Cancer Association of South Africa (CANSA)

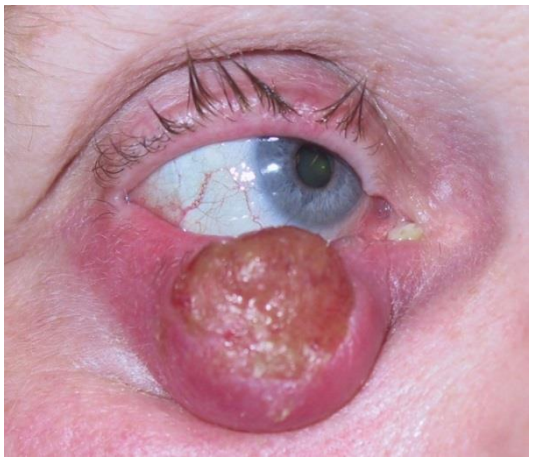
Research • Educate • Support

Fact Sheet on Sebaceous Gland Carcinoma

Introduction

Sebaceous gland carcinoma (SC) is a rare skin cancer. It is considered an aggressive cancer because it can spread.

Sebaceous glands are part of epidermal appendages. Neoplasms of the sebaceous glands may be benign, such as sebaceous hyperplasia or sebaceous gland adenomas. The malignant sebaceous gland carcinoma most commonly arises in the periocular area (around the eyes). Few cases of sebaceous cell carcinoma have been reported at extraocular sites.



[Picture Credit: Sebaceous Gland Carcinoma]

The most common site of origin is the meibomian glands of the eyelids, leading to the term meibomian gland carcinoma. However, this neoplasm can occur in other sebaceous glands, such as in the caruncle (the small, red portion of the corner of the eye that contains modified sebaceous and sweat glands), the glands of Zeis (the unilobar sebaceious glands located on the margin of the eyelid which service the eyelash), and in the eyebrow.

[Picture Credit: Caruncle]

Sebaceous cell carcinoma is a lethal eyelid malignancy and can masquerade as benign conditions. Error or delay in diagnosis is common, and this tumour carries a significant mortality rate with metastasis.
(eMedicine.Medscape; American Academy of Dermatology).

Incidence of Sebaceous Gland Carcinoma (SC) in South Africa

The National Cancer Registry (2010) does not provide any information regarding the incidence of sebaceous gland carcinoma.

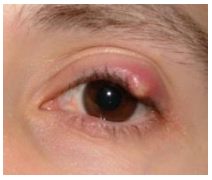
Signs and Symptoms of Sebaceous Gland Carcinoma (SC)
Many sebaceous carcinomas (SC) develop on an eyelid. When this rare skin cancer develops on an eyelid, the person may notice one or more the following:

- Slowly growing, often yellowish lump on the eyelid that feels firm, deep, and painless.
- Thickening of an eyelid, where lid meets lash.
- Yellow or reddish crust on eyelid, where lid meets lash.
- Growth on eyelid that looks like a pimple.
- Growth on eyelid that bleeds.
- Sore on eyelid that does not heal, or heals and reappears.

As the cancer progresses, it often looks like the person has pink eye. You may see growths on the upper and lower eyelid. The growths may open and ooze fluid. The eyelashes often fall out. As the cancer spreads, it can affect the eyesight.

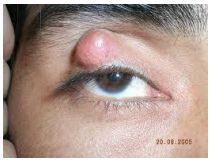
Mistaken identity: Stye, chalazion, or pink eye - SC is rare. Other growths that develop on the eyelid are much more common. Sometimes, SC is mistaken for one of these eye conditions:

- Stye**:** This is a common growth, which often looks like a pimple on the eyelid. Most styes feel tender when touched. SC tends to be painless. Without treatment, a stye can make blinking painful. The eyelid can swell, and the eyes may water. Most styes clear with treatment, which usually involves applying a warm compress 4 to 6 times a day.



