor for possible recurrence of the melanoma. The follow-up plans below are general guidelines for people with treated disease who have no current symptoms nor evidence of disease. Please note: These guidelines have been adopted from the Cancer Care Ontario-PEBC guideline and may differ by province.

Melanoma stage	Frequency
In situ melanoma	• Patients do not require oncologist follow-up after surgical treatment. • Follow-up full skin examination with a dermatologist should occur annually or as clinically indicated.
Stage I to IIA	• Patients do not require oncologist follow-up after surgical treatment. • Follow-up with a dermatologist should occur every six to 12 months or as clinically indicated.
High-risk stage IIB/C and stage IIIA	• Patients should receive clinical visits with an oncologist every six months in years 1 through 3, then annually until year 5. Patients may be discharged to care of dermatologist and family physician after five years if appropriate. • Follow-up with a dermatologist should occur every six to 12 months or as clinically indicated.
Stage IIIB to D and resected stage IV	• Patients should receive a clinical visit with an oncologist every three to six months in years 1 through 3 and every six months in years 4 to 5, or as clinically indicated. • Follow-up with a dermatologist should occur every six to 12 months or as clinically indicated.

Coping With Your New Diagnosis

Being diagnosed with melanoma can feel overwhelming. Processing information about the disease and making decisions about treatment options are usually the first tasks we face and are undoubtedly very important. Many people can feel bombarded with information and confused by a great deal of unfamiliar medical language. It can certainly be a lot to take in and be a big learning curve. Hopefully this booklet has been of help to understand melanoma and treatment of this disease.

Another important area to address is the emotional impact of a diagnosis. Everyone responds in a different way. You may experience a feeling of disbelief or feel shocked, overwhelmed, devastated, numb, afraid or angry. These emotions are normal and feelings that all new patients can relate to. It can feel like you are on a rollercoaster or feel like life as you know it has come to a complete halt.

Adjusting to and finding ways to cope with a melanoma diagnosis is an important part of healing, along with treatment. Below are some suggestions related to dealing with the challenges ahead as well as with some suggestions and tools for coping with the diagnosis.

Helpful Suggestions

Being diagnosed with cancer is like starting a new job. It is hard to know what to expect; it is a new role and culture that you need to adapt to. Treatment can be stressful and takes time and energy. It may be a challenge adjusting to this life change. This may be a time to step back, prioritize, delegate and try to focus on you as much as possible. Remember that you are not alone. **Melanoma Network of Canada can help with information, questions and support.**

Talk to your family about your diagnosis. One of the first thoughts to occur to some after hearing they have melanoma is "how am I going to tell my family?" Cancer definitely has an impact on the entire family. It is understandable to want to protect your loved ones from worry. Open communication is recommended by many experts. Talking about your treatment plan, available resources, along with an open discussion about your concerns and hopes can be key parts of the discussion. Although this is a stressful time, family connections can actually become stronger by working together on strategies to deal with this experience.

Learn about your disease and treatment options. This can help you understand the tests you undergo and the treatments that are recommended. If you would like to know more about your melanoma, ask your doctor for the details – the type, stage and prognosis. Ask for good sources of up-to-date information on your treatment options. Participating in your care, knowing what to

expect and your options may help you feel more in control and confident when making decisions. Some people prefer having less medical information - talk to your medical team about your preferences for receiving information. Sometimes "what I need to know right now" is a strategy that works.

Consider joining a support group or connecting with others who have experienced melanoma. Talking to others who have gone through similar experiences and have been treated for melanoma can be extremely helpful to some people. Cancer affects the whole person and their loved ones, so it is important to create a support network as part of managing your care. Melanoma Network of Canada has a Peer-to-Peer support program if you wish to connect with another melanoma patient or caregiver by phone that has had a similar experience. A Melanoma Network of Canada in-person support group may also be offered in your area. We welcome your call if you want further information.

Pay attention to how you feel emotionally and how you are coping. Professional help and support are available to you if you run into difficulties. It is normal for people diagnosed with cancer to worry or feel anxious or discouraged. If these emotions become excessive and interfere with your relationships and life in general, it may help to seek out professional support. If you are having difficulties concentrating, sleeping, or eating, or feel that you have lost interest in your usual activities, speak to your health care team and ask about counseling options and support services available. Many cancer centres have access to social workers, psychiatrists and psychologists who are covered through your provincial health insurance.

Take care of yourself. Make your well-being a priority during cancer treatment. Get enough sleep, choose a diet full of fruits and vegetables, make time for gentle exercise on days you feel up to it, and find time for things you enjoy, such as reading, meditating or listening to music. If you need to, let others take care of you for a while. This doesn't mean you're helpless or weak. It means you are using all your energy to get well!

Ask questions. Don't be afraid to ask your treatment team if you don't understand something. Melanoma can be complicated with complex treatment options. Good communication with your healthcare team is essential. Getting answers to your questions can help to ensure that you understand your diagnosis and treatment, and feel more satisfied with your overall care. Read the questions to ask your doctor contained in this booklet or on the Melanoma Network of Canada website (**www.melanomanetwork.ca/questions/**).

