a completely different type of cancer.

- Sometimes the new cancer is in the same organ or area of the body as the first cancer. For example, someone who was treated for a certain type of <u>colorectal</u> <u>cancer</u><sup>1</sup> can get another type of colorectal cancer as a second cancer.
- Or, a second cancer might develop in another organ or tissue. A second cancer is different from a <u>cancer recurrence</u><sup>2</sup> which is when the same type of cancer that a person had before comes back.

Because it can take many years for cancers to develop, second cancers have been studied in types of cancers for which successful treatments have been around the longest. That's why we know more about certain second cancers than others.

#### Who is at risk for second cancers?

It isn't always clear what causes a second cancer or who is most at risk. Some second cancers seem to have the same or similar risk factors as a first cancer. But, the risk is known to be higher for people with certain types of cancer, who had certain types of cancer treatment, or if they have a <u>family cancer syndrome</u><sup>3</sup>. But for other people, the risk for a second cancer may be lower or simply isn't known.

Risk factors for a second cancer include some of the same things that are a risk for a first cancer: a healthy lifestyle and environment, using tobacco products, family history and genetics, being overweight or obese, drinking too much alcohol, or the lack of good follow-up care or cancer screening after a first cancer.

When you have a first cancer can matter too. For example, survivors of childhood cancers can develop second cancers from some effects of treatment or because of hereditary or genetic problems. And, because a person's risk for cancer generally goes up as they age, an unrelated new cancer may develop later in a cancer survivor's life.

Sometimes there are specific lifestyle recommendations and monitoring needed if a person has certain non-cancer health problems that might affect them after treatment. There might also be specific cancer screening guidelines based on a person's level of risk or if they have a family cancer syndrome. But, in general, the same <u>cancer</u> <u>screening guidelines</u><sup>4</sup> should be followed as for people who have not had cancer.

#### **Hyperlinks**

- 1. <u>www.cancer.org/cancer/types/colon-rectal-cancer.html</u>
- 2. www.cancer.org/cancer/survivorship/long-term-health-concerns/recurrence.html
- 3. www.cancer.org/cancer/risk-prevention/genetics/family-cancer-syndromes.html
- 4. www.cancer.org/cancer/screening.html

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### **Second Cancers Related to Treatment**

It's not possible to predict who might get a second cancer, but sometimes having cancer treatment can put a person at higher risk for second cancers. As more new treatments emerge and standard treatments continue to be used, studies continue to look at how <u>genetics</u><sup>1</sup> and different cancer treatments interact, as well as links between the treatments, lifestyle habits, and known cancer-causing agents.

- Risk of developing second cancers after radiation therapy
- Risk of developing second cancers after chemotherapy and targeted therapy

#### Risk of developing second cancers after radiation therapy

Radiation therapy<sup>2</sup> was recognized as a possible cause of cancer many years ago. In

following years.

#### Solid tumors

There is also a risk for other cancers, which are mostly solid tumors, after having radiation therapy. Most of these cancers develop 10 years or more after radiation therapy. The effect of radiation on the risk of developing a solid tumor cancer depends on factors such as:

- The **age of the patient** when they were treated with radiation. For example, the risk of developing breast cancer after radiation is higher in those who were treated when they were young compared with those given radiation as adults. The chance of developing breast cancer after radiation seems to be highest in those exposed as children. Risk decreases as the age at the time of radiation increases; women who had radiation after the age of 40 have a lower risk of breast cancer. Your age when you get radiation treatment has a similar effect on the development of other solid tumors, including lung cancer, thyroid cancer, bone sarcoma, and gastrointestinal or related cancers (stomach, liver, colorectal, and pancreatic).
- The **dose of radiation**. In general, the risk of developing a solid tumor after radiation treatment goes up as the dose of radiation increases. Some cancers require larger doses of radiation than others, and certain treatment techniques use more radiation.
- The **area treated**. The area treated is also important, since these cancers tend to develop in or near the area that was treated with radiation. Certain organs, such as the breast and thyroid, seem to have a higher risk for developing cancers after exposed to radiation than other organs.