[Picture Credit: Stye]

- Chalazion**:** This common eye condition often causes an eyelid to swell. Most chalazions clear with treatment, which often requires the patient to apply warm compresses to the eye and use antibiotic eye drops.



[Picture Credit: Chalazion]

- Pink eye**:** Also called conjunctivitis, SC can look like pink eye that just won't go away - even with treatment.

[Picture Credit: Pink Eye]

(American Academy of Dermatology).

Risk and Causes of Sebaceous Gland Carcinoma (SC)
Like most cancers, the cause is far from fully understood. But these cancers can be associated with:

- Non-cancerous lumps (benign adenomas) of the sebaceous glands
- Exposure to radiation – previous radiotherapy or (less likely) repeated X-rays
- A genetic condition called Muir Torré syndrome

Muir Torré syndrome (MTS) can mean that there is another primary cancer elsewhere in the body. So people diagnosed with sebaceous gland cancer are often checked over for signs of cancer elsewhere. This can be frightening, but it is usually just a precaution.

Anyone can develop SC, but some people have a greater risk:

- Middle age or older. It is very rare for SC to develop before 30 years of age. Most people are 60 years of age or older, and the risk continues to increase with age.

- Weakened immune system. People who have a weakened immune system have a much greater risk. A weakened immune system may be caused by a medical condition or medication. Medical conditions that weaken the immune system include human immunodeficiency virus (HIV) and cancer. Medication taken after transplant surgery to prevent the body from rejecting the new organ and some medications used to treat psoriasis or arthritis also weaken the immune system.

- Received radiation treatments for a medical condition. People who received radiation treatments as a child have been diagnosed with this rare skin cancer in their 60s and 70s. SC also develops in children who receive radiation treatments for retinoblastoma, a cancer that develops in the eye.

- Muir-Torre syndrome (MTS). This is a rare medical condition. People get MTS from the genes that they inherit from their parents. MTS greatly increases the risk for developing several cancers. The risk is greatest for a type of colon cancer. Other cancers that a person with MTS has an increased risk of developing are SC, cancers of the uterus, stomach, ovaries, intestine, urinary tract, liver, and bile duct.

SC is often the first sign that a person has MTS.

Other risk factors include:
- Previous radiation therapy to the area for a variety of benign and malignant conditions, e.g. retinoblastoma
- History of oral thiazide diuretic use
- Mutations to the tumour suppressor gene p53
- Immunosuppression

Ocular sebaceous carcinomas occur more frequently in Asian populations and is more common in women, particularly those around 60 to 80 years of age.

Extraocular sebaceous carcinomas occur mainly in older adults and without predilection for male or female.
(DermNet NZ; SkinCancerNet).

Diagnosis of Sebaceous Gland Carcinoma (SC)
When a dermatologist suspects skin cancer, the dermatologist performs a biopsy. This procedure can be safely performed during an office visit. To perform a biopsy, the dermatologist will remove the suspicious lesion, or part of it, so that it can be examined under a microscope. This is the only way to know whether a patient has skin cancer.

If the biopsy confirms that the patient has SC, the dermatologist may also:

- Perform a full-body skin examination to check for other skin cancers and check the patient's lymph nodes for swelling.
- Ask if the patient or anyone in the patient's family has Muir-Torre Syndrome (MTS)
- Request that the patient have a thorough eye exam from an ophthalmologist if the SC occurs on an eyelid
- Write orders for additional medical tests. These tests may include a chest x-ray, blood tests, urinalysis, and colonoscopy. Women may get an order for a mammogram. The purpose of these tests is to check for other cancers that are common in people who have MTS
- Refer the patient to a medical geneticist. A medical geneticist can provide information about genetic testing and cancer screenings that may be appropriate

(SkinCancerNet).

Treatment of Sebaceous Glad Carcinoma (SC)
Treatment aims to remove the malignant lesion to prevent local or systemic spread.