Express your feelings: Talk to a trusted friend or family member, keep a journal or blog or express yourself through music, painting or drawing. Having opportunities to express how you are feeling can be a great relief.

Be well prepared for your medical appointments. Bring a list of all medications, vitamins or supplements you are taking and write down any symptoms you are experiencing. Take someone with you to the appointment. It can be difficult to remember all the information provided. Your support person can also talk with you after the appointment and they may remember something that you missed or forgot. Your time with your doctor is limited, so preparing a list of questions can help you make the most of your time together. List your questions from most important to least important, in case you run out of time.

Get organized: Find a system that works for you to keep track of your appointments, test results, questions for your team, prescriptions, side effects, etc. There are some good mobile apps available, or a simple binder might work for you.

Ask for and accept help: Reach out to friends and family. It may not be realistic to manage all of the responsibilities and tasks you accomplished pre-diagnosis. Going through and recovering from treatment is demanding and emotionally taxing. Friends and family appreciate the opportunity to help. Providing assistance can allow for family and friends to feel helpful and involved while at the same time benefitting you.

Find a stress outlet: This may be a good time to find a hobby, activity or pastime that allows you to take a break, provides distraction and lets you forget about your worries for a little while. No one can do cancer 24/7. This might also be a time to try out or learn some new stress relief tools such as mindfulness mediation.

Try to keep a hopeful outlook: Focusing on hope can improve the quality of your life throughout your cancer treatment. Hope is a concept that can change over time. It can be simple and short term like hoping for a good day with friends, or long term, such as hoping to be cancer free. It does not mean you have to be happy and positive all the time. It is about balance and being aware of and accepting all of your feelings.

Practical support: Financial questions, understanding drug coverage, parenting, and sorting out work can be just some of the practical issues that you are facing. Ask your healthcare team how to connect to a social worker who can assist you to navigate potential resources. Social workers can ensure that you are aware of resources and accessing any supports that you may be entitled to receive.

Dealing with uncertainty: This can be a time of much uncertainty and many unknowns. Trying to control things largely out of our control, (e.g. getting an infection after surgery), or setting up expectations about how things will turn out can be frustrating as well as exhausting. Adopting a mindset of flexibility can be helpful, along with giving yourself permission to not have all of the answers right now. This can initially be very difficult and uncomfortable, but finding some peace with living with uncertainty is possible.

Complementary and Alternative Medicines

Complementary and alternative medicine (CAM) includes vitamins, herbal preparations, nutritional supplements, and stress reduction. **Most CAMs have not been studied as treatments in cancer**. It is important to tell your treatment team about any CAMs you are taking. Some CAMs may interact with some cancer therapies. Complementary therapies that have been studied are acupuncture, which can provide pain relief in some conditions, and yoga and meditation, which can be effective for relaxation. These therapies may make you feel better. Your treatment team can advise you about which complementary therapies may help.

Preventing Melanoma and Skin Cancers

Practicing Sun Safety

People with melanoma have an increased risk of developing another melanoma. It is very important to take action to help prevent another melanoma or other form of skin cancer. Remember that the leading cause of melanomas is due to exposure to UV radiation. It is also important to know that UV radiation can penetrate windows, car windshields, and light clothing. Clouds do not protect from UV exposure. Follow these important preventive measures:

- Apply a broad-spectrum, water-resistant sunscreen with a sun protection factor (SPF) of at least 30 (SPF 50 or higher is even better for you) about 30 minutes before going out. Reapply every two hours, or more frequently after sweating or swimming. Wear sunscreen all year round. Do not use sunscreen to stay out in the sun longer.
- Limit your time in the sun.
- Do not use sunlamps or tanning beds. The risk of melanoma increases after a single use of a tanning bed.
- Avoid tanning.
- Avoid outdoor activities when the sun is strongest, between 11 am and 3 pm. If you are outdoors during peak hours of UV, then stay in the shade whenever possible.
- Protect yourself from sunlight reflected by water, ice, snow, sand, and pavement. UV rays reflecting off snow and ice are up to eight times stronger than reflection off water.
- Wear clothes made of tightly woven fabrics that cover your arms and legs or opt for sun protective clothing with an ultra-violet protection factor (UPF) of 50 or more.
- Wear a hat with a wide brim that shades your face, neck, and ears.
- Wear sunglasses with 100% UVA and UVB protection to protect your eyes and the skin around them.

