Cancer Association of South Africa (CANSA)

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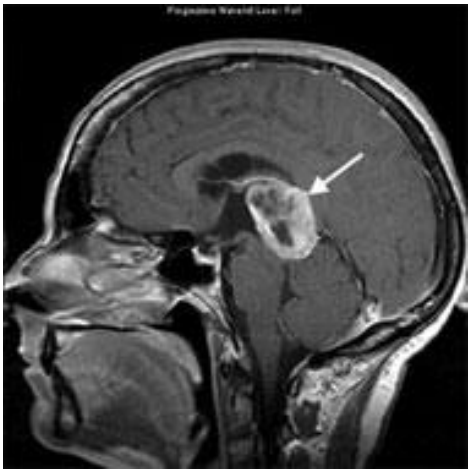
Fact Sheet on Pineoblastoma

Introduction

Pineoblastoma (also pinealoblastoma) is a malignant tumour of the pineal gland. A pineoblastoma is a supratentorial midline primitive neuroectodermal tumour. Pineoblastoma may occur in patients with hereditary uni- or bilateral retinoblastoma. When retinoblastoma patients present with pineoblastoma this is characterised as 'trilateral retinoblastoma'. Prognosis of patients with trilateral retinoblastoma is dismal, only a few patients have survived more than 5 years after diagnosis; all survivors were diagnosed with small tumours in a subclinical stage. Recent advances in (high-dose) chemotherapy treatment regimens and early detection have improved survival of patients with trilateral retinoblastoma to up to 50%. (Wikipedia).

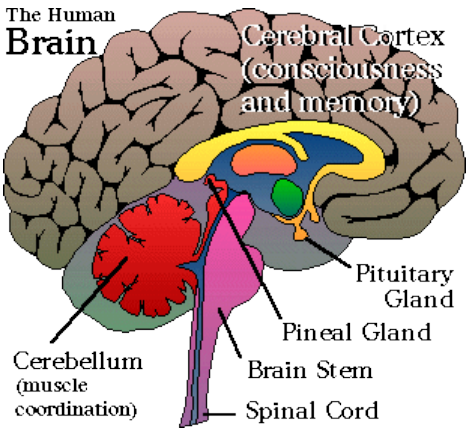


[Picture Credit: Pineoblastoma]

Pineal Tumours

These tumours originate from normal cells in the pineal gland. The pineal gland is located in the centre of the brain and is involved in the secretion of specific hormones.

[Picture Credit: Pineal Gland]



Tumour types occurring in the pineal region may or may not involve the pineal gland. Tumours that may occur in this region but are not necessarily pineal tumours include: germinoma, non-germinoma (eg, teratoma, endodermal sinus tumour, embryonal cell tumour, choriocarcinoma, and mixed tumours), meningioma, astrocytoma, ganglioglioma, and dermoid cysts.

There are three types of pineal tumours:

- Pineocytoma: Slow-growing, grade II tumour.
- Pineoblastoma: More aggressive, grade IV, malignant tumour. A grade III intermediate form has also been described.
- Mixed Pineal Tumour: Contains a combination of cell types.

(American Brain Tumor Association).

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Pineoblastoma

Pineoblastoma is one of several different types of tumours that arise in the area of the pineal gland, requiring different therapies. The exact diagnosis is critical for choosing the correct therapy. Pineal tumours typically present with hydrocephalus (a build-up of fluid pressure within the brain). A team of experts is needed for optimum therapy.

Pineal gland tumours as a group are rare, accounting for less than 1% of all primary brain tumours. Pineoblastomas represent just under half of all pineal gland tumours. Pineoblastoma usually occurs in children and young people between the ages of 20 and 40 years. It is equally common in males and females.

Pineoblastoma is more aggressive than other types of pineal gland tumours. Its fast growth usually causes cerebrospinal fluid (CSF) to build up in the brain. This condition is called hydrocephalus. While pineoblastoma may spread through the CSF in 10% to 20% of cases, most of the time the tumours do not spread to other parts of the body.

The cause of pineoblastoma is not known, although genetic abnormalities are suspected. (St Jude Children's Research Hospital).

Incidence of Pineoblastoma in South Africa

The National Cancer Registry (2013) does not provide any information regarding the incidence of Pineoblastoma in South Africa.

According to the National Cancer Registry (2013) the following number of brain and central nervous system cases was histologically diagnosed in South Africa during 2013:

Group - Males 2013	Actual No of Cases	Estimated Lifetime Risk	Percentage of All Cancers
All males	206	1:944	0,57%
Asian males	8	1:682	1,00%
Black males	63	1:3 093	0,59%
Coloured males	25	1:798	0,59%
White males	110	1:265	0,54%

Group - Females 2013	Actual No of Cases	Estimated Lifetime Risk	Percentage of All Cancers
All females	140	1:1 727	0,38%
Asian females	4	1:1 845	0,40%
Black females	50	1:4 827	0,32%
Coloured females	24	1:775	0,58%
White females	62	1:490	0,39%

The frequency of histologically diagnosed cases of cancer of the brain and central nervous system in South Africa for 2013 was as follows (National Cancer Registry, 2013):

Group - Males 2013	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	42	17	14	32	41	39	17	3
Asian males	1	1	1	1	1	2	1	0
Black males	21	6	5	12	10	6	0	0
Coloured males	5	1	2	6	4	5	1	0
White males	12	8	6	13	24	25	15	3

Group - Females 2013	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	28	10	21	14	22	29	14	2
Asian females	0	1	0	1	0	2	0	0
Black females	20	5	8	4	5	4	3	0
Coloured females	1	2	2	3	4	9	2	0
White females	4	2	10	6	13	14	9	1

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.