The treatment of sebaceous gland carcinoma is adequate surgical excision, with wide surgical margins and fresh frozen section controls to delineate the tumour edges. Lymph node evaluation is necessary to evaluate metastasis.

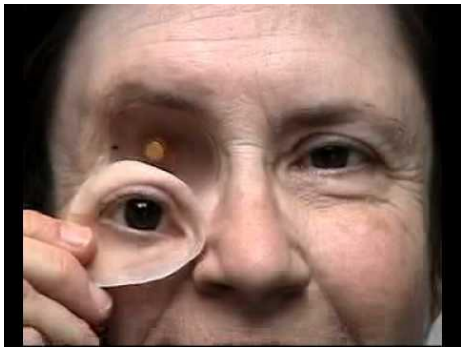
If diffuse involvement of the upper and lower eyelids is present, exenteration is required. Obtain a biopsy specimen of the areas of reddening of the conjunctiva that are suggestive of sebaceous gland carcinoma at the time of surgery.

Evisceration, Enucleation, and Exenteration are the three main surgical techniques by which all or part of the orbital contents are removed:

Evisceration is the removal of the contents of the globe while leaving the sclera and extraocular muscles intact.

Enucleation is the removal of the eye from the orbit while preserving all other orbital structures.

Exenteration is the most radical of the three procedures and involves removal of the eye, adnexa, and part of the bony orbit.



3-D Printed Facial Prosthesis offers new hope for eye cancer patients following exenteration. It is made to cover the hollow eye socket. It provides a more affordable alternative to traditional prosthetics

[Picture Credit: Exenteration

Monitoring for additional malignancies or metastatic sites is warranted. A marked increase in head and neck basal cell lesions is found in patients with previous eyelid malignancies. As many as 40% of patients also may have had or may develop other visceral malignancies. (eMedicine.Medscape; EyeWeb.Org).

Most patients diagnosed with SC are treated with surgery. Two types of surgery are used to remove SC:

Excision:
During this surgery, the surgeon removes the tumour and some surrounding tissue that looks healthy. This helps to remove cancer that may have travelled to an area that still looks healthy. An area can look healthy if it contains just a few cancer cells.

Mohs surgery:
Because many SCs develop on an eyelid or other area with little extra skin, Mohs (pronounced 'moes') surgery may be recommended. This specialised surgery is only used to treat skin cancer. This surgery allows the Mohs surgeon to remove less tissue yet remove the entire tumour.

During Mohs surgery, the Mohs surgeon cuts out the tumour plus a very small amount of healthy looking tissue surrounding the tumour. While the patient waits, the Mohs surgeon uses a microscope to look at what was removed. The surgeon is looking for cancer cells.

If the Mohs surgeon finds cancer cells at the edge of the removed tissue, the surgeon will remove another small amount of tissue and look at it under the microscope. This process continues until the surgeon no longer sees cancer cells along the edge of the removed tissue. The Mohs surgeon may refer to this edge as the 'margin'. When the Mohs surgeon no longer sees cancer cells along the edges, the surgeon may tell the patient that the 'margins look clear'.

After the cancer surgery, some patients need reconstructive surgery. This surgery is often performed immediately after the cancer surgery.

Surgery to remove lymph nodes:
When the cancer spreads to the lymph nodes, the patient may have surgery to remove the affected lymph nodes. Reports of patients surviving for many years after such surgery have been made.

Radiation treatment:
Radiation is not the first choice for treating SC. This treatment may be an option for:

- Easing a patient's pain if the cancer has spread.
- Treating patients who refuse or cannot withstand surgery.
- Treating patients who have had surgery but may still have some cancer.

Cryotherapy:
This treatment involves removing diseased skin by freezing it. More research is needed to find out whether this can be an effective treatment for SC.

Clinical trial:
Some patients are encouraged to join a clinical trial. A clinical trial is a type of research study. The purpose of a clinical trial is to study how well a new treatment or a new way of treating a disease works. For some patients, joining a clinical trial may be the best treatment option.
(American Academy of Dermatology).