Checking Your Skin

Check your entire skin once a month. A good time is after you shower or bathe. Checking your skin only takes about 10 or 15 minutes. Make sure the room has enough light and a full-length mirror. Use a hand-held mirror too. Learn where your moles, birthmarks, and other skin marks are and how they look and feel. Check for any change. People who check their skin regularly discover 53% of melanomas and family members discover 17% of melanomas. Finding melanoma at an early stage can lead to a 90% cure rate. Research has shown that checking your skin regularly can find melanomas at an early stage and decrease the risk of mortality by 63%.[3]

- Look at your face, neck, ears, and scalp. Because it is hard to check your scalp yourself, you may want to have a friend or relative help with this task.
- Look at your body from the front and back.
- Raise your arms and look at both sides of your body.
- Bend your elbows and look at your hands, including the palms and nails, and both arms.
- Look at the front, back, and sides of your legs.
- Look at your genital area and between your buttocks.
- Sit down and look at your feet, including the nails, soles, and between the toes.

Look for the following:

- A new mole that looks different
- A new firm flesh-coloured bump
- A change in any mole (remember ABCDE)
- A new red or dark flaky patch that may be raised
- A sore that does not heal

Examining your skin regularly helps you learn the normal appearance of your skin. If you find anything new and unusual, contact your doctor. It is also important to have your doctor examine your skin regularly. If you have many moles, it is helpful to have a dermatologist examine your skin.

Tip: The ugly duckling sign

Generally, most moles on a person's body look the same or similar. Melanomas, however, look different from all other moles. Usually, only one melanoma develops at one time. A mole that looks or feels different from other moles – the ugly duckling sign – needs to be checked by your doctor.

Take a picture and put a ruler as a scale of measure next to any unusual moles and keep a record to help you monitor and to be able to show to your doctor. There are many websites and apps available now that will help you monitor your moles. You also reduce your risk of melanoma by having your doctor remove any suspicious or abnormal moles.

Melanoma Network of Canada Support Services and Resources

Phone & Email Support

Available Monday to Friday, 9 am to 5 pm ET. We aim to respond to all inquires within 48 hours. All calls and emails and are confidential.

For support call **905-901-5121** or **1-877-560-8035** or email at **info@melanomanetwork.ca**.

Peer-to-Peer Melanoma Support

Providing a connection with a former patient or caregiver who has been down a similar path can provide immeasurable support. This program connects a trained volunteer who has been through a diagnosis with new patients, patients facing ongoing challenges with the disease, or their caregivers. This service is offered by telephone and can connect patients anywhere in Canada. Patients are able to ask questions and relieve some of their stress, worries, concerns, and fears that come from a diagnosis of melanoma. Peer-to-Peer support does not replace professional counseling or medical advice. If you are interested in becoming a Peer-to-Peer volunteer or would like to be matched with a fellow patient or caregiver please contact **info@melanomanetwork.ca**, call **905-901-5121** or **1-877-560-8035** or visit **www.melanomanetwork.ca/peer-to-peer/**.

Melanoma Support Groups

Join a melanoma patient and caregiver support group to meet with others facing a similar diagnosis. Led by skilled health care professionals along with melanoma survivors, these informal meetings are a great opportunity to share information, understanding, challenges, questions and insights. We provide an evening of encouragement, connection and support. Groups are free and held the first Wednesday of every month. For more information or to register, visit **www.melanomanetwork.ca/supportgroups** or email **info@melanomanetwork.ca**.

Melanoma Information Sessions

Each year, MNC hosts 10 patient meetings across Canada. The meetings provide an opportunity to hear about latest advancements in treatment and patient care and are a great opportunity to connect with other patients and members of our organization. Please check our events calendar for dates and times near you or contact **info@melanomanetwork.ca** or call **905-901-5121** or **1-877-560-8035**.

Melanoma Online Patient Forum

Our online discussion forum provides a place to ask questions or provide insights and information on your own experience with other patients and caregivers. It is a great way to get a timely response to your questions or concerns. Visit our Discussion Forum at **www.melanomanetwork.ca/forums**.

Patient & Caregiver Resources

Melanoma Patient Connection: Quarterly Newsletter

Our leading edge publications are designed and produced by MNC for melanoma patients, caregivers and physicians. All publications are in PDF format available to be downloaded. Alternatively, we can send you a printed copy. To view all MNC publications visit **www.melanomanetwork.ca/mncnewsletters**.

Melanoma: What You Need to Know

Available for download, by mail or at major cancer centres across Canada, this comprehensive booklet helps provide current and patient-friendly information covering topics such as types of melanoma, diagnosing, staging and treating melanoma. Visit **www.melanomanetwork.ca/mncpub/** or call **905-901-5121** or **1-877-560-8035**

Lymphedema for the Melanoma Patient

This guide to upper and lower limb lymphedema for the melanoma patient is a helpful tool to understand the care and treatment of lymphedema following surgery.

A Guide to Uveal Melanoma

A useful overview of this rare form of eye cancer. Written with the help of leading specialists in the country, it provides a good overview of this often challenging disease.

Melanoma Patient Education Video Library

Videos are available on our website and YouTube channel. Video topics include Patient Information Session recordings with leading Melanoma experts – oncologists, social workers, psychologists, drug navigators and more. Visit our YouTube channel **www.youtube.com/user/MelanomaCanada**.

