WHAT IS RETINOBLASTOMA?
Retinoblastoma is a cancerous tumor involving retinal cells. Normally, cells grow and divide to form new cells as our body needs them. When cells grow old, they die and new ones take their place. However, there are times when this orderly process goes wrong. New cells form even when the body does not need them or old cells do not die when they should.

Retinal cells line the back part of the inside of the eye. These cells comprise nerve tissue that senses light and transmits images to the brain through the optic nerve, somewhat like the film of a camera.

In retinoblastoma, the abnormal growth of retinal cells forms tumors inside the eye. It is the most common eye tumor in children worldwide, with more cases seen in developing countries. It usually occurs in very young children (below the age of 5 years) and may involve either one or both eyes. If detected early, it rarely spreads to other parts of the body and has a high chance of cure.

WHAT ARE THE TYPES OF RETINOBLASTOMA AND WHAT CAUSES IT?
There are two forms of retinoblastoma, the hereditary and nonhereditary forms. The nonhereditary type accounts for about 60% of all cases and most often involves only one eye. The remaining 40% have the hereditary type (meaning, the disease is passed from parent to child).

Hereditary retinoblastoma is caused by a gene mutation passed through the germ cell (sperm or egg cell) of an affected parent to child. These patients usually develop the disease at a very young age (usually < 18 months old) and usually affect both eyes. These patients may have some other family member also afflicted with retinoblastoma. Sometimes the retinoblastoma is first detected only in one eye but the other eye soon becomes affected. These patients are closely monitored up until the child is 7 years of age. A child with hereditary retinoblastoma is also at risk for developing pineal tumors in the brain. When this occurs, this is called trilateral retinoblastoma. They are also at risk for developing other types of cancer later in life. Therefore, regular follow up exams are important.

In nonhereditary types, the gene mutation happens after fertilization and manifests in only one eye. Although not usually passed on, monitoring of children of patients with presumed non-hereditary retinoblastoma is still recommended, as they have a 20% risk of developing the disease.

WHAT ARE THE SYMPTOMS OF RETINOBLASTOMA?
Most children with retinoblastoma will present with a “white pupil” (also called “cats eye”), which may often be seen in photographs. Pediatricians may also notice the presence of a white pupil instead of a red one when light is shined into it during routine well baby check ups. Some children have eye pain, redness, or a wandering or “crossed” eye. When any of these are detected, prompt referral to an eye specialist is warranted for a thorough eye evaluation. Further examination by an eye doctor with special interest in retinoblastoma may have to be done.

HOW IS THE DIAGNOSIS OF RETINOBLASTOMA MADE?
A careful health history, physical examination with specific attention to a thorough eye examination and several laboratory tests are done to prove the diagnosis of retinoblastoma, determine the stage and to determine if it has spread to other parts of the body.

A family history of retinoblastoma will be asked, as well as the patients past illnesses and treatments.

The physical examination may reveal the presence of the white pupil, crossed eyes, or redness. An ophthalmologist will also examine the eyes after giving medications to dilate or open the pupil, usually under anesthesia, to allow full visualization of the inside of the eye. Based on this examination, the tumor is classified according to the extent of involvement within the eye. The pediatric oncologist on the other hand may look for possible signs of disease involvement beyond the eye, particularly in cases of very large tumors since treatment decisions are based on extent of disease.
Special radiologic tests may be requested to better characterize the size of the tumor such as an eye ultrasound, MRI (Magnetic Resonance Imaging), or CT (Computerized Tomography) scan.

Retinoblastoma is usually diagnosed without a biopsy. Other tests that may be requested include a complete blood count, baseline liver and kidney function tests, urinalysis, hearing test and in suspected spread of disease to other parts of the body, examination of the bone marrow and spinal fluid, imaging of the brain, or a bone scan.

**HOW DOES ONE STAGE RETINOBLASTOMA?**

Staging refers to the process used to quantify the extent of disease either within the eye or if it has gone beyond the eye to other parts of the body. Knowing disease stage is important for treatment planning as well as knowing the child’s chance of cure.

Although there are many staging systems for retinoblastoma, for treatment purposes it is classified as either intraocular (confined within the eye), extraocular (involves tissue around and outside the eye), or metastatic (has spread to other parts of the body).