About Clinical Trials
Clinical trials are research studies that involve people. These studies test new ways to prevent, detect, diagnose, or treat diseases. People who take part in cancer clinical trials have an opportunity to contribute to scientists' knowledge about cancer and to help in the development of improved cancer treatments. They also receive state-of-the-art care from cancer experts.

Types of Clinical Trials
Cancer clinical trials differ according to their primary purpose. They include the following types:

Treatment - these trials test the effectiveness of new treatments or new ways of using current treatments in people who have cancer. The treatments tested may include new drugs or new combinations of currently used drugs, new surgery or radiation therapy techniques, and vaccines or other treatments that stimulate a person's immune system to fight cancer. Combinations of different treatment types may also be tested in these trials.

Prevention - these trials test new interventions that may lower the risk of developing certain types of cancer. Most cancer prevention trials involve healthy people who have not had cancer; however, they often only include people who have a higher than average risk of developing a specific type of cancer. Some cancer prevention trials involve people who have had cancer in the past; these trials test interventions that may help prevent the return (recurrence) of the original cancer or reduce the chance of developing a new type of cancer.

Screening - these trials test new ways of finding cancer early. When cancer is found early, it may be easier to treat and there may be a better chance of long-term survival. Cancer screening trials usually involve people who do not have any signs or symptoms of cancer. However, participation in these trials is often limited to people who have a higher than average risk of developing a certain type of cancer because they have a family history of that type of cancer or they have a history of exposure to cancer-causing substances (e.g., cigarette smoke).

Diagnostic - these trials study new tests or procedures that may help identify, or diagnose, cancer more accurately. Diagnostic trials usually involve people who have some signs or symptoms of cancer.

Quality of life or supportive care - these trials focus on the comfort and quality of life of cancer patients and cancer survivors. New ways to decrease the number or severity of side

effects of cancer or its treatment are often studied in these trials. How a specific type of cancer or its treatment affects a person's everyday life may also be studied.

Where Clinical Trials are Conducted

Cancer clinical trials take place in cities and towns in doctors' offices, cancer centres and other medical centres, community hospitals and clinics. A single trial may take place at one or two specialised medical centres only or at hundreds of offices, hospitals, and centres.

Each clinical trial is managed by a research team that can include doctors, nurses, research assistants, data analysts, and other specialists. The research team works closely with other health professionals, including other doctors and nurses, laboratory technicians, pharmacists, dieticians, and social workers, to provide medical and supportive care to people who take part in a clinical trial.

Research Team

The research team closely monitors the health of people taking part in the clinical trial and gives them specific instructions when necessary. To ensure the reliability of the trial's results, it is important for the participants to follow the research team's instructions. The instructions may include keeping logs or answering questionnaires. The research team may also seek to contact the participants regularly after the trial ends to get updates on their health.

Clinical Trial Protocol

Every clinical trial has a protocol, or action plan, that describes what will be done in the trial, how the trial will be conducted, and why each part of the trial is necessary. The protocol also includes guidelines for who can and cannot participate in the trial. These guidelines, called eligibility criteria, describe the characteristics that all interested people must have before they can take part in the trial. Eligibility criteria can include age, sex, medical history, and current health status. Eligibility criteria for cancer treatment trials often include the type and stage of cancer, as well as the type(s) of cancer treatment already received.

Enrolling people who have similar characteristics helps ensure that the outcome of a trial is due to the intervention being tested and not to other factors. In this way, eligibility criteria help researchers obtain the most accurate and meaningful results possible.

National and International Regulations

National and international regulations and policies have been developed to help ensure that research involving people is conducted according to strict scientific and ethical principles. In these regulations and policies, people who participate in research are usually referred to as "human subjects."

Informed Consent

Informed consent is a process through which people learn the important facts about a clinical trial to help them decide whether or not to take part in it, and continue to learn new information about the trial that helps them decide whether or not to continue participating in it.

