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An Introduction to Squamous Cell Carcinoma of the Head and Neck

### ReachMD Announcer:

Welcome to ReachMD. This medical industry feature, titled "Introduction to Squamous Cell Carcinoma of the Head and Neck (or SCCHN)" is sponsored by EMD Serono. This program is intended for US healthcare professionals. Your host is Dr. Lori Wirth. Dr. Wirth has been compensated for her participation in this program.

### Dr. Wirth:

Hello, my name is Doctor Lori Wirth. I'm a medical oncologist within the Head and Neck Oncology Program at Massachusetts General Hospital in Boston.

Welcome to our video titled: "Introduction to Squamous Cell Carcinoma of the Head and Neck."

### Chapter 1: "What is head and neck cancer?"

#### Dr. Wirth:

Squamous cell carcinoma of the head and neck, often referred to as SCCHN, is the name applied to a group of cancers that originate in the squamous cell epithelium of several sites and make up most head and neck cancers.<sup>1</sup>

SCCHN is considered early-stage, or stage I or II, when tumors are small.<sup>2</sup>

Locally advanced disease includes stages III, IVA, and IVB and is associated with larger tumors, with evidence of invasion to local lymph nodes and/or metastases in regional nodes.<sup>2</sup>

Most patients have locally advanced disease when they are first diagnosed with SCCHN.<sup>3</sup> Generally, these cases are treated with curative intent.<sup>3</sup>

Few patients, roughly 5% to 10%, present with distant metastases (stage IVC disease).<sup>2,4</sup>

However, about 50% of patients with locally advanced SCCHN will experience recurrence of local or regional disease and/or distant metastases after primary treatment.<sup>2</sup>

### Chapter 2: "Where do head and neck cancers occur?"

#### Dr. Wirth:

SCCHN occurs primarily in the oral cavity and the pharynx.<sup>5</sup>

The oral cavity includes the lips, gums, tongue, hard palate, the floor of the mouth, and the lining of the cheeks and lips.<sup>5</sup>

There are 3 parts of the pharynx: the oropharynx, larynx, and hypopharynx.<sup>5</sup>

There are 2 types of oropharynx, or throat, cancers: human papilloma virus (or HPV)—positive and HPV-negative cancers.<sup>5</sup>

These 2 types of oropharynx cancers have a very different disease course and utilize different treatment options.<sup>5</sup>

The larynx is what we generally refer to as the voice box, and the hypopharynx is the area around the voice box.<sup>5</sup>

Cancers that originate in the brain, eye, esophagus, thyroid gland, or skin of the head and neck are not classified as squamous cell

carcinoma of the head and neck.<sup>5</sup>

### Chapter 3: "How does SCCHN form and progress?"

#### Dr. Wirth:

SCCHN originates with atypical growth in cells of the mucosal lining of the oral cavity, pharynx, larynx, and sinuses, and progresses along an orderly series from:

- Squamous hyperplasia, or an increased thickness of the tissue due to an increased number of cells of the squamous epithelium, to
- Squamous dysplasia, or the presence of atypical cells among the squamous epithelium, to
- Local tumor formation,
- and eventually to invasive carcinoma<sup>6</sup>

Known genetic drivers of SCCHN are p53 mutations in HPV-negative SCCHN and PI3 kinase amplifications or mutations in HPV-positive SCCHN.<sup>2</sup>

It is important to note that most patients diagnosed with SCCHN do not have a history of a premalignant lesion.<sup>6</sup>

### Chapter 4: "What is the epidemiology of head and neck cancers?"

#### Dr. Wirth:

Head and neck cancers are the 7<sup>th</sup> most common cancers globally and are increasing in prevalence, with approximately 660,000 estimated new cases and 450,000 estimated deaths globally in 2020.<sup>7,8</sup>

In the United States, it is estimated that almost 66,920 new head and neck cancer cases and more than 15,000 deaths occurred in 2023, with SCCHN comprising more than 90% of these tumors.<sup>9-11</sup>