Symptoms and Diagnosis of Pineoblastoma

PNETs and pineoblastomas are aggressive tumours that tend to attach to parts of the brain that control movement, thought and sensation. Scientists have not been able to find an identifiable cause or risk factors for these tumours. There does not appear to be a genetic predisposition, meaning that these diseases do not seem to run in families.

Symptoms depend on the location of the tumour, and each child may experience symptoms differently. Common symptoms include headache, nausea and vomiting, fatigue, lethargy, seizures, behaviour or personality changes, unexplained weight loss or gain, difficulty looking upward and weakness on one side of the body.

In addition to a physical examination, medical history and neurological examination (which tests reflexes, muscle strength, eye and mouth movement, coordination and alertness), the doctor may requests tests, including diagnostic imaging.

Since these tumours are known to spread via cerebrospinal fluid, there is a high chance that they will invade other tissues of the brain and spine, so it is essential that your child have an MRI of both the brain and spine.

After all necessary tests are complete, the best treatment options can be identified.

Because the pineal gland sits just above and behind the third ventricle and the cerebral aqueduct, fluid-filled spaces in the brain, an enlarging tumour in this region can compress the aqueduct, cutting off the normal flow of fluid within the brain. This can lead to what is known as hydrocephalus which results in enlargement of the ventricles and increased pressure in the head. This can lead to symptoms such as headache, nausea, vomiting and finally neurological deterioration as it becomes more severe.
(Nervous System Diseases; St Jude Children's Research Hospital).

Diagnostic Imaging

Diagnostic imaging for paediatric cancer requires the use of specialised techniques and equipment to obtain pictures of the interior of the body, including soft tissues, organs and bones. For children with cancer, imaging studies are used to diagnose and stage tumours, evaluate and characterise masses, determine if the cancer has spread, establish which parts of a tumour are growing fastest, and – by monitoring a tumour's response to treatment – to guide state-of-the art treatment in addition to facilitating novel, experimental therapies.

Patients may require one of many different imaging procedures, including:

- X-ray – a quick, painless test that produces images of structures inside the body, especially the lungs, bones and some solid organs
- Fluoroscopy – a special X-ray technique that obtains moving, real-time images of the inside of a child's body
- Magnetic resonance imaging (MRI) – a diagnostic procedure that uses strong electromagnets, radio frequency waves and powerful computers to generate 3-D images of the body's organs, tissues and bones. MRI does not involve any ionizing radiation.
- Computed tomography (CT or CAT) – a non-invasive procedure that uses X-ray equipment and powerful computers to create detailed, cross-sectional images (slices) of a child's body
- Single Photon Emission Tomography (SPECT) and Positron emission tomography (PET) – a non-invasive diagnostic techniques that uses specific radiotracers to provide highly detailed images of the body and measures body functions such as blood flow, oxygen use and sugar metabolism to help evaluate how a child's tissues or organs are functioning and how cancers are responding to therapy.
- Ultrasound – the use of variable frequency sound waves and their echoes to produce cross-sectional images of the inside of the body
- Nuclear medicine and molecular imaging – the use of short-lived radiopharmaceuticals (tracers) and specialised cameras to show blood flow, functional and metabolic activity within organs and lesions

Interventional radiology is routinely used to manage abnormal blood vessels, perform biopsies and as an alternative to surgery, to treat blood clots and to provide minimally invasive therapy for certain tumours.
(Dana-Farber Boston Children's Cancer and Blood Disorders Center).

Treatment of Pineoblastoma

Treatment for pineoblastoma varies from patient to patient depending on specifics of each case such as age, tumour size and presenting symptoms. While other pineal tumours such as germinoma are very sensitive to radiation, surgical removal of pineoblastomas is often preferable. The aim of surgery can be to both obtain tumour tissue to analyse to make a definitive diagnosis and to remove as much of the tumour as possible. Various approaches to the pineal region can be used by neurosurgeons. In general, the procedures require a craniotomy (opening of the skull) in the posterior part of the head and is directed either above the cerebellum or between the occipital hemispheres to reach the pineal region.

Some patients will undergo other treatments such as radiation treatments for residual tumour or chemotherapy, particular in these malignant tumours.

Because the appropriate treatment varies considerably from patient to patient, each case should be evaluated and discussed with the patient's own treating physicians.
(Nervous System Diseases).

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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