## Risk of developing second cancers after chemotherapy and targeted therapy

#### Chemotherapy

Some types of <u>chemotherapy (chemo) drugs</u><sup>5</sup> have been linked with different kinds of second cancers. The cancers most often linked to chemo are myelodysplastic syndrome (MDS) and acute myelogenous leukemia (AML). Sometimes, MDS occurs first, then turns into AML. Acute lymphocytic leukemia (ALL) has also 0 0 rg gi5.35etestinal oedin 155

The risk gets higher with **higher drug doses**, **longer treatment time**, and **higher dose-intensity** (more drug given over a short period of time). Chemotherapy agents that have an increased risk for second cancers include:

- Alkylating agents (mechlorethamine, chlorambucil, cyclophosphamide, melphalan, lomustine, carmustine, busulfan)
- Platinum-based drugs (cisplatin, carboplatin)
- Anthracycline topoisomerase II inhibitors (etoposide or VP-16, teniposide, mitoxantrone)

#### Targeted therapy drugs

Some drugs used to treat cancer are called targeted therapy drugs because they were designed to find and attack certain genes or proteins that are in specific types of cancer. Targeted therapies are newer, so not a lot is known about the risk for second cancer yet. More will be known as more patients get these types of drugs and become survivors who are monitored for future health problems and second cancers.

Vemurafenib (Zelboraf<sup>®</sup>) and dabrafenib (Tafinlar<sup>®</sup>) are drugs that target the BRAF protein. They are used to treat melanoma and are being studied for use in other cancers. People taking these drugs have a higher risk of <u>squamous cell carcinomas of the skin</u><sup>6</sup>.

#### **Hyperlinks**

- 1. <u>www.cancer.org/cancer/risk-prevention/genetics.html</u>
- 2. www.cancer.org/cancer/managing-cancer/treatment-types/radiation.html
- 3. <u>www.cancer.org/cancer/types/leukemia.html</u>
- 4. www.cancer.org/cancer/types/myelodysplastic-syndrome.html
- 5. <u>www.cancer.org/cancer/managing-cancer/treatment-types/chemotherapy.html</u>
- 6. www.cancer.org/cancer/types/basal-and-squamous-cell-skin-cancer.html

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# Second Cancer Risks Related to Lifestyle and Environment

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### Second Cancer Risks Related to Family History and Genetics

It's not possible to predict who might get a second cancer, but certain <u>gene changes</u><sup>1</sup> or hereditary (family) cancer syndromes can put a person at higher risk for some second cancers. However, most cancers are not clearly linked to the genes we inherit from our parents. Studies continue to look at the links between genetics, lifestyle habits, and known cancer-causing agents.

<u>Family cancer syndromes</u><sup>2</sup> are caused by abnormal gene changes (variants or mutations) that are often inherited from a parent. These syndromes can be linked to a higher risk for one or more kinds of cancer. For example, women with hereditary breast and ovarian cancer (HBOC) syndrome, which is most often caused by mutations in the genes *BRCA1* and *BRCA2*, have a high risk of breast, ovarian, and some other

cancers. Another example is <u>hereditary non-polyposis colorectal cancer syndrome</u> (<u>HNPCC</u>)<sup>3</sup>, also known as **Lynch syndrome**, which is linked to a high risk for colorectum, endometrial, ovarian, bladder, stomach, pancreatic, and some other cancers.

Genetic counseling and testing<sup>4</sup>

of Oncology. 11th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2019:2155-2173.

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# Lowering the Risk of Getting a Second Cancer

While it's not possible to predict who might get a second cancer, it's very important that cancer survivors understand their risk for future health problems and second cancers. Talk with your health care team about what problems you might need to watch for more

- 2. www.cancer.org/cancer/risk-prevention/genetics/family-cancer-syndromes.html
- 3. <u>www.cancer.org/cancer/screening/american-cancer-society-guidelines-for-the-early-detection-of-cancer.html</u>
- 4. <u>www.cancer.org/cancer/risk-prevention/tobacco.html</u>
- 5. <u>www.cancer.org/cancer/risk-prevention/diet-physical-activity/body-weight-and-</u> <u>cancer-risk.html</u>
- 6. <u>www.cancer.org/cancer/risk-prevention/diet-physical-activity/acs-guidelines-</u> nutrition-physical-activity-cancer-prevention/guidelines.html
- 7. www.cancer.org/cancer.html

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