### Chapter 5: "What are the early signs and symptoms of SCCHN?"

#### Dr. Wirth:

Early signs and symptoms of SCCHN vary slightly by location<sup>5</sup> and can be easily missed by clinicians. Symptoms that are unilateral, rather than bilateral, are of particular concern and can potentially indicate the presence of head and neck cancer.<sup>12</sup>

Tumors of the oral cavity are often more noticeable by patients and health care providers<sup>6</sup> and can present as<sup>5</sup>:

- Patches or ulcers on the gums, tongue, or lining of the mouth
- Bleeding and/or pain in the mouth

Thus, oral cancers are often diagnosed at earlier stages either by a primary care physician, dentist, or other health care providers<sup>6</sup>

Cancers forming in the hypopharynx, oropharynx, nasopharynx, or larynx are more hidden anatomically and, thus, may go unnoticed until later stages.<sup>6</sup> Symptoms for these cancers include<sup>6</sup>:

- Difficulty eating or swallowing
- Earache
- A change in voice or persistent hoarseness
- A lump or mass in the neck
- And sinus congestion

Referral to a specialist, such as an otolaryngologist or medical oncologist, is generally recommended when these signs or symptoms are recognized.

### Chapter 6: "What are some of the recognizable precursors for SCCHN?"

#### Dr. Wirth:

For oral cancers, precursors may present as potentially malignant oral epithelial lesions, including leukoplakia. Leukoplakia are white patches on the oral epithelium, which cannot be rubbed off or otherwise characterized clinically. These potential malignant growths may appear as multiple leukoplakic lesions and/or with visible growth or spread.<sup>13</sup>

A particularly notable form of leukoplakia is proliferative verrucous leukoplakia, which refers to a spectrum of multifocal and multicentric white lesions, with diverse histologic features, that is characterized by progressive spread and displays progression to SCCHN in roughly 50% of cases.<sup>14</sup>

Erythroplakia is a red lesion that is typically well-defined with a “velvety” texture.<sup>13</sup>

Leukoerythroplakia, or erythroleukoplakia, is a subset of erythroplakia and may include red and white areas, which may be associated with a burning sensation and/or soreness.<sup>13</sup>

Erythroplakia is less common than leukoplakia but, while exact transformation rates are unknown, up to 85% of erythroplakias show signs of malignancy at the time of biopsy.<sup>13</sup>

As most patients who develop SCCHN do not show a history of premalignant lesions, it is important for health care providers, including dentists, to recognize these potentially malignant lesions and characterize their size and disposition to account for any change or progressive growth, as referral to specialists for biopsy and characterization can allow for early intervention.<sup>13</sup>

### Chapter 7: "What are the risk factors for Head & Neck Cancer?"

#### Dr. Wirth:

SCCHN develops following exposure to a combination of environmental factors, genetic changes, and other risk factors.<sup>1</sup> Environmental risk factors include<sup>5</sup>:

- Infection with HPV
- Tobacco use, with risk increasing with the length and/or frequency of use
- Secondhand smoke can also increase the risk for developing or experiencing the recurrence of SCCHN, even among individuals who have not personally smoked
- Excessive alcohol use, which can lead to SCCHN as an independent risk factor
  - Excessive alcohol use has been found to compound the carcinogenic effects of smoking, meaning the risk of developing cancer is greater for individuals who use both tobacco and alcohol<sup>1</sup>
- Betel nut or paan chewing
- Radiation exposure
- Occupational exposure (for example, to wood dust)
- Genetic alterations such as Fanconi anemia
- Ancestry: Asian ancestry increases the risk of nasopharyngeal carcinoma

Additionally, head and neck cancers are found more commonly in men than in women.<sup>5</sup>

The risk of developing head and neck cancers increases with age, with most diagnoses occurring in patients over 50 years of age.<sup>5</sup>