Strides for Melanoma

Each year in September, MNC puts on a national walk for melanoma awareness in Canada. Connect with melanoma patients, survivors, caregivers and friends to support one another for a future without melanoma.

For walk locations and registration information visit our website at **www.melanomanetwork.ca** or call us at **1-877-566-8035**.

Glossary

ABCDE
A memory acronym for characteristics of moles that might be cancer.
A=Asymmetry
B=Border
C=Colour
D=Diameter
E=Evolving or changing.

Acral lentiginous melanoma
An uncommon type of melanoma that looks like a bruise on the palms or soles, or like a dark stripe in a nail.

Adjuvant therapy
Additional cancer treatment given after the primary treatment (usually surgery), to lower the risk that the cancer will come back. Adjuvant therapy may include biological therapies (such as cytokines, immunotherapies, targeted therapies), chemotherapy, or radiation therapy.

Advanced melanoma
Cancer that has spread beyond the area near the main tumour.

Aldesleukin (IL-2, Interleukin 2, Proleukin)
A type of interleukin, a chemical messenger or substance that can improve the body's response to disease. It stimulates the growth of certain disease-fighting blood cells in the immune system. A type of protein molecule produced by lymphocytes that activates other lymphocytes in the immune system.

Anesthesia
A controlled loss of feeling with or without loss of wakefulness.

Anesthetic
A drug or other substance that causes a controlled loss of feeling or awareness with or without loss of wakefulness.

Angiolymphatic invasion
Melanoma that has invaded lymph or blood vessels.

Asymmetry
Asymmetry of a skin spot; one half does not match the other.

Autoimmune disorders
Diseases that cause the immune system to attack the body.

Biological therapy (biotherapy)
Treatment to stimulate or restore the ability of the immune (defense) system to fight infection and disease. Biological therapy is any form of treatment that uses the body's immune system to fight infection and disease or to protect the body from some of the side effects of treatment.

Biopsy
A medical procedure that collects tissue.

Blood vessel
A tube that carries blood throughout the body.

Breslow depth (thickness)
A measure of how deeply a melanoma tumour has grown into the skin. The tumour thickness (depth) is usually measured from the top of the tumour to the deepest tumour cells. If the tumour is ulcerated (the skin is broken), it is measured from the base of the ulcer to the deepest tumour cells. Breslow thickness is used to help determine the stage of cancer. Thicker tumours are linked with lower survival rates. Also called Breslow depth. The depth a melanoma lesion extends below the skin surface is measured in millimetres.

Cancer
An abnormal growth of cells which tend to proliferate in an uncontrolled way and, in some cases, to metastasize (spread).

Cell
The individual unit that makes up all of the tissues of the body.

Chemotherapy
Drugs that kill cancer cells.

Clinical trial
Research comparing new and current treatments to find out which is better.

Cobimetinib (Cotellic)
Cobimetinib is a kinase inhibitor indicated for the treatment of patients with unresectable or metastatic melanoma with a BRAF V600E or V600K mutation, in combination with vemurafenib (Zelboraf).

Computed tomography (CT) scan
A procedure that uses a computer linked to an x-ray machine to make a series of detailed pictures of areas inside the body. The pictures are taken from different angles and are used to create 3-dimensional (3-D) views of tissues and organs. A CT scan may be used to help diagnose disease, plan treatment, or find out how well treatment is working. Also called CAT scan.

Connective tissue
Supportive and binding fibres.

Cytokine
A type of protein that is made by certain immune and non-immune cells and has an effect on the immune system. Some cytokines stimulate the immune system and others slow it down. They can also be made in the laboratory and used to help the body fight cancer, infections, and other diseases. Examples of cytokines are interleukins, interferons, and colony-stimulating factors (filgrastim, sargramostim).

Dabrafenib (Tafinlar)
A targeted BRAF inhibitor therapy prescribed for patients with a BRAF V600 mutation. It is a monotherapy oral treatment for advanced melanoma. Dabrafenib blocks the activity of a mutated protein called BRAF, a molecule that helps regulate cell growth. It is often prescribed in combination with trametinib (Mekinist).

Deep margin
Normal-looking tissue underneath a tumour.

Deep margin status
Presence or absence of cancer cells in the normal-looking tissue under a tumour.

Dermal mitotic rate
A measure of how many tumour cells are actually growing.

Dermatologist
A doctor who specializes in diseases of the skin.

Dermatopathologist
Physician who has special training in diagnosing disease on the basis of microscopic examination of the skin.

Dermis
The second layer of skin that is beneath the epidermis.

Dermoscopy
Dermoscopy is a widely used noninvasive diagnostic technique. It improves the diagnostic accuracy for pigmented lesions in comparison with examination with the unaided eye. The use of a dermatoscope allows for a more thorough examination of skin structures and patterns.