During the first part of the informed consent process, people are given detailed information about a trial, including information about the purpose of the trial, the tests and other procedures that will be required, and the possible benefits and harms of taking part in the trial. Besides talking with a doctor or nurse, potential trial participants are given a form, called an informed consent form, that provides information about the trial in writing. People who agree to take part in the trial are asked to sign the form. However, signing this form does not mean that a person must remain in the trial. Anyone can choose to leave a trial at any time—either before it starts or at any time during the trial or during the follow-up period. It is important for people who decide to leave a trial to get information from the research team about how to leave the trial safely.

The informed consent process continues throughout a trial. If new benefits, risks, or side effects are discovered during the course of a trial, the researchers must inform the participants so they can decide whether or not they want to continue to take part in the trial. In some cases, participants who want to continue to take part in a trial may be asked to sign a new informed consent form.

New interventions are often studied in a stepwise fashion, with each step representing a different "phase" in the clinical research process. The following phases are used for cancer treatment trials:

Phases of a Clinical Trial

Phase 0. These trials represent the earliest step in testing new treatments in humans. In a phase 0 trial, a very small dose of a chemical or biologic agent is given to a small number of people (approximately 10-15) to gather preliminary information about how the agent is processed by the body (pharmacokinetics) and how the agent affects the body (pharmacodynamics). Because the agents are given in such small amounts, no information is obtained about their safety or effectiveness in treating cancer. Phase 0 trials are also called micro-dosing studies, exploratory Investigational New Drug (IND) trials, or early phase I trials. The people who take part in these trials usually have advanced disease, and no known, effective treatment options are available to them.

Phase I (also called phase 1). These trials are conducted mainly to evaluate the safety of chemical or biologic agents or other types of interventions (e.g., a new radiation therapy technique). They help determine the maximum dose that can be given safely (also known as the maximum tolerated dose) and whether an intervention causes harmful side effects. Phase I trials enrol small numbers of people (20 or more) who have advanced cancer that cannot be treated effectively with standard (usual) treatments or for which no standard treatment exists. Although evaluating the effectiveness of interventions is not a primary goal of these trials, doctors do look for evidence that the interventions might be useful as treatments.

Phase II (also called phase 2). These trials test the effectiveness of interventions in people who have a specific type of cancer or related cancers. They also continue to look at the safety of interventions. Phase II trials usually enrol fewer than 100 people but may include as many as 300. The people who participate in phase II trials may or may not have been treated previously with standard therapy for their type of cancer. If a person has been treated previously, their eligibility to participate in a specific trial may depend on the type and amount of prior treatment they received. Although phase II trials can give some indication of whether

or not an intervention works, they are almost never designed to show whether an intervention is better than standard therapy.

Phase III (also called phase 3). These trials compare the effectiveness of a new intervention, or new use of an existing intervention, with the current standard of care (usual treatment) for a particular type of cancer. Phase III trials also examine how the side effects of the new intervention compare with those of the usual treatment. If the new intervention is more effective than the usual treatment and/or is easier to tolerate, it may become the new standard of care.

Phase III trials usually involve large groups of people (100 to several thousand), who are randomly assigned to one of two treatment groups, or "trial arms": (1) a control group, in which everyone in the group receives usual treatment for their type of cancer, or 2) an investigational or experimental group, in which everyone in the group receives the new intervention or new use of an existing intervention. The trial participants are assigned to their individual groups by random assignment, or randomisation. Randomisation helps ensure that the groups have similar characteristics. This balance is necessary so the researchers can have confidence that any differences they observe in how the two groups respond to the treatments they receive are due to the treatments and not to other differences between the groups.

Randomisation is usually done by a computer program to ensure that human choices do not influence the assignment to groups. The trial participants cannot request to be in a particular group, and the researchers cannot influence how people are assigned to the groups. Usually, neither the participants nor their doctors know what treatment the participants are receiving.

