Cancer Association of South Africa (CANSA)

Fact Sheet
on
Bowen's Disease

Introduction

Skin cancer develops primarily on areas of sun-exposed skin, including the scalp, face, lips, ears, neck, chest, arms and hands, and on the legs in women. But it can also form on areas that rarely see the light of day — the palms, beneath the fingernails or toenails, and the genital area.

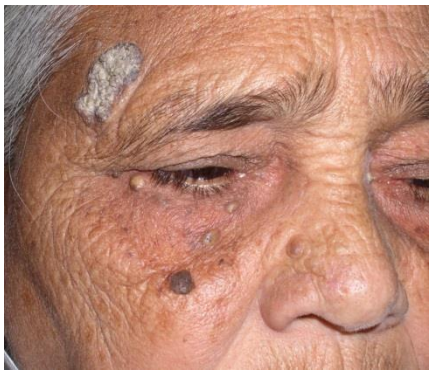
[Picture Credit: John T Bowen]

Skin cancer affects people of all skin tones, including those with darker complexions. When melanoma occurs in people with dark skin tones, it is more likely to occur in areas not normally exposed to the sun.
(Mayo Clinic).

Bowen's Disease

Bowen's disease is a very early form of squamous cell skin cancer. It is also called squamous cell carcinoma *in situ*. It was named after Prof John Templeton Bowen (1857-1940).

Doctors call Bowen's disease pre-invasive. That means that there are cancer cells there but they are only in the outermost layer of skin, the epidermis. Sometimes it can spread along the skin surface.



[Picture Credit: Bowen's Disease]

If left untreated, there is a small chance that Bowen's disease can spread into the deeper layers of the skin. This means it has become an invasive cancer and it can then spread into the lymphatic system. It takes a long time for Bowen's disease to develop into an invasive cancer. But the risk of developing into a cancer remains until Bowen's disease is treated.

Like squamous cell cancer of the skin, Bowen's disease can grow anywhere. It is most common on the trunk, arms or legs. The phrase Bowen's disease is often used for squamous cell carcinoma *in situ* around the genitals or anus.
(Cancer Research UK; Wikipedia).

Incidence of Squamous Cell Carcinoma (SCC) in South Africa
According to the National Cancer Registry (2012) the following number of squamous cell carcinoma (SCC) cases was histologically diagnosed in South Africa during 2012:

Group - Males 2012	Actual No of Cases	Estimated Lifetime Risk	Percentage of All Cancers
All males	3 347	1:42	10,43%
Asian males	23	1:313	2,73%
Black males	417	1:269	3,58%
Coloured males	353	1:35	8,15%
White males	3 054	1:13	15,23%

Group - Females 2012	Actual No of Cases	Estimated Lifetime Risk	Percentage of All Cancers
All females	2 612	1:98	6,04%
Asian females	26	1:323	2,40%
Black females	374	1:483	1,93%
Coloured females	242	1:92	10,03%
White females	1 969	1:26	12,41%

The frequency of histologically diagnosed cases of squamous cell carcinoma (SCC) in South Africa for 2012 was as follows (National Cancer Registry, 2012):

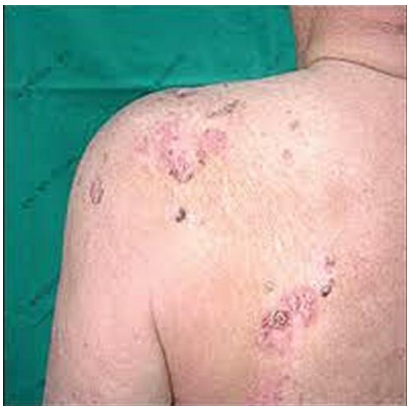
Group - Males 2012	0 – 19 Years	20 – 29 Years	30 – 39 Years	40 – 49 Years	50 – 59 Years	60 – 69 Years	70 – 79 Years	80+ Years
All males	5	10	79	201	511	1 010	1 127	854
Asian males	0	1	0	2	4	7	4	5
Black males	4	6	37	51	86	94	76	47
Coloured males	0	0	8	20	46	103	96	77
White males	1	5	42	124	413	779	836	483

Group - Females 2012	0 – 19 Years	20 – 29 Years	30 – 39 Years	40 – 49 Years	50 – 59 Years	60 – 69 Years	70 – 79 Years	80+ Years
All females	4	22	60	136	330	505	723	785
Asian females	1	1	0	1	5	7	3	6
Black females	1	17	49	46	68	50	66	66
Coloured females	1	0	2	17	36	45	63	72
White females	1	4	8	72	221	402	591	640

N.B. In the event that the totals in any of the above tables do not tally, this may be the result of uncertainties as to the age, race or sex of the individual. The totals for 'all males' and 'all females', however, always reflect the correct totals.

Signs and Symptoms of Bowen's Disease
Bowen's disease can occur anywhere on the body but it is usually found on the lower legs. To begin with, it often looks like a red, scaly patch, or sometimes like raised spots or warts. The affected skin may become itchy, sore and may bleed. As Bowen's disease can look like other skin conditions such as eczema or psoriasis, it is important to get any skin problems checked by a doctor (MacMillan Cancer Support).