Desmoplastic melanoma
Desmoplastic melanoma is a rare subtype of melanoma that is commonly found on sun-exposed areas, such as the head and neck, and is usually seen in older patients. It comprises less than 4% of invasive melanomas.

Diagnosis
Identification of a disease.

Distant metastasis
Cancer cells have spread to a part of the body far away from the first (primary) melanoma tumour.

Dysplastic nevus
A mole that is large or has irregular borders or inconsistent colours; abnormal mole has a fried egg appearance.

Early stage
Cancer that has had little growth in nearby tissues.

Epidermis
Outer layer of skin.

Excisional biopsy
Technique in which a lesion is removed from the skin by cutting out the affected area as well as a portion of normal skin surrounding the lesion. This technique is also used to remove larger lesions.

Excisional lymph node biopsy
Surgery to remove the entire, enlarged lymph node(s).

Family history
The family structure and relationships within the family, including information about diseases in family members.

Fine-needle aspiration
Use of a thin needle to remove fluid or tissue from the body.

Gland
An organ that makes fluids or chemicals the body needs.

Glucose
A natural sugar in the body used by cells for energy.

Histologic subtype
Grouping of cancer types based on cancer cell qualities.

Hormones
Chemicals in the body that activate cells or organs.

Imaging tests
Medical tests that take pictures of the inside of the body.

Immune system
The body's natural defense against disease.

Immunotherapy
Treatment that uses the immune system to fight disease.

In Situ
In situ melanoma is the earliest form of melanoma (considered stage 0). It is the easiest to treat (by excision) and almost always curable. *In situ* means that the tumour has not invaded beyond the epidermis, the outermost layer of the skin.

In-transit metastases
Cancer that has spread into lymph vessels near the first tumour but not into lymph nodes (groups of special disease-fighting cells).

Incisional biopsy
Surgery to remove part of a tumour.

Interferon (intron-a)
Interferon is a type of immunotherapy patients receive as adjuvant therapy offered to patients with a high risk of recurrence to reduce the risk of melanoma relapse.

Ipilimumab (Yervoy)
Ipilimumab is a type of immunotherapy known as a checkpoint inhibitor or an anti-CTLA-4 inhibitor, which helps your own immune system attack cancer cells. Ipilimumab blocks the activity of CTLA-4, a protein that prevents T cells from attacking your normal body cells and cancer cells. It is prescribed for melanoma that is unresectable or metastatic and given intravenously. It is often used in combination with nivolumab (Opdivo).

Lactate dehydrogenase (LDH)
An enzyme found in the blood and other body tissues.

Lentigo maligna melanoma
A type of melanoma that gets mistaken for a sunspot. It is an early form of melanoma in which the malignant cells are confined to the tissue of origin, the epidermis, hence it is often reported as *in situ* melanoma. It occurs in sun-damaged skin so is generally found on the face or neck, particularly the nose and cheek and commonly seen in the elderly.

Lesion
Tissue that has been damaged by disease or injury.

Local recurrence
Cancer that has come back after treatment in or near the same place as the first tumour. A satellite recurrence is a type of local recurrence.

Lymph
A clear fluid containing white blood cells.

Lymph node
A collection of immune cells grouped together in a special way.

Lymph node biopsy
Removal of all or part of a lymph node (groups of special disease-fighting cells located throughout the body) to test for disease.

Lymph vessels
Tubes that carry lymph – a clear fluid containing white blood cells that fight disease and infection – throughout the body and connect lymph nodes to one another. Also called lymphatic channels.

Lymphedema
A condition in which extra lymph fluid builds up in tissues and causes swelling. It may occur in an arm or leg if lymph vessels are blocked, damaged, or removed by surgery.

Magnetic resonance imaging (MRI)
A procedure in which radio waves and a powerful magnet linked to a computer are used to create detailed pictures of areas inside the body. These pictures can show the difference between normal and diseased tissue. MRI makes better images of organs and soft tissue than other scanning techniques, such as computed tomography (CT) or x-ray. MRI is especially useful for imaging the brain, the spine, the soft tissue of joints, and the inside of bones.

Malignant
Cancerous; growing out of control.

Medical history
All health events and medications taken to date.

Medical oncologist
A doctor who specializes in drug treatments for cancer.

Melanin
A pigment that gives colour to skin and eyes and helps protect it from damage by ultraviolet light.

Melanocytes
Skin cells of the epidermis.

Melanoma
A form of skin cancer that begins in melanocytes (cells that make the pigment melanin). It may begin in a mole (skin melanoma), but can also begin in other pigmented tissues, such as in the eye or in the intestines.

Metastases
Tumours formed by cancer cells that have spread from the first tumour to other parts of the body.

Metastasis
The spread of cancer cells from the first tumour to another body part.

Metastatic
Containing cancer cells that have spread from the first tumour.

Metastasize
The growth of cancer beyond local tissue.

Microsatellitosis
Tiny tumours near the main tumour seen with a microscope.