### Chapter 8: "What is the association between SCCHN and HPV?"

#### Dr. Wirth:

HPV is a group of more than 200 related viruses and is the most common sexually transmitted infection.<sup>15</sup>

SCCHN can be caused by high-risk HPV infection, usually HPV 16.<sup>1</sup> HPV-positive SCCHN is a biologically different disease from HPV-negative SCCHN, with different risk factors, tumor sites, and outcomes.<sup>1,2</sup>

HPV-positive SCCHN generally presents in oropharyngeal sites and occurs more commonly in younger patients, who generally have better prognoses or outcomes.<sup>2,5,15</sup>

HPV-negative SCCHN generally occurs more frequently in nonoropharyngeal sites. Patients diagnosed with HPV-negative SCCHN are generally older and have worse prognoses than those with HPV-positive cancers.<sup>2,5,16</sup>

### Chapter 9: "How do patients present at diagnosis and what are the recurrence rates?"

#### Dr. Wirth:

About 30% to 40% of patients present with early-stage cancer at the time of their diagnosis, with an expected long-term disease-free survival rate of about 60% to 90%.<sup>17</sup>

Most patients, about 60% to 70%, are diagnosed after they have progressed to locally advanced disease, or stage III, IVA, or IVB cancer, which is associated with larger tumors with evidence of invasion to local lymph nodes and/or metastases in regional nodes.<sup>2,17</sup>

Although these patients present with locally advanced disease, they still have the potential for curative outcomes with the appropriate therapy.<sup>3</sup> However, as mentioned earlier, approximately half of patients with locally advanced SCCHN will experience recurrence after primary treatment.<sup>2</sup>

Recurrence of SCCHN may depend on several factors such as cancer site, HPV status, and treatment interventions received.<sup>18</sup>

#### **Chapter 10: “How are head and neck cancers diagnosed?”**

**Dr. Wirth:**

Several confirmatory diagnostic tests can be used to diagnose SCCHN.<sup>19</sup>

One diagnostic test is a physical or oral examination that includes checking the neck, lips, gums, cheeks, nose, mouth, throat, and tongue for lumps and/or other abnormalities.<sup>19</sup>

Another diagnostic test is endoscopy, which is a visual examination of potential tumor sites with equipment that allows specialists to see inside the narrow passages of the throat and sinuses.<sup>19</sup>

A biopsy, which involves removal of tissue that is examined by a pathologist using a microscope to determine whether cancerous cells are present, may also confirm the diagnosis.<sup>19</sup>

Molecular testing can be used to look for signs of HPV infection or the expression of specific genes or proteins within a collected sample, such as saliva or epithelial cells.<sup>19</sup>

Imaging techniques are important diagnostic tools that allow health care professionals to detect the presence of tumors.<sup>19</sup>

These techniques include CT, PET, and MRI scanning, which can be used to produce detailed images of internal organs using magnetic fields, x rays, and/or the location and abundance of contrast agents that accumulate in certain tissues, such as tumors.<sup>19</sup>

While imaging is helpful in confirming a diagnosis of head and neck cancer, one pitfall is that the anatomy of the head and neck is very challenging, meaning that imaging scans may be difficult to interpret for individuals who do not routinely evaluate the disease.<sup>20</sup>

To obtain an accurate diagnosis, it is important to order the right imaging study and communicate the patient’s localizing symptoms to the radiologist.<sup>20</sup>

#### **Chapter 11: Summary**

**Dr. Wirth:**

In summary, SCCHN is a group of cancers in the oral cavity, oropharynx, hypopharynx, and larynx that make up about 90% of all head and neck cancers, with increasing prevalence.<sup>1,11</sup>

Most patients are diagnosed in the locally advanced stage, and up to half of those patients experience disease recurrence after primary treatment.<sup>2,3</sup>

SCCHN can be associated with high disease burden and poor survival outcomes.<sup>7,8</sup>

Novel and effective treatment options are therefore required to improve outcomes for patients with SCCHN.<sup>2</sup>

**ReachMD Announcer:**

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