[Picture Credit: Bowen's Disease 2]



Diagnosis of Bowen's Disease

Diagnosis of Bowen's Disease is done by means of a shave or punch biopsy for histological diagnosis. Where possible, a hair follicle should be included in the biopsy material.

The following conditions are considered as part of a differential diagnosis:

- Actinic Keratosis
- Basal Cell Carcinoma
- Lichen Simplex Chronicus
- Paget Disease (mammary)
- Psoriasis (plaque)
- Squamous Cell Carcinoma
- Tinea Corporis

(Patient.co.uk).

Risk Factors of Bowen's Disease

Risk factors for Bowen's Disease include:

Sun damage - exposure to sunlight (especially with fair skin) is a strong risk factor

Other irradiation damage - radiotherapy, photochemotherapy

Carcinogens - particularly arsenic. Exposure to inorganic arsenic is less common than it was. Arsenic used to be found in Fowler's solution (used to treat psoriasis), in Gay's solution (used to treat asthma), in contaminated well water and in some pesticides

Viral infection - There is a strong association with human papillomavirus (HPV), particularly in genital and perianal lesions. (Often HPV-16 but several other HPV types have been implicated.)

Immunosuppression - therapeutic following organ transplants, or Aids. Malignant and premalignant skin tumours are more common in patients who have received organ transplants. The risk may depend on the immunosuppressive regime used. The literature also contains a number of reports of Bowen's disease, quite often extensive, in patients with Aids

Chronic skin injury or dermatoses - rarely, it arises in pre-existing skin lesions such as seborrhoeic keratoses
(Patient.co.uk).

Staging of Skin Cancer

Doctors use a staging system that is common to all cancers. It is called the TNM system:

- The T indicates the size and depth of the tumour
- The N shows whether the cancer has spread to the lymph nodes
- The M shows whether the cancer has spread to another part of the body (metastasis)

The number system
Once the TNM categories (types) have all been decided, the information is put together to give a number stage from 0 to 4. The lower the stage, the earlier the cancer has been diagnosed. Most squamous cell skin cancers are diagnosed at stage 1 or 2.

Stage 0
Stage 0 is also called Bowen's disease or carcinoma in situ. Carcinoma means there are cancer cells there. In situ means the cells are still in the place where they started to develop. So the cells have started to turn into cancer, but they have not yet spread or grown into surrounding areas of the skin. If it is not treated, Bowen's disease can develop into a squamous cell skin cancer. So your doctor may describe this stage as pre-cancerous or pre malignant.

Stage 1
Stage 1 means the cancer is 2cm across or less and has 1 or no high risk features.

- High risk features mean the cancer
- Is more than 2mm thick
- Has grown into the lower dermis
- Has grown into the space around a nerve (perineural invasion)
- Started on the ear or lip
- Looks very abnormal under the microscope (the cells are poorly differentiated or undifferentiated)

Stage 2
Stage 2 means the cancer is more than 2cm across, or has 2 or more high risk features.

Stage 3
Stage 3 means the cancer

- Has grown into the bones in the face, such as the jaw bone or the bone around the eye,

OR

- Has spread to a nearby lymph node (or lymph gland) on the same side of the body (and is less than 3cm)

Stage 4
Stage 4 means the cancer

- Has grown into the spine, ribs or lower part of the skull, OR
- Has spread to a lymph node that is more than 3cm OR to an internal organ, such as the lungs

Staging can be quite complicated, so do talk to your doctor or clinical nurse specialist about what your stage of cancer is and what it means.
(Cancer Research UK).

Treatment of Bowen's Disease
There are a number of treatment options and your dermatologist will take into consideration where the patch is on your body, as well as the size, thickness and number of patches you have before deciding on the most appropriate procedure.

They will also consider how well your skin is likely to heal afterwards – for example, skin on the lower legs tends to be tight, fragile and slow to heal.

Treatment options include:

- Cryotherapy – Liquid nitrogen is sprayed onto the affected skin to freeze it. The procedure may be painful and the skin may remain a bit uncomfortable for a few days. The treated area may blister and weep. The patch will scab over afterwards and usually fall off within a few weeks, removing the affected skin.
- Imiquimod cream or chemotherapy cream, such as 5-fluorouracil – This is applied to the affected skin regularly over a period of time. It may cause your skin to become red and inflamed before it gets better.
- Curettage and cautery – The affected area of skin is scraped away under local anaesthetic, and heat or electricity is used to stop any bleeding, leaving the area to scab over and heal after a few weeks.
- Photodynamic therapy – A light-sensitive cream is applied to the affected skin, and a laser is directed onto the skin four to six hours later, to destroy the abnormal cells. The treatment session lasts about 20-45 minutes. A dressing covers the area afterwards, to protect it from light. You may need more than one session.
- Surgery – The abnormal skin is cut out and stitches may be needed afterwards. It is not the best option if the patch is large or if there are several patches.
- Talk to a dermatologist about which treatment is most suitable.
- In a minority of cases, the dermatologist may just advise monitoring the Bowen's disease closely, as it is very slow-growing and (because of the treatment's side effects) may not be worth treating.

(NHS.UK).

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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