Mitosis (mitoses)
Mitosis is the process whereby cells divide into two separate cells, each with their own nucleus. Cancer is unchecked cell division, or growth. Mutations in genes can cause cancer by accelerating cell division rates or inhibiting normal controls on the system, such as cell cycle arrest or programmed cell death. As a mass of cancerous cells grows, it can develop into a tumour.

Mole
A dense area of melanin.

Nevus
Medical term for mole.

Nivolumab (Opdivo)
Nivolumab is a drug therapy known as a checkpoint inhibitor - a type of immunotherapy that helps make cancer cells more vulnerable to attack from the body's own immune system. It promotes the tumour-killing effects of T cells (white blood cells that help your body fight disease) and is used to treat advanced melanoma that is unresectable or has spread to organs and other parts of the body. In addition, nivolumab is also used as adjuvant therapy, that is, treatment after complete surgical resection of melanoma to reduce the risk of the melanoma returning. It is often used in combination with ipilimumab (Yervoy).

Nodular melanoma
A type of melanoma that has a dome shape and quickly grows into the dermis.

Palliative non-curative therapy
Palliative non-curative therapies are given without curative intent when no cure can be expected. Care includes treatment to relieve the symptoms and reduce the suffering caused by cancer and other life-limiting diseases.

Pathologic stage
A cancer stage given by a pathologist based on tissue samples.

Pathology report
A document with information about cancer cells and tissue that were removed from the body and examined with a microscope for disease.

Pathologist
A specialist in pathology; one who interprets and diagnoses the changes caused by disease in tissues and body fluids.

Pembrolizumab (Keytruda)
Pembrolizumab is an anti-PD-1 inhibitor, which is a type of immunotherapy known as a checkpoint inhibitor. It helps make cancer cells more vulnerable to attack by the body's own immune system and promotes the tumour-killing effects of T cells (white blood cells that help your body fight disease). It is used to treat advanced melanoma that is unresectable or has spread to organs and other parts of the body.

Peripheral margin
Normal-looking tissue from around the sides of a tumour.

Peripheral margin status
Presence or absence of cancer cells in the normal-looking tissue around the sides of a tumour.

Persistent (recurrent) melanoma
Cancer not completely removed or destroyed by treatment; persistent melanoma is found in or right next to the surgical scar where the first melanoma was removed. Also called true local scar recurrence.

Pigment
Substance with colour.

Platelets
A type of blood cell responsible for blood clotting.

Positron emission tomography (PET) scan
A procedure in which a small amount of radioactive glucose (sugar) is injected into a vein, and a scanner is used to make detailed, computerized pictures of areas inside the body where the glucose is taken up. Because cancer cells often take up more glucose than normal cells, the pictures can be used to find cancer cells in the body.

Primary tumour
Initial tumour or the body site where it forms.

Prognosis
The likely course and outcome of a disease.

Punch biopsy
A procedure in which a small round piece of tissue about the size of a pencil eraser is removed using a sharp, hollow, circular instrument, commonly used to check for melanoma.

Pure desmoplasia
Presence or absence of dense connective tissue.

Radiation oncologist
A doctor who specializes in the treatment of cancer with radiation.

Radiation therapy (radiotherapy)
The use of high-energy rays to damage cancer cells, stopping them from growing and dividing. Like surgery, radiation therapy is a local treatment that affects cancer cells only in the treated area.

Radioactive
Containing a powerful energy called radiation.

Recurrence
Cancer that has recurred (come back), usually after a period of time during which the cancer could not be detected. The cancer may come back to the same place as the original (primary) tumour or to another place in the body. Also called recurrent cancer.

Regimen
A treatment plan that specifies the dosage, schedule, and duration of treatment.

Regional lymph node recurrence
Cancer that has come back after treatment in lymph nodes (groups of special disease-fighting cells) near the first melanoma.

Regional lymph nodes
Groups of special disease-fighting cells located near the tumour.

Risk factor
Something that increases the chance of getting a disease.

Screening
Regular tests used to detect a disease.

Second-line therapy
The treatment given after the first treatment fails.

Sentinel lymph node
The first major node that lymph travels to after leaving the tumour area.

Sentinel lymph node biopsy
A sentinel lymph node biopsy (SLNB) is a procedure in which the sentinel lymph node is identified, removed, and examined to determine whether cancer cells are present.

Shave biopsy
Surgery to remove a thin tissue sample from the top of a tumour.

Side effect
An unplanned physical or emotional response to treatment.

Skin biopsy
Removal of a sample of tissue from the skin to test for disease.

Stage (of cancer)
Measure of the extent of a malignancy, arrived at by examining features of the primary tumour and searching for evidence of metastasis.

Subcutaneous tissue
Layer of fat and connective tissue under the dermis.

Superficial spreading melanoma
The most common type of melanoma; it generally spreads from a new or existing mole.

Surgery
An operation to remove or repair a part of the body.

