Viva-University Children's Cancer Centre Opens at NUH

The Viva-University Children's Cancer Centre opened in March this year as part of the University Children's Medical Institute, National University Hospital (NUH), Singapore. The center will also work closely with the National University Cancer Institute (NCIS), Singapore and St. Jude Children's Research Hospital in Memphis, Tennessee, USA. Recently, the Viva Children's Cancer Program received a S$12 million gift from the Goh Foundation to help advance knowledge in the treatment of childhood cancer in Singapore. In an email interview with APBN, Associate Professor Allen Yeoh, Medical Director of the Viva-University Children's Cancer Centre explains the goals of the center, the unique situation faced by children with leukemia and how their treatment can be improved through better collaboration and coordination.

APBN: **Tell us about the special challenges of treating children's leukemia and other cancers.**

Allen Yeoh: Children are not smaller versions of adults; the spectrum of childhood cancers and their treatments is very wide indeed. For example, acute lymphoblastic leukemia (ALL) accounts for 30% of all newly diagnosed childhood cancers in Singapore and worldwide but is not even in the top 10 cancers in adults. Conversely, carcinomas of the lung and breast which are the most common form of cancers in adult males and females, are rare in children.

A successful management of any child with cancer must involve managing the whole family as well. This is because we need to tap the support of the parents, extended family like grandparents and help the siblings adjust to the family's focus on the sick child. This will require a lot of patience, detailed explanation and harnessing the family to be the extended medical team to care for the child. The parents are the 24/7 nurse and doctor caring for the sick child.

APBN: Why is children's leukemia on the rise in Singapore?

Allen Yeoh: The Singapore Cancer Registry in Singapore has collected comprehensive population based incidence of cancers in Singapore since 1968. In their review from 1968 to 2002, there is a modest 20% increase in incidence of childhood ALL among males and less than 10% increase in female children. This has tilted the scale in favor of a striking male predominance for childhood ALL in the world (1.2:1).

The perception that childhood leukemias are on the rise, however is true. This is because of greater public awareness and the high cure rates of childhood ALLs. Prior to 1973, most children with ALL in Singapore died within six months of diagnosis. Now, in Singapore, more than 80% of children with ALL are cured. They go to school and lead a healthy life. So it is common to hear that a child living in the next block has leukemia or someone from your child's school has leukemia. The increased awareness has led to an exaggerated perception that leukemia in children is on the rise.

APBN: Besides leukemia, what are the other common cancers afflicting children in Singapore?

Allen Yeoh: Peculiar to Singapore and Asian countries, germ-cell tumors have shown a 3-fold rise in incidence since 1968. It is not clear why this is so. After leukemias, brain tumors are the most common form of childhood cancers. This is because children are inherently born with larger brains compared to their body. In fact the most rapid development of the brain occurs within the first five years of life before it plateaus off. This period of rapid growth is highly susceptible to development of cancer.

APBN: The main focus of the Viva-University Children's Cancer Center is children's leukemia treatment and care. Why was this particular cancer chosen?

Allen Yeoh: Childhood leukemias were chosen because it is most common. In combination, childhood acute lymphoblastic and myeloid leukemias account for 4 out of every 10 new cancer cases diagnosed each year. Despite its high cure rates, relapse from childhood leukemias is the 4th most common form of cancer. Taken together, this has the highest impact and hence is the strategic focus of the St Jude-Viva Programme.

APBN: Have China and India achieved high cure rates for childhood leukemias comparable to the West? If not, why?

Allen Yeoh: There are pockets of excellence in China and India where childhood leukemias are curable. For example, centers like All India Institute of Medicine and Tata Memorial Hospital in India boast of ~60% cure rates for childhood ALL. However beyond these centers of excellence, the results have been much poorer. Many factors work against achievement of a high cure rate in these countries. Diagnosis of leukemias requires considerable laboratory and clinical expertise which is usually available in tertiary centers but not in rural hospitals leading to delayed or even wrong diagnoses. Treatment of childhood leukemias requires excellent supportive care, blood products and a constant supply of chemotherapy drugs. Many of the public hospitals in low income countries are underfunded, overcrowded and understaffed. Low population densities sometimes force families to travel exceedingly long distances to get to a center which can treat them. This may take more than six hours or even a whole day. Parents have to give up their livelihood to bring the child to hospital. In Singapore, no child is more than 30 minutes away from NUH by car.

APBN: Will the center be conducting clinical trials? If so, what phases are these trials in?

Allen Yeoh: Currently the Viva-University Children's Cancer Centre conducts Phase III multi-center trials in leukemia. We hope to work with pharmaceutical partners to run Phase I/II trials in new therapeutics drugs in children.

APBN: Tell us more about the Viva-Goh Foundation Professorship in Paediatric Oncology.