People who participate in phase III trials may or may not have been treated previously. If they have been treated previously, their eligibility to participate in a specific trial may depend on the type and the amount of prior treatment they received.

In most cases, an intervention will move into phase III testing only after it has shown promise in phase I and phase II trials.

Phase IV (also called phase 4). These trials further evaluate the effectiveness and long-term safety of drugs or other interventions. They usually take place after a drug or intervention has been approved by the medicine regulatory office for standard use. Several hundred to several thousand people may take part in a phase IV trial. These trials are also known as post-marketing surveillance trials. They are generally sponsored by drug companies.

Sometimes clinical trial phases may be combined (e.g., phase I/II or phase II/III trials) to minimize the risks to participants and/or to allow faster development of a new intervention.

Although treatment trials are always assigned a phase, other clinical trials (e.g., screening, prevention, diagnostic, and quality-of-life trials) may not be labelled this way.

Use of Placebos

The use of placebos as comparison or "control" interventions in cancer treatment trials is rare. If a placebo is used by itself, it is because no standard treatment exists. In this case, a trial would compare the effects of a new treatment with the effects of a placebo. More often,

however, placebos are given along with a standard treatment. For example, a trial might compare the effects of a standard treatment plus a new treatment with the effects of the same standard treatment plus a placebo.

Possible benefits of taking part in a clinical trial

The benefits of participating in a clinical trial include the following:

- Trial participants have access to promising new interventions that are generally not available outside of a clinical trial.
- The intervention being studied may be more effective than standard therapy. If it is more effective, trial participants may be the first to benefit from it.
- Trial participants receive regular and careful medical attention from a research team that includes doctors, nurses, and other health professionals.
- The results of the trial may help other people who need cancer treatment in the future.
- Trial participants are helping scientists learn more about cancer (e.g., how it grows, how it acts, and what influences its growth and spread).

Potential harms associated with taking part in a clinical trial

The potential harms of participating in a clinical trial include the following:

- The new intervention being studied may not be better than standard therapy, or it may have harmful side effects that doctors do not expect or that are worse than those associated with standard therapy.
- Trial participants may be required to make more visits to the doctor than they would if they were not in a clinical trial and/or may need to travel farther for those visits.

Correlative research studies, and how they are related to clinical trials

In addition to answering questions about the effectiveness of new interventions, clinical trials provide the opportunity for additional research. These additional research studies, called correlative or ancillary studies, may use blood, tumour, or other tissue specimens (also known as 'biospecimens') obtained from trial participants before, during, or after treatment. For example, the molecular characteristics of tumour specimens collected during a trial might be analysed to see if there is a relationship between the presence of a certain gene mutation or the amount of a specific protein and how trial participants responded to the treatment they received. Information obtained from these types of studies could lead to more accurate predictions about how individual patients will respond to certain cancer treatments, improved ways of finding cancer earlier, new methods of identifying people who have an increased risk of cancer, and new approaches to try to prevent cancer.

Clinical trial participants must give their permission before biospecimens obtained from them can be used for research purposes.

When a clinical trial is over

After a clinical trial is completed, the researchers look carefully at the data collected during the trial to understand the meaning of the findings and to plan further research. After a phase I or phase II trial, the researchers decide whether or not to move on to the next phase or stop testing the intervention because it was not safe or effective. When a phase III trial is completed, the researchers analyse the data to determine whether the results have medical

importance and, if so, whether the tested intervention could become the new standard of care.

The results of clinical trials are often published in peer-reviewed scientific journals. Peer review is a process by which cancer research experts not associated with a trial review the study report before it is published to make sure that the data are sound, the data analysis was performed correctly, and the conclusions are appropriate. If the results are particularly important, they may be reported by the media and discussed at a scientific meeting and by patient advocacy groups before they are published in a journal. Once a new intervention has proven safe and effective in a clinical trial, it may become a new standard of care.
(National Cancer Institute).

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