Surgical oncologist
A surgeon who has special training in performing biopsies and other surgical procedures in cancer patients.

Systemic therapy
Drugs used throughout the entire body to kill cancer cells that have spread far.

Targeted therapy
Treatment that stops cancer cell growth by attacking a specific or unique feature of the cancer.

Trametinib (Mekinist)
Trametinib is a type of oral targeted therapy called a MEK inhibitor. It is used alone (monotherapy) or in combination with dabrafenib (Tafinlar) to treat melanoma in patients whose cancer has a mutated (changed) form of the BRAF gene called a BRAF V600 mutation. Trametinib blocks proteins called MEK1 and MEK1. This may help keep cancer cells from growing and may kill them.

Tumour
A tissue mass made from an abnormal growth of cells.

Tumour location
The area of the body that contains the tumour.

Tumour regression
An inflammation response to tumour cells, resulting in a decrease in the size of the tumour.

Ulceration status
Presence or absence of a tumour's top skin layer.

Ultraviolet light
Light energy with a wavelength shorter than visible light but longer than x-rays.

Vemurafenib (Zelboraf)
Vemurafenib is an oral drug known as a BRAF enzyme inhibitor, developed for the treatment of adult patients with BRAF V600 mutation-positive unresectable or metastatic melanoma. Vemurafenib blocks the activity of the mutated BRAF protein which has signaled cells to develop abnormally and divide out of control. It is often prescribed in combination with cobimetinib (Cotellic).

Vertical growth phase
The direction of tumour growth is down into the skin.

White blood cells
A type of blood cell that fights disease as part of the immune system.

X-ray
Use of small amounts of radiation to make pictures of organs and structures inside the body.

References

1. Canadian Cancer Society's Advisory Committee on Cancer Statistics. Canadian Cancer Statistics 2017 [Internet]. Toronto: Canadian Cancer Society; 2017 Jun [cited 2018 Mar 28]. Available from: **www.cancer.ca/Canadian-Cancer-Statistics-2017-EN**

2. Nessim C, Rotstein L, Goldstein D, Sun A, Hogg D, McCready D, et al. Princess Margaret Cancer Centre Clinical Practice Guidelines: Melanoma [Internet]. Toronto: University Health Network; 2015 Aug [cited 2018 Sep 27]. 21 p. Available from: **www.uhn.ca/PrincessMargaret/Health_Professionals/Programs_Departments/Documents/CPG_Melanoma.pdf**.

3. Canadian Dermatology Association. Melanoma [Internet]. 2018 [cited 2018 Sept 28]. Available from: **www.dermatology.ca/public-patients/skin/melanoma/**

4. Chamberlain AJ, Fritschi L, Giles GG, Dowling JP, Kelly JW. Nodular type and older age as the most significant associations of thick melanoma in Victoria, Australia. Arch Dermatol. 2002 May;138(5):609-14.

5. Murray CS, Stockton DL, Doherty VR. Thick melanoma: the challenge persists. Br J Dermatol. 2005 Jan;152(1):104-9.

6. Liu W, Dowling JP, Murray WK, McArthur GA, Thompson JF, Wolfe R, Kelly JW. Rate of growth in melanomas: characteristics and associations of rapidly growing melanomas. Arch Dermatol. 2006 Dec;142(12):1551-8.

7. Richard MA, Grob JJ, Avril MF, Delaunay M, Thirion X, Wolkenstein P, et al. Melanoma and tumor thickness: challenges of early diagnosis. Arch Dermatol. 1999 Mar;135(3):269-74.

8. Kelly JW. Nodular melanoma: how current approaches to early detection are failing. J Drugs Dermatol. 2005;4(6):790-3.

9. Patrick RJ, Fenske NA, Messina JL. Primary mucosal melanoma. J Am Acad Dermatol. 2007 May;56(5):828-34.

10. Carvajal RD, Schwartz GK, Tezel T, Marr B, Francis JH, Nathan PD. Metastatic disease from uveal melanoma: treatment options and future prospects. Br J Ophthalmol. 2017 Jan;101(1):38-44. doi: 10.1136/bjophthalmol-2016-309034.

11. Kujala E, Mäkitie T, Kivelä T. Very long-term prognosis of patients with malignant uveal melanoma. Invest Ophthalmol Vis Sci. 2003 Nov;44(11):4651-9.

12. Khoja L, Atenafu E, Joshua A, and The International Rare Cancer's Initiative-Ocular Melanoma Group. Meta-analysis of phase II trials in metastatic uveal melanoma (MUM) to determine progression-free (PFS) and overall survival (OS) benchmarks for future phase II trials: An irci-ocular melanoma initiative. J of Clin Onc. 2016; 34 Suppl 15:S9567. doi: 10.1200/JCO.2016.34.15_suppl.9567.

13. Yang J, Manson DK, Marr BP, Carvajal RD. Treatment of uveal melanoma: where are we now? Ther Adv Med Oncol. 2018 Feb 21;10:1758834018757175. doi: 10.1177/1758834018757175.