Allen Yeoh: The Viva-Goh Foundation Professor will chair the Viva Programme and execute the whole strategic plan. The Professorship is critical as he decides the battle plan and harnesses the available resources to improve care of children with cancer.

APBN: Tell us more about the four research programs for Bone Marrow Transplant, Childhood Leukemia, Bone Cancer and After Completion of Therapy.

Allen Yeoh: Bone marrow transplantation focuses on using immune cells to fight low residual levels of highly resistant leukemia cells that cannot be eradicated by chemotherapy. The team will study what components of the bone marrow are critical and how to engineer the best graft from transplantation. Childhood leukemia will focus on personalizing chemotherapy for each child to maximize cure and minimize long term side-effects. We will also work to bring our successful treatment to adults. Bone cancer – we have an outstanding multidisciplinary team in musculoskeletal oncology. The team consists of orthopedic surgical oncologists who can remove the cancerous bone, reconstruct the resulting gap while preserving the limbs and function. Our pediatric oncologists are able to administer effective multi-agent chemotherapy that can cure more than 75% of these children. For research in after completion of therapy, as seven out of ten children with cancer in Singapore are long-term survivors, it is critical for us to look at the late effects of treatment in these children and design measures to prevent these disabilities from becoming a handicap.

APBN: What novel technologies, drugs and methods would you be exploring in these research programs?

Allen Yeoh: We are focusing on using immune cells to fight residual levels of highly resistant leukemia cells after intensive chemotherapy. Previously this was done by bone marrow transplant where it may be a hit and miss. We will be able to better select the donors and engineer the bone marrow to remove the harmful T-cells which may attack the patient, while preserving the important immune cells like NK-cells which can attack the residual leukemia cells.

APBN: What shifts in cancer treatment trends have you observed in the last 10 years?

Allen Yeoh: In the 1970s, there was no cure. In the 1980s, we cure at all costs. This involved radiation of the brain in all children with ALL to eradicate leukemia cells hiding there. As a result, many children suffered from decreased IQ and long-term side-effects. In the 1990s, we started risk-stratified therapy where the intensity of therapy was adjusted to the predicted risk of relapse. In the 2000s, we were able to tailor therapy more accurately. Now treatment can be safely reduced in many children without compromising cure.

APBN: What path do you expect cancer treatment to follow in the next 10 – 20 years?

Allen Yeoh: I anticipate a more personalized form of therapy where treatment is optimized to maximize cure and minimize side-effects. For example, our Malaysia-Singapore ALL 2003 study has successfully tailored treatment primarily based on the patients' response to the early part of the therapy. Indeed, we have actually reduced the intensity of therapy in one out of three children with ALL who had very rapid complete response without compromising the outcome. With cancer and the patients' genetic factors better characterized, we will soon be able to choose the best combination of drugs to target cure.

APBN: What do you think is lacking in Singapore, in terms of cancer prevention, diagnosis and treatment?

Allen Yeoh: We have most of the cost-effective measures in Singapore. Newer molecular diagnostics are making their way from the laboratory to the clinics. For example, we have designed and validated many molecular and pharmacogenetic biomarkers and transferred them to clinical use in our Molecular Diagnostic Centre at the National University Hospital in Singapore.

APBN: What do you think is lacking in the global hunt for a cancer cure?

Allen Yeoh: Collaboration and Coordination. Curing cancer requires our brightest minds to collaborate and focus our efforts to find cures. With improving cures, demonstration of effective therapy requires large patient numbers in multi-center collaborative trials. Coordination of efforts is important. That is why large agencies like the National Cancer Institute have been able to set trends and make major inroads in research by coordinating the efforts. ■

About Associate Professor Allen Yeoh

Associate Professor Yeoh is a Senior Consultant and Assistant Professor in the Division of Paediatric Haematology-Oncology, The Children's Medical Institute, NUH and Yong Loo Lin School of Medicine, NUS. He was trained in NUS and NUH and was in the St Jude Children's Research Hospital as a Clinical Fellow from 1999 to 2001.

Dr Yeoh's interest is in childhood leukemia. He is currently the principal investigator of the multi-center Malaysia-Singapore ALL and AML trials competitively funded by NMRC and A*STAR/Singapore Cancer Syndicate. Currently these trials have been highly successful with more than 80% and more than 60% projected cure. He is the first Singapore doctor to receive the American Society of Hematology Merit Award for his pioneering work in gene expression profiling in leukemia. His work was one of the most cited articles in this field in 2003.

Dr Yeoh is also the recipient of numerous National and International Awards including the Singapore Youth Award 2002, NUS Office of Life Sciences Award 2002, Asian Innovation Award (Gold) 2003 and the NMRC-BMRC Clinician Scientist Award 2005.