**HOW IS THE TREATMENT PLANNED AND WHO ARE INVOLVED IN THE TREATMENT?**

In planning the treatment for a child with retinoblastoma, certain factors that impact on the chance of recovery are taken into consideration. This includes the stage of the disease, the potential for preserving useful vision, the size and number of tumors within the eye and whether trilateral retinoblastoma occurs.

The pediatric oncologist and ophthalmologist are the main physicians involved in the care of these patients. Pediatric oncologists are pediatricians specially trained in the treatment of childhood cancer. An ophthalmologist with special training in retinoblastoma care, particularly ocular oncologists, pediatric ophthalmologists and retina specialists, are necessary for the diagnosis, treatment and monitoring of these children. At the same time, the expertise of other specialty physicians is required for complete care of the child (also called multidisciplinary care) - for diagnosis, treatment and supportive care. These physicians include geneticists, neurologists, radiologists, radiation oncologists, pediatric surgeons, oncology nurses, pharmacists, psychologists, social workers, physical and occupational therapists, etc. The members of the multidisciplinary care team all contribute to the treatment and support of the child.

**WHAT ARE THE AVAILABLE TREATMENT OPTIONS FOR RETINOBLASTOMA?**

There are currently several treatment options for a child with retinoblastoma, although outcome still depends on the extent of disease. The multidisciplinary team will determine the specific treatment modalities to be employed on an individual basis.

For patients whose disease is confined within the eye (intraocular), treatment is determined by the size and number of tumors within the eye and the potential for preserving useful vision. In patients in whom both eyes are affected, great care is taken to try to preserve vision in at least one eye. Several treatment modalities are available for local control of the tumor and will be discussed shortly.

Enucleation involves removal of the eye and part of the optic nerve. This is done in cases when the tumor is very large and useful vision is no longer possible. The eye and the optic nerve will also be examined to find out if there are signs that the tumor may have started to spread beyond the eye.

Cryotherapy involves the use of special instrument to freeze and destroy tumor cells.

Photocoagulation uses laser light to destroy the blood vessels that feed the tumor, thus starving the tumor and it subsequently dies.

Heat may also be used to destroy the tumor. This is called thermotherapy.

Enucleation, cryotherapy, photocoagulation and thermotherapy are performed by an ophthalmologist specially trained to do these procedures.
Radiation therapy uses high-energy X-rays or other radiation energy to kill cancer cells. For retinoblastoma, several methods of delivering radiation may be employed. The type of method will vary depending on the patient’s particular need. This includes intensity modulated radiation therapy (IMRT), stereotactic radiation therapy, proton beam radiotherapy and plaque radiotherapy. Radiation therapy is administered by a radiation oncologist.

Chemotherapy is the use of drugs to kill cancer cells. It may be given by mouth or injected through a vein or muscle (systemic therapy). For children with retinoblastoma, chemotherapy is given to decrease the size of the tumor to allow better local therapy (cryotherapy, photocoagulation, thermotherapy, radiation therapy). This is called chemoreduction. In patients with widespread disease, more intensive systemic chemotherapy may be needed.

There are also studies currently being conducted to evaluate newer ways of delivering chemotherapy such as: (1) injecting the drug through the membrane covering the muscles around the eye and nerves found at the back of the eye (called subtenon chemotherapy) and (2) through a catheter up to the artery that nourishes the eye.

The treatment of extraocular retinoblastoma is more challenging as there is currently no single standard mode of chemotherapy. In general, a combination of systemic chemotherapy and radiation therapy are employed. Also under investigation is the use of very high doses of chemotherapy followed by the transplantation of blood forming stem cells for patients with very advanced disease.

Aside from the treatment methods mentioned, the management of children with retinoblastoma includes genetic counseling. A geneticist is a specialist trained in discussing with families about inherited diseases. As mentioned previously, siblings of a child with retinoblastoma are also screened since they may be at risk for developing the disease. Counseling is important since some of these patients also have a lifelong risk of developing other cancers and are at risk of passing the development of retinoblastoma to their offspring.

This information is made possible through the efforts of the Philippine Society of Pediatric Oncology, Inc. (PSPO), a subspecialty society of the Philippine Pediatric Society (PPS). For details regarding the treatment of individual patients, it is strongly recommended that they confer with their pediatric oncologist.