14. Lens MB, Newton-Bishop JA, Boon AP. Desmoplastic malignant melanoma: a systematic review. Br J Dermatol. 2005 Apr;152(4):673-8.

15. Hamid O, Carvajal RD, Morton DL, Faries M. Unusual melanomas. In Raghavan D, Blanke CD, Johnson DH, Moots PL, Reaman GH, Rose PG, et al, editors. Textbook of uncommon cancer, 4th Edition. Wiley-Blackwell; 2012 Nov. p. 691-708.

Additional References

Alberta Provincial Cutaneous Tumour Team. Optimal excision margins for primary cutaneous melanoma [Internet]. Alberta Health Services; 2013. 10 p. Available from: **www.albertahealthservices.ca/assets/info/hp/cancer/if-hp-cancer-guide-cu010-optimal-margins.pdf**.

Alberta Provincial Cutaneous Tumour Team. Preoperative and pretreatment investigations for malignant melanoma [Internet]. Alberta Health Services; 2013. 9 p. Available from: **www.albertahealthservices.ca/assets/info/hp/cancer/if-hp-cancer-guide-cu007-preop-pretreat-invest.pdf**.

Alberta Provincial Cutaneous Tumour Team. Systemic therapy for unresectable stage III or metastatic cutaneous melanoma [Internet]. Alberta Health Services; 2012 [revised 2015]. 14 p. Available from: **www.albertahealthservices.ca/assets/info/hp/cancer/if-hp-cancer-guide-cu012-systemic-therapy.pdf**.

Bichakjian CK, Halpern AC, Johnson TM, Foote Hood A, Grichnik JM, Swetter SM, et al. Guidelines of care for the management of primary cutaneous melanoma. American Academy of Dermatology. J Am Acad Dermatol. 2011 Nov;65(5):1032-47. doi: 10.1016/j.jaad.2011.04.031.

British Columbia Cancer Agency. Melanoma: Biopsy proven malignant melanoma [Internet]. 2013. Available from: **www.bccancer.bc.ca/health-professionals/clinical-resources/cancer-management-guidelines/skin/melanoma**.

British Columbia Cancer Agency. Melanoma: Surveillance and early detection in high risk patients [Internet]. 2013. Available from: **www.bccancer.bc.ca/health-professionals/clinical-resources/cancer-management-guidelines/skin/melanoma**.

Cancer Care Ontario. Single-agent interleukin-2 in the treatment of metastatic melanoma [Internet]. 2011. 50 p. Available from: **www.archive.cancercare.on.ca/common/pages/UserFile.aspx?fileId=34367**.

Cancer Care Ontario. Systemic adjuvant therapy for patients at high risk for recurrent melanoma [Internet]. 2005 [updated 2009]. 88 p. Available from: **www.archive.cancercare.on.ca/common/pages/UserFile.aspx?fileId=34373**.

Kottschade LA, Grotz TE, Dronca RS, Salomao DR, Pulido JS, Wasif N, et al. Rare presentations of primary melanoma and special populations: a systematic review. Am J Clin Oncol. 2014 Dec;37(6):635-41. doi: 10.1097/COC.0b013e3182868e82.

Mayo Clinic. Melanoma [Internet]. [cited 2012 Nov 7]. Available from: **www.mayoclinic.com/health/melanoma/DS00439**.

McGuire ST, Secrest AM, Andrulonis R, Ferris LK. Surveillance of patients for early detection of melanoma: patterns in dermatologist vs patient discovery. Arch Dermatol. 2011 Jun;147(6):673-8. doi: 10.1001/archdermatol.2011.135.

National Cancer Institute. Skin Cancer (Including Melanoma)—Patient Version [Internet].

U.S. Department of Health and Human Services. National Institutes of Health. Available from: **www.cancer.gov/types/skin**.

National Comprehensive Cancer Network. NCCN Guidelines for Patients: Melanoma [Internet]. 2018. Available from: **www.nccn.org/patients/guidelines/melanoma**.

Rajagopal S, Souter LH, Baetz T, McWhirter E, Knight G, Rosen CF, et al. Follow-up of Patients with Cutaneous Melanoma who were Treated with Curative Intent [Internet]. Cancer Care Ontario; 2015 [cited 2015, Nov 3]. 6 p. Available from: **www.archive.cancercare.on.ca/common/pages/UserFile.aspx?fileId=352598**.

Notes

Melanoma Network of Canada
Sun Safe Sun Aware

Our Mission:
We support individuals whose lives has been changed by melanoma. We are advancing the prevention of melanoma through advocacy and education.

Melanoma Network of Canada
Phone: 905-901-5121 | Toll Free: 1-877-560-8035
www.melanomanetwork.ca

Charitable Registration # BN 85491 3050 RR0001

We would like to thank and acknowledge Merck Canada for providing partial funding for this publication.